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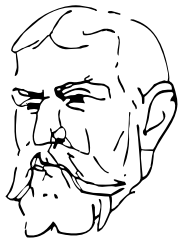

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CONTENTS

ORIGINAL ARTICLES

ORIGINAL ARTICLE

PREVENTIVE EXAMINATIONS OF CHILDREN IN DIFFERENT COUNTRIES: SIMILARITIES AND DIFFERENCES

DOI: 10.36740/WLek202205101

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ABSTRACT

The aim: The aim of this study was to compare, analize and establish differences the recommendations for well-child visits and screenings till the age of 5 years in different countries .

Materials and methods: The comparative analysis of the data from governmental recommendations for pediatricians from Germany, Ukraine and Poland is conducted. It was used the guideline for medical care for a child under 3 years (The Order №149) and for a healthy child from 4 to 18 years (The Order №434) in Ukraine, the book «Kinderuntersuchungsheft» in Germany and child's examination book «Książeczka zdrowia dziecka» in Poland.

Results: The number of visits to children by the doctors in Ukraine is 1.5-2 times higher than in other countries and the nurses visit are absent in Germany. The neonatal screening for genetic and metabolic diseases, updated in 2021 in Ukraine, corresponds to such screenings in other countries. Physical examination is performed in accordance with WHO standards in Ukraine, while in Poland and Germany the growth references are specially developed for the pediatric population. There was a difference in the age of hearing screening, examination of the hip joints, tactics for assessing vision by a pediatrician. The use of vitamin D, fluoride, iodine and vitamin K is recommended in Poland and Germany from the birth, while in Ukraine only vitamins are used.

Conclusions: It was found that the differences and similarities in preventive program in Ukraine, Poland and Germany. The results of this study may be useful for improving primary pediatric care.

KEY WORDS: preventive medicine, child, neonatal screening

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INTRODUCTION

Providing high-level medical care is a priority for the children's outpatient health care system. Well-child visits provide dynamic monitoring of the child's physical development, timely administration of necessary preventive vaccinations, doctor`s consultation on breastfeeding and childcare [1,2]. Early screening of development and behavior children is necessary to identify development delays and to facilitate timely treatment. [3] Unfortunately, quite often at pediatric appointments doctors focuses on the treating diseases and does not pay attention to the prevention [4]. Therefore, preventive visits should be separated from the visits in which the doctor deals with developmental problems, treats acute or chronic diseases [5]. According to researchers, preventive pediatric care should be family-oriented and have community support [6]. Parents often search the information on child care, nutrition, etc. in the internet, but health professionals need to give parents an opportunity to discuss what they have found. [7] Regular routine visits to the pediatrician contribute to the early diagnostic of the pathological processes. The list of recommended screenings and the number of preventive visits to the doctor are determined by each country in accordance with health guarantee and insurance programs. Comparative analysis of preventive screening programs will help to identify differences and similarities between programs in different countries. The results of this study may be useful for improving primary pediatric care.

THE AIM

The aim of this study was to compare and establish differences the recommendations for well-child visits and screenings till the age of 5 years in different countries.

MATERIALS AND METHODS

Governmental recommendations for pediatricians from Germany, Ukraine and Poland were used to compare the system of preventive care for healthy children. In Ukraine, a guideline (The Order №149)[8] for medical care for a healthy child under 3 years and guideline (The Order №434) [9] for a healthy child from 4 to 18 years have been developed for pediatricians and approved by The Ministry of Health of Ukraine. To evaluate the system of preventive

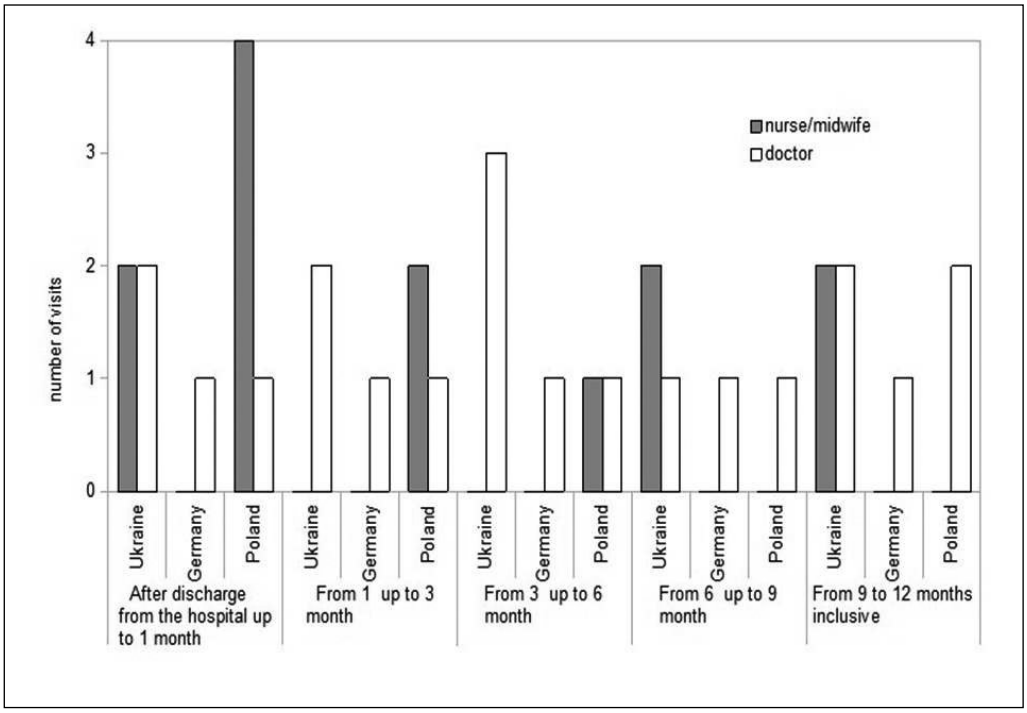

Fig. 1. Numbers of visits doctors and nurses to children during 1 years after the birth.

Table I. Recommendations for Screening in Ukraine, Poland, Germany

	Ukraine	Poland	Germany
Genetic and metabolic disorders	20 diseases [14]	23 diseases [15]	20 diseases [10]
Hearing screening	First 3 days: Transitory evoked otoacoustic emission. 3 month: automated auditory brainstem response [17]	First 3 days : Transitory evoked otoacoustic emission, automated auditory brainstem response [11]	First 3 days : Transitory evoked otoacoustic emission, automated auditory brainstem response [10]
Congenital heart defect	EchoCG is performed when signs of congenital heart disease are detected [8]	Pulse oximetry: SaO2<96% - EchoCG [11]	Pulse oximetry screening (measurement at the foot), if incorrect –EchoCG [10]
Screening for hip joint dysplasia	Pediatrician checking the symptoms of Barlow, Ortolani. Orthopaedist and sonography at the 3 month [8]	Pediatrician checking the symptoms of Barlow, Ortolani, sonography at the 6th-9th week [11]	Pediatrician checking the symptoms of Barlow, Ortolani, sonography at the 4th–5th week [10]
Vision	Pediatrician checking the morphological deviations, fixation of gaze. If incorrect – ophthalmologist consultation, visual acuity test from 5 year [8,9]	Pediatrician checking the morphological deviations, fixation of gaze. Cover-test, Hirschberg -test visual acuity test from 5 year [11]	Pediatrician checking the morphological deviations, fixation of gaze. Brukner test, visual acuity test from 3 year [10]
Iron deficiency	Complete blood count at 9 monthand 5 years for all [8]	Complete blood count in children from risk group 6-9 weeks [11]	Complete blood count in children from risk group [10]

children examinations in Germany the book «Your child's medical records (Kinderuntersuchungsheft)» was used [10]. The data on the preventive examinations of a child in Poland were taken from the child's examination book «Książeczka zdrowia dziecka»[11]. At our study we evaluated such features of preventive program as the number of visits to the doctor, the structure of the pediatrics' visit, the responsibilities of the pediatrician, consultations with other specialists, laboratory tests and recommendations for supplements. Additionally, we used evidence-based recommendation according to the rating system [12,13] if such data were available.

RESULTS

The child care program includes visits by a doctor and a nurse or midwife. The number of visits for each country is presented in fig.1.

As shown in the figure, the total numbers of visits by doctors for 1 year of life in Ukraine is 13 visits, while in Poland – 6 visits, in Germany – 5 visits. At the same time, a nurse or midwife meets the child at home or in a clinic in Ukraine 6 times, in Poland 7 times, in Germany there are no scheduled visits to the nurse. After the 1-st year in Ukraine and Poland next visit is recommended after 6 month, then in all countries it is 1 times per year up to 5 years.

HISTORY

According to the recommendations for the visits during the first 2 weeks in all countries, the doctor should carefully collect the child's medical history, results of neonatal screening, pay special attention to the presence of hereditary and chronic diseases, allergies, immune system defects in the family. Subsequently, during each visit, the doctor collects information about breastfeeding and its difficulties, the child's sleep, defecation and urination and make examination of organs and systems. It is very important to evaluate immunization history in every visit.(grade C) [Katherine Turner]. In Ukraine, unlike Poland and Germany, vaccines against pneumococcal infection, rotavirus and meningococcus are not included in the mandatory vaccination schedule.

SCREENING

Screening recommendations at the different countries are outlined in table I.

From October 2021 in Ukraine, as well as in Germany and Poland, the screening of inborn errors of metabolism includes cystic fibrosis , hypothyroidism, congenital adrenogenital syndrome which are all performed with conventional methods (blood screening). There is also the screening for phenylketonuria, Maple Syrup Urine Disease, fatty acid oxidation disorders, medium-chain acyl-CoA dehydrogenase (MCAD) deficiency, long-chain 3-hydroxyacyl-CoA dehydrogenase (LCHAD) deficiency, very long-chain acyl-CoA dehydrogenase deficiency (VLCADD), carnitine inborn errors of metabolism, isovaleric academia, glutaric acidemia type 1, tyrosinemia type 1, which are performed with tandem mass spectrometry. There are recommendations to perform the screenings for severe combined immunodeficiency, sickle cell disease und 5q-assosiated Spinal muscular atrophy. [14-16,18].

COMMUNICATION

Effective communication between the doctor and the parents increases the parental adherence to medical care. It is important to assess the psycho-emotional situation in the family, symptoms of parental stress. The guideline in Poland recommends to assess the signs of the postnatal depression. The Edinburgh Postnatal Depression Scale (EPDS) is the most common, but this questionnaire is not the only advertised. [19]. This evidence -based recommendation is the B Grade [12,13]. The psycho-emotional state of the mother and the support of the family significantly affect the duration of breastfeeding and health of the child. The significant effect of breastfeeding for more than 6 months on the relationship between mother and child has been proven [20]

NEUROMOTOR DEVELOPMENT AND PSYCHOSOCIAL ASSESSMENT

In all countries, the doctor evaluate neuro-motor development according to age. This assessment consists of such parameters as: coarse and fine motor skills, perception and cognition, social and emotional skills and regulation and stimulation. Reflexes from the neonatal period are also evaluated. It is important that in the manuals for doctors which were used for comparison, there are no scales or questionnaires to assess the psychosocial condition of the child. The American Academy of Pediatrics recommends screening for autism at 18-24 month (Grade C) [12,13]. It is no standardized tools, but M-CHAT questionnaire can be recommended for early screening of autism disorders. [21]

PHYSICAL EXAMINATION

At every visit doctor should perform a physical examination of the child. It is necessary to measure the height, weight, circumference of the head and chest and compare these results with the standards according to the age and sex of the child. In Ukraine all the measurements are compared with World Health Organization (WHO) percentiles and z-scores. The graphs of growth standards for Polish children are compared with the WHO only for children from 0 to 3 years. According to the results of the OLA study growth reference for children from 3 to 18 years have been significantly different from WHO recommendation [22]. The German book «Your child's medical records (Kinderuntersuchungsheft)» contains the information on growth reference that is recommended for children from 0 to 7 years. Percentile curves are based on the results of examination 17,147 boys and 17,275 girls aged 0-18. The survey of a large cohort of Polish and German children showed the differences between the recommended WHO and OLA study percentiles. [22]

LABORATORY INVESTIGATION

Screening for the iron-deficiency anemia (complete blood count) is recommended in Ukraine at the age of 9 months and in 5 years old for all children. In Poland and Germany it is recommended to perform the complete blood count with the purpose of early screening for iron-deficiency anemia in children from the risk groups, especially for premature children. Iron deficiency in infancy might lead

to the subsequent poor neurocognitive development; and there is a possibility that the prevention of neurodevelopmental consequences may require the screening and early treatment of multiple nutritional deficiencies, rather than iron deficiency only [23]. In Ukraine, for the children of 4 and 5 years old the tests for parasites, stool ova, urinalysis and blood glucose test are also recommended.

SUPPLEMENTS

Vitamin K is commonly recommended to be used after birth for the prevention of hemorrhagic disease of the newborn (HDN). In Ukraine it is a single dose (1.0 mg) of intramuscular vitamin K after birth. In Germany and Poland it is given oral three times: after birth, on the 4-6 days and 4-6 weeks at a dose of 2 mg. Vitamin K deficiency bleeding is the serious problem for newborn and young infants. It is necessary for parents to get prenatal education about vitamin K supplementation according to ESPGHAN recommendations [24].

Prevention of vitamin D deficiency and rickets is recommended in all countries. In Ukraine

it is recommended to start prophylactic dose of vitamin D for children under 3 years 1000 IU / day to be followed apply to all healthy children from the second months of life up to 3 years daily, except three months in summer [25]. In Germany and Poland the recommended vitamin D supplementation is at a dose of 400-500 MO per day for the first year of life and then just for risk groups [26].

In Ukraine fluoride supplementation is conducted depending on the child's dietary requirements and the fluoride level in the water, its intake with food (soy products, hypoallergenic foodstuffs, mineral water). Pediatric guidelines do not indicate the need to recommend fluoride supplements to children. But in Germany and Poland fluoroprophylaxis is recommended from neonatal period. Until regular exposure to fluoride in appropriate amounts is achieved (fluoride-enriched table salt and fluoridated toothpaste), the daily intake of a fluoride supplement is recommended for infants and children is recommended. [27] In addition, in Germany also prescribes iodine prophylaxis (iodine salt, mineral water).

DISCUSSION

The comparative study of the preventive programs in Ukraine, Poland and Germany show some differences and similarities. It is established and shown in Fig.1 that the number of visits to the doctor in Ukraine is more than in Poland and Germany, i.e. 13, 6 and 5, respectively. However, Poland demonstrates larger number of nursery/midwife visits up to the first 6 weeks of child life. It gives an undisputable advantages for families in controlling child care and breastfeeding. A frequent visits allow to establish trust relationship families to believe in care communications and further treatment with medical personnel (doctors, nursery). Decreased parental adherence to doctor visits is also seen as an increased risk of hospitalizations in young children [28].

According to the updated recommendations from 2021 in Ukraine, the list of diseases for neonatal screening is almost the same as in Germany and Poland, however, it is only available in large cities. It is very important to make screenings for severe combined immunodeficiency, sickle cell disease and 5q-assosiated Spinal muscular atrophy. The early treatment of SMA seems to be crucial for maximizing the therapeutic effects. Up to 30–60% (depending on the age of treatment initiation and the patient's baseline functional status) of children with SMA1, treated after the onset of disease symptoms, achieve the ability to sit by themselves without help [29]. So, the screening all the newborns for SMA is the best strategy for the successful treatment.

In the results of comparison of the methods of physical assessment of the child it was found that Germany and Poland conducted their own research to determine the growth references of child, while in Ukraine WHO recommendations are used. It is very important to assess the physical parameters in accordance with the country and ethnic characteristics.

The comparison of the pediatric visits (Table I) found that in Germany and Poland the pediatricians have more functionality. In addition to the physical examination of the child, auscultation of the heart and lungs and palpation, the doctor evaluates hearing and vision, sonography of the hip joints. The recommendations for visiting another specialist are provided only if the problems are identified. In Ukraine, the specialized examinations of vision, hearing and hip joints are conducted by ophthalmologist, otolaryngologist and orthopedist specialists. It is important that hearing screening in Poland and Germany is conducted in the first 3 days after the birth by two methods (Transitory evoked otoacoustic emission, automated auditory brainstem response), while in Ukraine only one method is used. Unfortunately, parents do not always pay attention to the results of neonatal screening and do not carry out the next examination at 3 months.

The examination of vision by pediatricians in Ukraine is limited to the external assessment of the eye, morphological deviations, fixation of gaze. German pediatricians are recommended to take the Brukner test, while pediatricians in Poland use Cover-test and Hirschberg test. The assessment of visual acuity is carried out from 3 to 5 years, which correspond to the international studies (Grade B)[12,13].

It is established that the analysis of sonography of the hip joints is performed at different ages in Poland, Germany and Ukraine, i.e. at 6-9 weeks, 4-5 weeks and 3 months, respectively (Table I). There is no international consensus in the world on the age at which ultrasound screening should be performed. This leads to the significant differences in screening programs across Europe, but it is recommended in the most countries to prevent the serious disability of the hip [30].

In Ukraine, there are no systematic studies to determine the level of vitamin D in the population. There are also no updated recommendations for the supplement of vitamin D. According to the European study, 400 IU daily

is a sufficient dose for infants and children 1 year of age to prevent the development of vitamin D deficiency. In Germany and Poland vitamin D supplementation is only recommended for older children having the risk factors and chronic diseases routine [26]. In Ukraine the doctors prescribe a test on 25(OH) to recommend an individual dose of treatment for D deficiency.

For the majority of European Countries, the EAPD recommends the appropriate use of fluoride toothpaste in conjunction with good oral hygiene. [27] In addition to oral fluoride supplements, it is also recommended to use fluoride gel during a visit to the doctor to protect teeth from caries (Grade B) [12,13]

CONCLUSIONS

The comparative analysis of the preventive screening programs of children in Ukraine, Poland and Germany, by involving the list of the proposed parameters, is carried out. As the results the proper differences and similarities were identified and analyzed.

There were found the differences in number of visits to children by the doctors and nurses, growth references, age of child for hearing screening and sonography of the hip joint, screening of iron deficiencies and supplements support. The similarity of approaches to neonatal screening, age assessment of visual acuity test, assessment of neuro-motor and psychosocial development is noted.

Thus, in order to improve the provision of medical care it is recommended to start the systematic study to determine the growth references of children in Ukraine. It is also necessary to provide more opportunities for pediatricians, at least in using new methods for vision assessment. The improved prevention with supplements (vitamin K, vitamin D, fluoride) in accordance with the international guidelines should be recommended for children. The results of this study may be useful for improving the primary pediatric care of children.

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ORIGINAL ARTICLE

POSSIBILITIES OF RENOPROTECTION IN PATIENTS WITH CHRONIC KIDNEY DISEASE AND HYPERURICEMIA

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ABSTRACT

The aim: To determine efficacy and safety of allopurinol and febuxostat in treatment of patients with CKD to reduce the sUA level and analyze its influence on glomerular filtration rate (GFR).

Materials and methods: The study included 45 CKD patients (stages 3b-5) without other severe/decompensated diseases and contraindications to the allopurinol/febuxostat. All patients underwent a comprehensive clinical and laboratory examination, and were divided into the study groups: Group I (28 patients, 61,3±3,2 y.o., CKD3b-12, CKD4-10, on hemodialysis-6 patients) received febuxostat, Group II (24 patients, 60,7±4,1y.o., CKD3b-9, CKD4-10, on hemodialysis -5 patients) took allopurinol.

Results: Achievement of the target level of sUA was significantly often registered in Group I: after 1 month – in 45.5% (in group II – in 15.9%, $p<0.001$); after 3 months – in 67.5% (in group II – 21.2% $p<0.01$); after 6 months, these figures were 90% and 37.1%, respectively ($p<0.01$). sUA level <300 μmol/l was accompanied by significant positive GFR changes in group I patients; in group II there was a gradual progression of GFR deterioration in 31.8% of patients.

Conclusions: In patients with pre-dialysis stages of CKD febuxostat demonstrates renoprotective abilities. Use of febuxostat in patients with CKD stage 3b-4 and in patients on hemodialysis is safe and more effective for target sUA level achievement than the use of allopurinol.

KEY WORDS: chronic kidney disease, hyperuricemia, febuxsostat, allopurinol, glomerular filtration rate, renoprotection

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INTRODUCTION

Over the last few decades, there has been a significant increase in the incidence of chronic kidney disease (CKD) incidence around the world. Thus, according to the CDC USA, the frequency of this pathology is becoming epidemic and the prevalence of CKD stage 3 reaches 11.5% [1]. At this stage of the pathological process, CKD is a progressive and irreversible condition that significantly reduces the quality of life and life expectancy, requires significant medical and social investments in treatment and care of such patients. Taking into account the lack of effective pharmacologic treatment for CKD and the long asymptomatic course of this pathology and therefore the "escape" of such patients from the attention of health professionals at early stages of disease, there is an urgent need in identification of the risk factors for increasing prevalence of CKD in different populations to determine the most effective approaches to prevention of renal damage and development of renoprotective drugs. One of the intensively investigated factor which have systemic negative impact on metabolic processes, cardio-vascular disease morbidity and mortality and directly connected with renal function is hyperuricemia (HU) [2-7].

At present the number of current epidemiological studies indicate a significant effect of serum uric acid (sUA) on the development and progression of CKD. According to the study of Obermayr R. P. et al., 2008 [8], where the data from 21,475 healthy individuals was analyzed, even a slightly elevated sUA level (> 7.0 mg/dL (> 416 μmol/l) was associated with a doubling of the risk of developing CKD. In a study of 13,338 participants with preserved renal function – the risk of CKD increases 1.1-fold for every 1.0 mg/dL (59.5 μmol/l) increase of sUA concetration after age and other metabolic parameters adjustment [9].

The negative influence of HU on renal condition and function today is explained by a number of pathogenetic mechanisms that continue to be studied. Among them are: the development of HU-related hyperuricosuria and hyperglycemia with formation of UA crystals deposits in nephron collecting tubules in lower urine pH, which promotes further crystal formation and adhesion to the tubular epithelium; initiation of chronic inflammatory reaction in focuses of crystal deposition, including kidneys [7-10]. Non-crystallization effects of HU were demonstrated in experimental animals: even a mild increase in sUA led to

the systemic elevation of blood pressure and glomerular hypertension in rats due to the development of systemic endothelial dysfunction.

The same mechanism of action of HU is indicated by other experimental data. In vitro it has been shown that HU reduces the synthesis of NO, thereby contributing to the development of the local endothelial dysfunction; in experiment also have been confirmed that HU caused arteriolopathy of the afferent arteries of the glomeruli and trigger the development of tubulo-interstitial fibrosis by activating RAAS; it is also shown that UA activates cytoplasmic phospholipase A2 and inflammatory transcription of NF-κB, which leads to inhibition of proliferation in proximal tubules. Other identified effects of HU include a systemic increase in the synthesis of proinflammatory cytokines (including tumor necrosis factor alpha) and a local increase in chemokine expression (including MCF-1, monocyte chemotaxis factor) in the kidneys and COX-2 in blood vessels. Reduction of the sUA level reduces tubulo-interstitial sclerosis – both in the nephrectomy model and in diabetic nephropathy [7, 10-12].

According to the results of the retrospective cohort study of healthy men aged 20-60 years, conducted in Japan using the annual survey and laboratory monitoring of the employees of several big companies in the period 2009-2014 (12,413 people) found the prevalence of HU in this cohort 21%, demonstrated and confirmed important significant relationships of sUA with other metabolic processes. Thus, significantly higher levels of glycated hemoglobin and lower levels of high-density lipoprotein cholesterol (HDL cholesterol) were found in men with HU. Analysis of data included in the study for 5 years of observation showed that the development of HU contributed to a decrease in GFR, and a decrease in the initially increased level of sUA – helped to slolw GFR loss: the difference for some subgroups in this study was up to 4.5 times [2]; the same study showed that the level of sUA was crucial for reducing GFR during 5 years of follow-up.

At the same time, current studies of allopurinol use in treatment of CKD patients failed to demonstrated it efficacy for slowing the CKD progression [11]. Given the significant increase in the number of adverse events with the use of therapeutic doses of allopurinol on the background of initially reduced GFR (including severe) and existing recommendations to reduce the dose in the presence of CKD, which in most cases does not achieve target levels in patients with GFR < 60ml/min., the study of probable renoprotective effect of non-purine selective inhibitor of xanthine oxidase – febuxostat attracts a lot of attention from researchers around the world. Thus, a meta-analysis of the observational and controlled trials [12, 13] showed that the use of febuxostat in patients with CKD and HU reduced serum creatinine slightly; moreover, in patients with CKD and HU with GFR of 15-60 ml/min/1.73 m^2, it was found that the use of febuxostat reduced the rate of progression of GFR loss. Other authors indicate that in such patients febuxostat effectively reduces the level of sUA and has a positive effect on GFR, albuminuria and blood pressure [14]. Nevertheless there are no recommendations about febuxostat use for its renoprotective action in the published CKD international guidelines, because of declared lack of scientific data about the subject.

At present time also the target levels of sUA are set only for patients with HU and gout, while the optimal values of UA in serum for prevention / inhibition of CKD progression (GFR loss) – remain unclear.

THE AIM

To determine the efficacy and safety of allopurinol and febuxostat in treatment of patients with CKD to reduce the level of sUA and to analyze the effect of such treatment on glomerular filtration rate (GFR).

MATERIALS AND METHODS

The study was conducted in 2020-2021 at the Department of Family Medicine, Department of Nephrology and Renal Replacement Therapy (National Healthcare University of Ukraine, Kyiv, Ukraine) based on KNP KOR "Kyiv Regional Clinical Hospital", Department of Traumatology and Orthopedics of Bogomolets National Medical University; Hemodialysis Center of the Brovarsky Multidisciplinary Clinical Hospital; Clinic of Modern Rheumatology (Kyiv, Ukraine); Department of Internal Diseases No 2 (I. Horbachevsky Ternopil Medical University, Ternopil, Ukraine). Study design and procedures were approved by Ethic Committee of the KNP KOR "Kyiv Regional Clinical Hospital". The study included 45 patients with HU (serum UA>416μmol/l) and CKD (stages 3b-5). All patients gave their consent to participate in the study. Patients with recent acute kidney injury, acute renal failure, acute glomerulonephritis, advanced heart failure, with kidney transplant, systemic connective tissue diseases, infections, cancer, other severe/decompensated diseases, Hb <80 g/l; ALT and/or AST >3 times exceed the normal limit; and other conditions that could affect the parameters studied and the patient's life expectancy; contraindications to the use of allopurinol/febuxostat – were not included. At the time of enrollment in the study, patients were either not taking ULT or had completed a 2-week withdrawal period (10 patients). The target level of UA for patients with pre-dialysis stages of CKD was set at 300 μmol/l, for patients on hemodialysis – was not set.

All patients underwent a comprehensive clinical and laboratory examination, which included medical history, complete physical and joint examination, laboratory tests (full blood count, creatinine, UA, ALT, AST, blood glucose, HbA1c), GFR calculation (CKD- EPI). Further the patients were divided by their consent into one of the study groups for the treatment of HU: group I received febuxostat (40-120 mg/day), group II – allopurinol (50-300 mg/day – for patients with pre-dialysis CKD stages and up to 800 mg/day – for patients on hemodialysis). Clinical and laboratory examination was repeated after 2 weeks, 3 months and 6 months of treatment; sUA levels were determined with

Table I. Clinical and laboratory characteristics of the study patients

Parameter	Group I , n=28	Group II, n=24	P
Mean age, years	61,3±3,2	60,7±4,1	>0.05
Males, n/%	17 / 61,2	14/58,8	>0.05
CKD 3b, n/%	12/43,2	9/37,8	>0.05
CKD 4, n/%	10/35,7	10/41,7	>0.05
Patients on hemodialysis, n/%	6/21,6	5/20,8	>0.05
Comorbidities:			
Gout, n/%	16/57,6	13/54,6	>0.05
Chronic anemia, (Hb 81-119 g/l)	12/42,9	10/41,7	>0.05
NAFLD, n/%	16/57,6	15/62,5	>0.05
AH, n/%	100%	100%	>0.05
DM, n/%	10/35,7	7/29,4	>0.05
CVD, n/%	15/54,0	13/54,6	>0.05
Urolithiasis, n/%	4/14,4	4/16,4	>0.05
sUA, µmol/l	682,12±23,1	676,48±30,23	>0.05
GFR, ml/min	26,8±8,5	27,4±10,1	>0.05

Note: NAFLD – non-alcoholic fatty liver disease; AH – arterial hypertension; DM – diabetes mellitus; CVD – cardio-vascular disease.

Table II. Dynamics of sUA level and GFR in patients of both groups with pre-dialysis stages of CKD

Group /timepoint	Group I N=22		Group II N=19	
	sUA, µmol/l	GFR ml/min	sUA, µmol/l	GFR ml/min
Baseline	553,1±15,8	30,4±	539,8±19,3	31,2±2,6
In 1 month	429,7±25,1*	31,5±	466,5±29,3	31,0±
In 3 months	372,8±13,6*	33,5±2,8*	433,5±36,7	29,7
In 6 months	302,5±11,5*	34,1±3,1*	447,2±25,1	29,1

Note: *- the difference with group II is significant, p<0.05

Table III. Changes in sUA levels (µmol/l) in hemodialysis subgroups of patients during 6 months of study

Group/ timepoint	Group I N=6	Group II N=5
Baseline	686,5±24,7	650,6±27,3
In 1 month	574,6±20,2*	600,7±24,3
In 3 months	476,5±15,8*	574,8±22,9
In 6 months	380,1±25,1*	586,3±30,3

Note: *- the difference with Group II and with the level of the previous visit is significant, p<0.05.

individual frequency, depending on the dynamics of the indicator. Doses of ULT drugs were corrected depending on the dynamics of sUA, taking into account GFR (for allopurinol).

Statistic analysis was performed with program Statistica 10 with use of non-parametric methods and Mann-Witney U-test; the difference between parameters was considered significant in p<0.05.

The characteristics of the patients included in the study are presented in Table I.

As its shown in Table I all included patients had 3-5 comorbidities and took rather wide spectrum of concomitant medications for its treatment according to the national guidelines, the treatment remained stable during the study period.

RESULTS

All participants showed a significant decrease in the level of sUA under the influence of ULT drugs, however, the achievement of the target level of UA was significantly more often registered in Group I. The dynamics of the indicators in patients with pre-dialysis CKD stages is shown in Table II.

Analysis of the dynamics of sUA decrease in the studied groups showed that after 1 month of treatment 10 patients

reached the target level of sUA in group I (45.5%) and 3 patients in group II (15.9%), p<0.001; after 3 months of treatment in group I 67.5% reached the target level of sUA, and in group II – 21.2% (p<0.01); after 6 months, these figures were 90% and 37.1%, respectively (p<0.01), while it should be noted that in group II, all patients who reached the sUA level about 300 μmol/l were in CKD 3 subgroup. We have not find any significant differences in sUA level achieved in 3 and 6 month of treatment in patients with different comorbidities.

At each study visit, the GFR (using the CKD-EPI formula) was re-determined in all patients, and as can be seen from the data presented in Table II, the achievement of sUA levels less than 300 μmol/L was accompanied by significant positive GFR dynamics in most patients (in 90% of patients, GFR increased compared with the baseline, on average – in group I – by 3.1±0.51 ml/min, while in group II there was a gradual progression of GFR deterioration – in 31.8% of patients, a downward trend – in other patients in the group. Starting from month 3 timepoint of the study GFR was significantly higher in patients of Group I, independently from comorbidities profile, comparing to patients from Group II (p<0,05).

An analysis of the dynamics of sUA levels in patients from the hemodialysis group showed the achievement of significantly lower level in patients treated with febuxostat comparing to the baseline and to the group treated with allopurinol (Table III).

During the study period, no serious adverse events (AE) were registered in study patients, mild and moderate adverse events (in total – 8 events) in the form of epigastric discomfort, transient increase in ALT / AST (up to 3 times from the upper limit of the laboratory normal level) and skin rashes were registered in 5 patients (2 patients took febuxostat and 3 – allopurinol). Development of AEs did not lead to the discontinuation in study participation in any cases, but made impossible to increase the dose of allopurinol in 3 patients. It is worth to note that all cases of increase in ALT and / or AST level were determined in patients with comorbid non-alcoholic fatty liver disease.

DISCUSSION

The problem of the increasing incidence of CKD in the world's population with the subsequent development of the end-stage renal disease requires clarification of not only the risk factors for this serious condition, but also the search for pharmacological drugs with renoprotective properties. Unfortunately, to date, the renoprotective activity of drugs with a previously proven positive effect on the kidney function (primarily – drugs that effect the RAAS system) is being questioned. At the same time, the number of experimental and clinical studies are pointing on the negative impact of elevated serum uric acid levels on kidney function, development of metabolic disorders and comorbid diseases. Some researchers state that it is absolutely necessary to reduce the level of serum uric acid in order to prevent or slow down the progression of GFR loss in patients with CKD, prevention of CVD, metabolic syndrome and other pathological conditions, however, recommendations for the use of urate-lowering therapy for these purposes have not been approved. In our study, we compared the efficacy and safety of the use of classical ULT drugs – febuxostat and allopurinol for the treatment of HU in patients with CKD 3b-5 stage and analyzed the dynamics of GFR during 6 months of follow-up. It should be noted that the study was conducted in real practice, where all patients had 3-5 comorbid diseases and, in addition to HU and CKD, received a wide range of drug therapy for concomitant diseases, which could have influence on the study results. Another limitation of the study is rather small number of cases analyzed and the relatively short follow-up period. An analysis of the results of the use of ULT in the above mentioned groups of patients showed that febuxostat is more effective than allopurinol in achieving target levels of sUA in patients with pre-dialysis stages of CKD, with the same level of adverse events. The use of this ULT drug allowed a statistically significant improvement in GFR in this subgroup of patients, which suggests the presence of renoprotective properties in febuxostat, possibly associated not only with the achieved level of sUA, but also with the pleiotropic effects of this drug.

In hemodialysis patients, febuxostat was also more effective than allopurinol in achieving significantly lower sUA levels during the study period, the effect of which on patient health needs to be further investigated.

CONCLUSIONS

Use of febuxostat in patients with CKD stage 3b-4 and in patients on hemodialysis is more effective in reducing the level of sUA and achieving the target level of sUA than the use of allopurinol in the absence of serious adverse events within 6 months of therapy. In patients with pre-dialysis stages of CKD, the use of febuxostat as part of treatment is accompanied by stabilization or a significant increase in GFR, which requires further research to confirm the renoprotective properties of febuxostat and develop a standard treatment algorithm, possibly starting at earlier stages of CKD.

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ORIGINAL ARTICLE

HEPATIC VASCULAR TUMORS IN CHILDREN: POTENTIAL RISKS, OPTIMAL IMAGING AND THE ROLE OF SURGICAL INTERVENTION

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ABSTRACT

The aim: To revise the case-series of hepatic vascular tumors (HVT), particularly to identify optimal visualization, management and role of surgical intervention.

Materials and methods: Out of 96 children with hepatic tumors who hospitalized in a single center from 2011 to 2020, 20 (20,8%) were diagnosed HVT. Hepatic Hemangiomas (HHs) were presented in 19 patients and Kaposiform hemangioendotelioma (KHE) in one case. To determine the type of HH we used radiological classification. For visualisation contrast-enhanced MRI (n=7, 30%) and cCT (n=15,70%) were used. Follow-up period was 14-77 months.

Results: All HVT were revealed by sonogram at the age of 0-5 m, with 4 (20%) diagnosed prenatally. Male to female ratio was 3:2. Beta-blockers were prescribed to 12 patients with HHs. Treatment duration was from 6 to 24 month. Steroid therapy was initial in cases when it was impossible to prescribe the curative dose of beta-blockers. Complications of propranolol treatment were transitory bradycardia (n=7) and transitory hypoglycemia (n=2). After vincristine chemotherapy decreases the tumor size by 54%, that allowed a safe liver resection. 4 (20%) patients – two multifocal HHs, one diffuse HH and in patient with KHE manifested congestive heart failure and pulmonary hypertension Mortality rate is 5% (n=1), this patient died against progressive cardiovascular failure.

Conclusions: life-threatening complication of HVT was congestive heart failure. Early treatment is beneficial for complications prevention. Surgical treatment is optional for KHE when can be removed safely.

KEY WORDS: Hepatic Hemangioma, Kaposiform hemangioendotelioma, children

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INTRODUCTION

Hepatic tumors are rare in children, representing up to 5% of all tumors diagnosed in fetuses and neonates [1]. Among them, according to different authors data, benign hepatic vascular tumors (HVT) amount from 8,6% [2] to 60% [3]. Hepatic Hemangioma (HH) is a benign vascular tumor, asymptomatic in most cases, usually detected as incidental finding while examination for other reasons. However sometimes HH are huge and provoke dangerous complications. Symptomatic HHs mortality rate is up to 16 – 20% [4, 5]. Kaposiform hemangioendotelioma (KHE) is a rare symptomatic GLUT-1-negative tumor with a great risk of complications development and high mortality rate [6, 7]. While numerous multicentral randomised researches on hemangiomas of superficial localization are represented in the medical literature widely, with a consensus on diagnostics and management [8], there are occasional articles on HH, dedicated to separate groups studying [9 ,10].

THE AIM

To revise the case-series of HVT, particularly to identify the type-specific character of clinical presentation, optimal visualization, management and role of surgical intervention.

MATERIALS AND METHODS

Out of 96 children with hepatic tumors who underwent treatment and or dynamic observation within a single center from January 2011 to January 2020, 20 (20,8%) were diagnosed HVT. The diagnosis of HVT was determined under ISSVA 2018 systemic classification [11], which divides vascular tumors into benign, locally aggressive and malign. The last named are rejected from the study. Hepatic hemangiomas (HH) are benign HVT, presented in 19 patients of the study, Kaposiform hemangioendotelioma (KHE) is classified as locally aggressive or borderline vascular tumor, presented in the only one patient of the group. To determine the type of HH we used radiological classification, which divides HH into focal, multifocal and diffuse [12].

Clinical examination started with history-taking, prenatal screening, age at first symptom noticing, clinical presentation analysis, and skin lesions presence. Ultrasound activity assessment of HVT followed, in a grey scale and Color Doppler mode, according to the method, developed in our clinic [13]. Routine laboratory examination included blood count and platelet count; coagulation profile with D-dimer and fibrinogen levels evaluation; considering the risks of hypothyreosis development in HH patients thyroxine, triiodothyronine and TTG levels were determined; metabolic panel (BUN, creatinine, blood sugar).

Table I. Characteristic of patients with hepatic vascular tutors

№	Sex	Prenatal diagnosis	HH type	Follow up, months	Skin lesions	Presentation	Treatment	Outcome
1	F	-	focal	77	-	Asymptomatic	observation	Tumor regression
2	F	+	focal	67	-	Asymptomatic	observation	Tumor regression
3	F	-	diffuse	62	-	High transaminases rate, coagulopathy	beta-blockers	recovery
4	M	+	diffuse	52	-	hypothyreosis	beta-blockers	recovery
5	M	-	diffuse	45	-	Cardiac failure and pulmonary hypertension, coagulopathy hypothyreosis	Corticosteroids + beta-blockers	recovery
6	M	-	focal	64	-	Asymptomatic	Laparoscopic biopsy and beta-blockers	Tumor regression
7	M	-	focal	57	-	Asymptomatic	observation	Tumor regression
8	M	-	multifocal	32	+	Asymptomatic	beta-blockers	recovery
9	M	-	multifocal	34	+	Asymptomatic	beta-blockers	recovery
10	M	+	multifocal	22	-	asymptomatic	beta-blockers	recovery
11	M	-	diffuse	70	-	Jaundice hypothyreosis	beta-blockers	Tumor regression
12	M	-	multifocal	27	+	Asymptomatic	beta-blockers	recovery
13	F	-	multifocal	44	+	Bleeding from tracheostomy wound, coagulopathy	beta-blockers	recovery
14	F	-	multifocal	58	+	Asymptomatic	beta-blockers	recovery
15	M	-	multifocal	56	+	Asymptomatic	beta-blockers	recovery
16	M	-	multifocal	52	+	Asymptomatic	beta-blockers	recovery
17	F	-	multifocal	-	+	Cardiac failure and pulmonary hypertension	Corticosteroids	died
18	F	-	multifocal	60	+	Cardiac failure and pulmonary hypertension	Corticosteroids + beta-blockers	recovery
19	M	-	multifocal	43	+	Asymptomatic	beta-blockers	Tumor regression
20	F	+	KHE	14	-	Cardiac failure and pulmonary hypertension	Vincristine – 11 courses; surgery	recovery

Pretreatment testing also included ECG and echocardiography with a view to risks of cardiac failure development, with following close monitoring in symptomatic patients and while beta-blockers dose titration. For visualization we used contrast-enhanced MRI (n=7, 30%) and contrast-enhanced CT (n=15, 70%), with one patient had both visualizing options with following implementation of radiological classification. In one case liver biopsy was performed once with Glucose transporter protein type 1 (GLUT1) level determination. Median follow-up period was 49,3 months, range14±77.

RESULTS

All HVT were revealed by sonogram at the age of 0-5 m (range 52,3±43,29 days), 4 (20%) HVT were diagnosed

Fig. 1. Male O., 4 m.o., numerous skin infantile hemangiomas (photo) and multifocal HH (MRI, axial view)

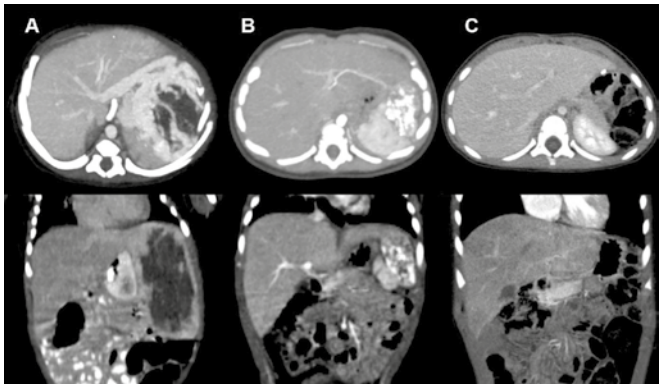

Fig. 2. Female C, Kaposiform hemangioendotelioma. CT scans of a series of studies (axial and coronal) A. Initial scan shows massive hypervascular tumor in the left lobe of the liver, associated with the branches of the portal vein. B. After neoadjuvant chemotherapy, the volume decreased significantly, tumor partially calcified. C. After radical resection of the tumor, restoration of the shape of the liver.

prenatally, 3 by ultrasound screening for multiple skin lesions, 17 (85%) in general within first three months of life. Male to female ratio was 3:2 (12 males to 8 females). Patients' data are represented in Table I.

HH was diagnosed in 19 patients, with 11 (55%) multifocal, 4 (20%) diffuse, and 4 (20%) focal. One patient was diagnosed KHE.

Focal HHs were diagnosed prenatally in two children. Ultrasound findings included large lesion with echoic border; the diagnosis was confirmed after birth by ultrasound and weighted CT-scan, with the finding of the spherical solitary tumor with clear margins that intensively accumulates contrast at peripheral margin with its lower density in the center.

Among 11 children with multifocal HH numerous skin infantile hemangiomas were present in 10 (90,9%) patients, the number of skin lesions varied from 8 to a couple of dozens (Fig. 1).

Ultrasound findings in multifocal HHs were represented by numerous well-delineated hypoechogenic lesions of different diameter, up to 30 mm, with echogenic center and peripheral halo. Imaging features of multifocal HH in weighted CT-scan were numerous spherical lesions, that intensively accumulate contrast from their peripheral margins to the center and surrounded by healthy liver tissue.

Diffuse HH had a clinical presentation right after birth. They presented signs of liver failure, hepatomegaly and coagulopathy, including transitory low platelet count. Hypothyreosis was diagnosed in 3 cases of diffuse HH.

Conservative treatment was provided to all HH patients: beta-blockers monotherapy (n=12), combined therapy of beta-blockers and corticosteroids (n=2), corticosteroids monotherapy (n=1). Thyroid replacement therapy was considered in patients with hypothyreosis (n=3).

4 patients were under dynamic observation, with laparoscopic biopsy performed to one of them to obtain a clearer diagnosis that was followed by beta-blockers treatment. Patient with KHE underwent combined treatment: vincristine administration in allowed to perform safe surgical resection of vascular tumor.

Beta-blockers was prescribed to 12 patients (4 – diffuse HHs and 8 with multifocal HHs). Treatment duration was from 6 to 24 months, mean duration was 14,9±4,3. Beta-blockers show the great efficacy for these lesions. Steroid therapy in combination with beta-blockers was considered in patients with early manifestation of liver failure and coagulopathy for a period of beta-blockers dose titration with gradual withdrawal of steroids after reaching the curative dose of beta-blockers. Congenital HH is potentially not sensitive to beta-blockers treatment, so mentioned patients (n=4) underwent dynamic observation.

Considering all potential complications of beta-blockers when prescribed to young children, the treatment was initiated within inpatient department with dose titration from 0,5 mg/kg/day to curative dose of 2 mg/kg/day. Propranolol treatment continued outpatiently in selected dosage. Along with that mothers of patients were taught to follow the regimen of treatment, that mandatory included information about alarm signs that might indicate the complications of therapy.

Complications of propranolol treatment were transitory bradycardia (n=7) and transitory hypoglycemia (n=2). Bronchial obstruction that resulted into treatment-limiting was observed in one case. HH size hasn't essentially changed after beta-blockers elimination, though its activity was increased for 6 months, manifesting high transam-

inases rates. It took 10 months to transaminase rates to decrease to normal. 2 children with multifocal and one child with diffuse HH, who presented signs of respiratory and cardiovascular failure, were initially treated with corticosteroids in a daily dosage of 3-4 mg/kg. At the age of 3 weeks in two other patients, propranolol treatment started with dose titration (from 0,5 to 2 mg/kg/day) with gradual steroids elimination.

Propranolol treatment resulted into HH blood supply reduction, metabolic panel normalization, hypothyreosis signs elimination (in 1.5-2 months) and HH involution.

It was impossible to initiate propranolol treatment in a 3m.o. patient with multifocal HH and numerous skin hemangiomas who presented with cardiac failure. The reason was she was hemodynamically unstable and required inotropic support. This child was treated with corticosteroids in a dosage of 8 mg/kg/day (recalculated against prednisone). Despite all efforts intensive care team haven't managed to stabilize her condition and this patient died against progressive cardiovascular failure. Three other patients with cardiac failure were stabilised, that afforded to start beta-blockers and eventually resulted into recovery. CT findings of mentioned patients were replacement of liver tissue by vascular neoplasms with anomalous vascular shunts.

A patient with KHE was diagnosed prenatally by ultrasound screening, where hepatomegaly caused by fast-flow vascular tumor were seen. When admitted to the hospital at the age of 1 m.o. she manifested acute cardiac failure and coagulopathy. Objective findings included abdominal distention, acrocyanosis, respiratory embarrassment. The diagnosis of HVT was confirmed by CT (fig.2A), that also showed spleen was affected. Vincristine chemotherapy was prescribed to decrease the tumor size and affect the ssecondary respitatory distress resulted from compartment syndrome. As a result of the treatment tumor size was reduced by 54% (fig. 2B), that allowed a safe surgical removal of the tumor accompanied by splenectomy. Atypical resection of left lateral section was performed by crash-clamp parenchymal dissection. Recovery followed.

CD31 and CD34 expression as immunohistochemical markers of endothelial transdifferentiation intumor tissue confirm the diagnosis.

DISCUSSION

Infantile hemangioma is a widespread pathology in babies. According to different sources its frequency is 4 to 10% among children aged 0-1y.o. [8]. In most cases this data represents the frequency of superficial lesions. It is impossible to perform an objective determination of internal organs hemangiomas portion, as indefinite part of them are asymptomatic. Partially some confusion is brought by ambiguous terminology, that may be used by different authors. The term "liver hemangioma" is used to describe both infantile hemangiomas, and other vascular malformations, that are diagnosed at any other age [8, 14].

Liver is a critical site for vascular tumors localization, as there is a big potential risk of complications, and high mortality rate [4]. Congestive heart failure, acute liver failure, hypothyreosis and abdominal compartment syndrome should be mentioned among the most dangerous HHs complications [12]. Compartment syndrome results into secondary respiratory distress. In our series 4 (20%) patients manifested cardiac failure at admission; two of them required ICU immediately.

Mortality rate in children with infantile HHs is up to 11 – 20% according to recent publications, but the real number is likely to be higher [17]; and up to 2/3 of symptomatic patients with KHE die. HH tissue contains macro- and micro- arteriovenous shunts, that are the reason of congestive heart failure development [18].

Most publications state they prefer noninvasive methods for HHs diagnosing, MRI in particular [12, 19] and CT scans. For patients of younger age CT benefit is possibility to perform examination without sedation, but its disadvantage is radiation exposure. In cases of untypical clinical presentation combined with skin lesions absence there is a need in tumor biopsy with following determination of Glut1 protein level [20]. Lesion biopsy is not a routine diagnostic option for HVT, most authors consider HVT biopsy hazardous for the risk of uncontrolled bleeding development or rapid tumor growth induction [1, 7].

Congenital hemangioma evolution process takes place prenatally and reaches the full development by the moment of birth and can be diagnosed within prenatal screening [12, 19]. Otherwise involution is partial their size is constant, or involution is partial [12]. In most cases such patients are under compulsory outpatient observation. In children with focal HH transitory thrombocytopenia can be observed because of thromboses within the affected tissue. Hemorrhages into the tumor usually take place when fetal blood flow redevelops into postnatal blood flow. Calcifications can also be found, and their number is growing along with tumor involution [12].

Multifocal and diffuse HHs are infantile hemangiomas, they are characterized by rapid growth during first 12 months of life followed by slow involution during next 1 – 5 years [12]. Multifocal HH are the most frequently combined with numerous skin lesions [14, 19]. In prospective study of 151 patients with more than 5 skin hemangiomas, liver lesions were found in 24 (16%) cases. Treatment required only in 2 (8,3%) children [21]. In other research it is shown that there is a high risk of HH in patients with 10 skin lesions and more [10].

Specific feature of diffuse HH is the absence of healthy liver tissue in affected liver region, as it is totally substituted with tumor tissue. Clinical course is more severe than in patients with focal or multifocal HH [22]. Cardiac failure is infrequent, as arteriovenous shunts are not common with diffuse HH unlike with multifocal. Usually they present with abnormal liver function and coagulation disorders. One case of severe hypothyreosis in a child with diffuse HH gave an impetus to detect D3 rate in the tumor [23]. All infantile hemangiomas speed up type-3 iodothyronine deiodinase (D3) metabolism. In proportion to hemangio-

ma involution, hypothyreosis signs eliminate. In our study, three of the four patients with diffuse HH had hypothyreosis and required substitution therapy.

According to Boston Vascular Anomalies Center, KHE occurrence is 0,91 to 100000 newborns [2]. When suspected at initial ultrasound, the following visualization is chosen – enhanced CT or MRI [3, 7]. KHE is typically larger than other vascular lesions on CT. It can be represented as mass without strict borders, sometimes developing a "lost signal phenomenon" for numerous high-flow vessels [8]. Most severe KHE's complications include thrombocytopenia, coagulopathy, hemolytic anemia, intraperitoneal bleedings, heart failure with or without pulmonary hypertension, hypothyreosis [7, 15, 16]. In children with heart failure manifestation it is obligatory to detect and measure the vascular shunts. In our patient with KHE shunts were detected by CT-scan. Adequate visualization together with clinical correlation allows confirming the diagnosis without biopsy.

The role of surgical treatment dramatically changed since the time of vascular tumors biological classification implementation into medical practice, along with antiangioproliferative drugs with their minimal adverse effects and the possibility to determine the prognosed life cycle of infantile hemangioma [12, 14]. Previously, corticosteroids, vincristine and interferon-α were used as a systemic therapy [9]. There is an effective combined systemic treatment for patients with cardiac failure symptoms, which includes corticosteroids and beta-blockers [19]. Surgical treatment retains its relevance for treatment of KHE. If the tumor can be removed without undue risk to the patient, we will get all the symptoms gone [16].

CONCLUSIONS

Life-threatening complication of HHs and liver vascular tumors is congestive heart failure, caused by vascular shunts within mentioned lesions.

Beta-blockers (propranolol) treatment was used in all patients with infantile HHs and showed excellent efficacy, resulting into recovery in 12 and tumor regression in 2 patients.

Surgical treatment is a great treatment option for patients with KHE, when they can be safely resected.

Early treatment is beneficial for complications prevention in initially asymptomatic patients with large intrahepatic arteriovenous shunts, who could have developed cardiac failure.

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The Authors declare no conflict of interest.

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ORIGINAL ARTICLE

SINGLE NUCLEOTIDE POLYMORPHISM RS4696480 OF *TLR2* GENE ASSOCIATES WITH SEVERITY OF ATOPIC DERMATITIS IN CHILDREN, BUT NOT WITH IGE SENSITIZATION TO MALASSEZIA

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ABSTRACT

The aim: Malassezia has been linked to atopic dermatitis, and TLRs are suggested to mediate influence of Malassezia spp on human cells. The aim of the study was to examine if *TLR2* rs4696480 polymorphism predisposes to atopic dermatitis, IgE sensitization to Malassezia or to severe phenotype of atopic dermatitis.

Materials and methods: The study included 103 patients with eczema and 84 healthy children. Specific IgE against Malassezia mix (m227) was analyzed in 47 patients using immunochemiluminescent method on the ImmunoCAP 100 (Thermo Fisher Scientific Inc., Phadia, Sweden). Genotyping for *TLR2* rs4696480 was performed by using Real-time PCR.

Results: Increased IgE to Malassezia spp. was observed in 34,3 % of children with eczema. Higher Malassezia spp.-specific IgE titre positively correlated with duration of atopic dermatitis and a higher total IgE. There were no difference in allele distribution among patients and control group (OR=1.096 (0.549- 2.191) for AT, OR=0.946 (0.430– 2.078) for TT, p > 0,05). *TLR2* polymorphism rs4696480 was not associated with Malassezia spp.-sIgE. AA-genotype was significantly more frequent among patients with severe and moderate-to-severe AD (OR=6.395 (1.240-32.991).

Conclusions: AA variant of *TLR2* rs4696480 polymorphism predisposes to severe phenotype of AD.

KEY WORDS: SNP; *TLR2*; Malassezia; atopic dermatitis; children

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INTRODUCTION

Atopic dermatitis (AD), the most common skin disease in infants and children, is a complex disease with a multifactorial etiology, including dysregulation of the immune system and dysfunction of the epidermal barrier, which are affected by both genetic and environmental factors [1].

Malassezia has been linked to a number of skin conditions, including AD. This is the most common fungal genus of healthy skin, but these yeasts also show pathogenic potential under appropriate conditions. The close relationship between skin and IgE-binding allergens in Malassezia in AD has been shown previously [2, 3]. They interact with almost all cellular components of the normal epidermis, including keratinocytes, Langerhans cells, melanocytes, and the host's immune system. It is known that Malassezia yeast is of great importance to the development of sensitization in AD. Malassezia colonizes human skin after birth, and therefore, as a commensal, must be normally recognized by the human immune system. The presence of SNPs in the PRR genes may be a prerequisite for the development of AD in children. Despite the current knowledge about the association of Malassezia species with the development of AD, the mechanisms underlying their change in their condition from commensal to pathogenic still need to be further elucidated.

TLR are members of the PRR family, which recognize various preserved microbial components or PAMP. TLR2 recognizes components of gram-positive bacteria and yeast, such as lipotechoic acid, peptidoglycan, lipoproteins or zymosan [2]. Recognition of PAMP by TLR initiates a signaling cascade that results in the production of proinflammatory cytokines, chemokines, antimicrobial peptides, and inducible enzymes in the skin by activating transcription factors, activator protein (AP) -1, and nuclear factor (NF) κB [3-5]. TLRs are suggested to mediate influence of Malassezia on human cells. It has been discovered that TLR2, in particular, can recognize components of many yeasts including Malassezia [5]. Some studies conducted recently, confirmed the significance of TLRs for the immune response of human cells against Malassezia. For example, Malassezia induces the expression of TLR2 and TLR4 on human keratinocytes, which mediate the increased production of the antimicrobial peptide human beta–defensin 2 and the chemokine CXLC8. Others contribute to the pro–inflammatory response of dendritic cells against Malassezia to TLR–mediated mechanisms [6-8].

THE AIM

In the present study we investigate the frequencies of *TLR2* gene polymorphism T16934A (rs4696480) in children with AD to explore the association between the polymorphism and the sensibilization to Malassezia yeasts.

MATERIALS AND METHODS

The study included patients with AD (n = 103); aged 6 month to 18 years 6 [3;10] from department of allergy at Kyiv City Children Clinical Hospital №2 and 84 children aged 12 month to 18 years (6 [5;9]) without allergic disease at the time of examination or according to history data. This study was approved by the ethical committee of the O. Bogomolets natioanal medical university, all patients/parents of affected children gave informed consent to participate.

OUTCOME MEASURES

The diagnosis of AD was established according to the criteria of Hanifin & Rajka [9], by the patient's history. Clinical parameters of patients including age, gender, age of onset and severity of eczema, AD distribution (exclusive head–neck type eczema vs diffuse AD including head and neck involvement), concomitant allergic diseases, parental history of atopy, total IgE and sIgE to Malassezia. Scoring of AD severity and blood sampling to determine IgE levels were performed at the same visit.

ASSESSMENT OF ATOPIC DERMATITIS SEVERITY

The severity of AD was assessed using SCORing Atopic Dermatitis (SCORAD) index. A SCORAD < 25 indicated mild AD, a SCORAD between 25 and 50 indicated moderate AD, and a SCORAD > 50 (with a maximum index of 103) indicated severe AD [10].

TESTING OF IGE ANTIBODIES

Specific IgE against Malassezia mix (m227), a mixture of 3 Malassezia species (Malassezia sympodialis, Malassezia globosa, and Malassezia restricta), was analyzed in 47 patients. Serum samples from patients were collected during visits and stored at –20°C until analysis. All samples were analysed together for the presence of total IgE antibodies and allergenspecific IgE antibodies to Malassezia spp. (m227) using immunochemiluminescent method on the ImmunoCAP 100 (Thermo Fisher Scientific Inc., Phadia, Sweden). The results were classified into classes: 0 (less than 0.35 kU \ l), 1 (0.35–0.7 kU \ l), 2 (0.7–3.5 kU \ l), 3 (3.5– 17.5 kU \ l), 4 (17.5 –50 kU \ l), 5 (50–100 kU \ l) and 6 (100 kU \ l). Class 1 or higher was defined as positive. The results of specific IgE to Malassezia were matched with patient-related parameters (gender, age, head–neck type eczema, SCORAD, age of onset, total IgE, concomitant allergic diseases).

SELECTION OF SNP

An SNP *TLR2* rs4696480 (A>T), which was located in intron region, was selected for genotyping, as it can affect expression of *TLR2* and is reported to be common in European populations.

DNA EXTRACTION

Buccal epithelium was taken by using buccal brushes, skin samples samples were collected from the forearm by swabbing with the following freezing of samples and their storage at -20°C. DNA for genotyping was extracted from the samples by using NeoPrep 100 DNA (Neogen, Ukraine) according to manufacturer's protocol. The concentration of total DNA was determined by using a NanoDrop spectrophotometer ND1000 (NanoDrop Technologies Inc., USA).

qPCR GENOTYPING

Amplification reactions were performed by using a 7500 Fast Real-time PCR System ("Applied Biosystems", USA) in a final reaction volume of 20 µl, which contained 2X TaqMan Universal Master Mix ("Applied Biosystems", USA), assay C__27994607_10 and the template DNA. The thermal cycling conditions involved a denaturation step at 95°C for 20 s, followed by 40 cycles of amplification at 95°C for 3 s and 60°C for 30 s. Analysis of the data was carried out with 7500 Fast Real-Time PCR Software. The primer sequences of rs4696480 *TLR2* polymorphism were follows: For TLR2-F 5' AACAGAAATTTATCCATTCATGGTT 3', Rev TLR2-R 5' AGCAGTTTATTGTGAGAATGAGTTT 3' (https://www.ncbi.nlm.nih.gov/SNP/):

STATISTICAL ANALYSIS

Since the distribution of most of the sample characteristics differed from the Gaussian (normal) distribution, the statistical sample was heterogeneous, and therefore non-parametric statistical methods were used. Quantitative data for each of the study groups were presented as median – Me[QI; QIII], categorical (dichotomous qualitative) variables – as the frequency of each of the values (n) and the percentage (%) in the group.

In the analysis of influence sensitization to Malassezia spp. on AD, Mann-Whitney U-test was used to compare differences between groups for quantitative data and Fisher's test was used for categorical variables. Spearman's ranking criterion (ρ) was used to assess the correlation between quantitative traits. A p-value < 0.05 was considered statistically significant.

Statistical processing was performed using EZR software version 1.32 (graphical interface R (version 2.13.0)).

SNPAnalyzer (web-based software) was used to examine Hardy-Weinberg equilibrium. χ^2 test was performed to investigate if there was any difference in the frequency of the genotype and the allele between the AD patient group and the healthy control group.

RESULTS

103 children between 6 months and 18 years of age were investigated in our study. The average age of children in

Table I. Characteristics of studied patients

Age, years, median (range)	**6 [3;10]**	
Male:Female	53:50	
SCORAD, median (range)	36,8 [30;60]	Minimum 0 Maximum 80
Categorised SCORAD, patients, %	35,9	
Mild (<25)	23,3	
Moderate (25–50)	20,5	
Severe (>50)	26,2	
Concomitant allergic diseases		
allergic rhinitis	32,0	
asthma	18,4	
allergic rhinitis+ asthma	14,6	
Early onset, %	85,0	
Sensitisation to Malassezia spp., %	34,3	

Table II. *TLR2* rs4696480 polymorphism genotype distribution among patients and control group and the association with clinical parameters of AD.

Clinical parameter	**AA n (%)**	**AT n (%)**	**TT n (%)**	**p–values by OR**
AD (n=103)	29 (28,1)	46 (44,7)	28 (27,2)	> 0,05
Controls (n=84)	23 (27,4)	40 (47,6)	21 (25,0)	
Severity by SCORAD				
Mild (n=23)	2 (8,7)	12 (52,2)	9 (39,1)	< 0,05
severe and moderate-to-severe (n=80)	27 (33,8)	34 (42,5)	19 (23,75)	
Age of onset				
early (before 18 mo) (n=86)	25 (29,1)	40 (46,5)	21 (24,4)	> 0,05
late (after 18 mo) (n=17)	4 (23,5)	6 (35,3)	7 (41,2)	
Asthma				
yes (n=16)	5 (31,3)	8 (50,0)	3 (18,7)	> 0,05
no (n=87)	24 (27,6)	38 (43,7)	25 (28,7)	
Allergic rhinitis				
yes (n=34)	10 (29,4)	15 (44,1)	9 (26,5)	> 0,05
no (n=69)	19 (27,5)	31 (44,9)	19 (27,5)	
Serum total IgE				
High total IgE (n=53)	12 (22,6)	23 (43,4)	18 (34,0)	> 0,05
Normal total IgE (n=50)	17 (34,0)	23 (46,0)	10 (20,0)	
sIgE to Malassezia				
yes (n=12)	4 (33,3)	6 (50,0)	2 (16,7)	> 0,05
no (n=35)	9 (25,7)	15 (42,9)	11 (31,4)	
Parental histoty of atopy				
yes (n=37)	11 (29,7)	16 (43,2)	10 (27,0)	> 0,05
no (n=66)	18 (27,3)	30 (45,5)	18 (27,3)	

the main group was 6 [3;10] years, including 53 boys and 50 girls. The clinical characteristics of patients are summarised in Table I.

Serum IgE to Malassezia was evaluated in 47 children. Increased IgE to Malassezia spp. was observed in 12 (34,3%) children with AD. Among them 4 (33,3 %) children had class 1 of sensitization, 3 (25,0 %) children had 3rd class, 5 (41,7 %) children - the 4th class. Among children with positive IgE to Malassezia, there were 6 male and 6 female ($p > 0.05$).

We have found a relationship between higher Malassezia spp.-specific IgE titre and a higher total IgE and the age of the onset, but not the severity and the duration of eczema. Data are presented on Figures 1-4.

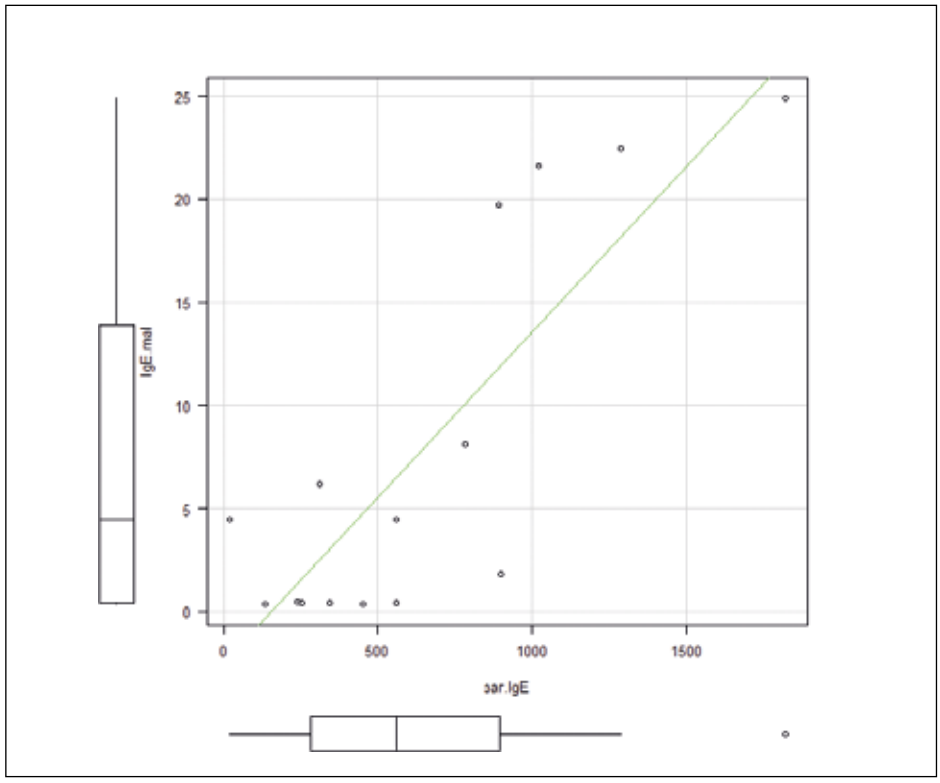

Fig. 1. Correlation of total IgE and Malassezia spp.-specific IgE, p=0,00625

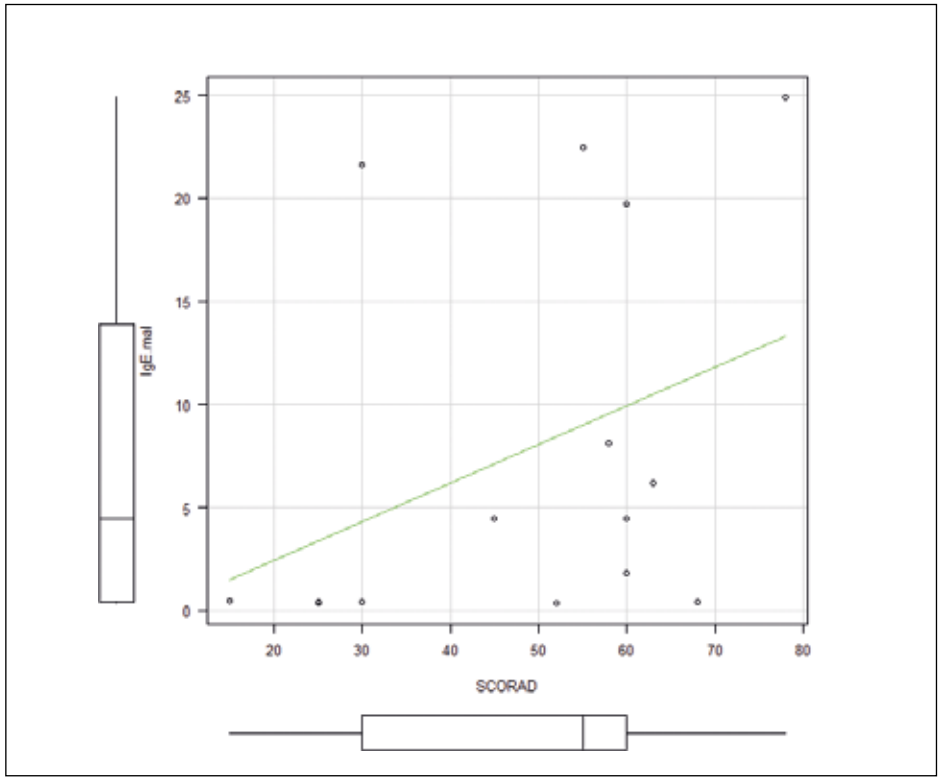

Fig. 2. Correlation of SCORAD and Malassezia spp.-specific IgE, p=0,133

GENOTYPING

We found that SNP was in Hardy-Weinberg equilibrium. There was no difference in genotype distribution among patients and control group (OR=1.096 (0.549-2.191) for AT, OR=0.946 (0.430– 2.078) for TT, p > 0,05) (Table II).

We investigated the association of the *TLR2* rs4696480 polymorphism with clinical parameters of AD (severity on the SCORAD scale, age of the onset, presence of concomitant allergic diseases, serum total IgE level, presence of sIgE to Malassezia, the parental history of the atopy). AA-genotype was significantly more frequent among patients with severe and moderate-to-severe AD (OR=6.395 (1.240-32.991) (Figure 5). Other clinical parameters and features of the phenotype were not related to the genotype of patients (Table II).

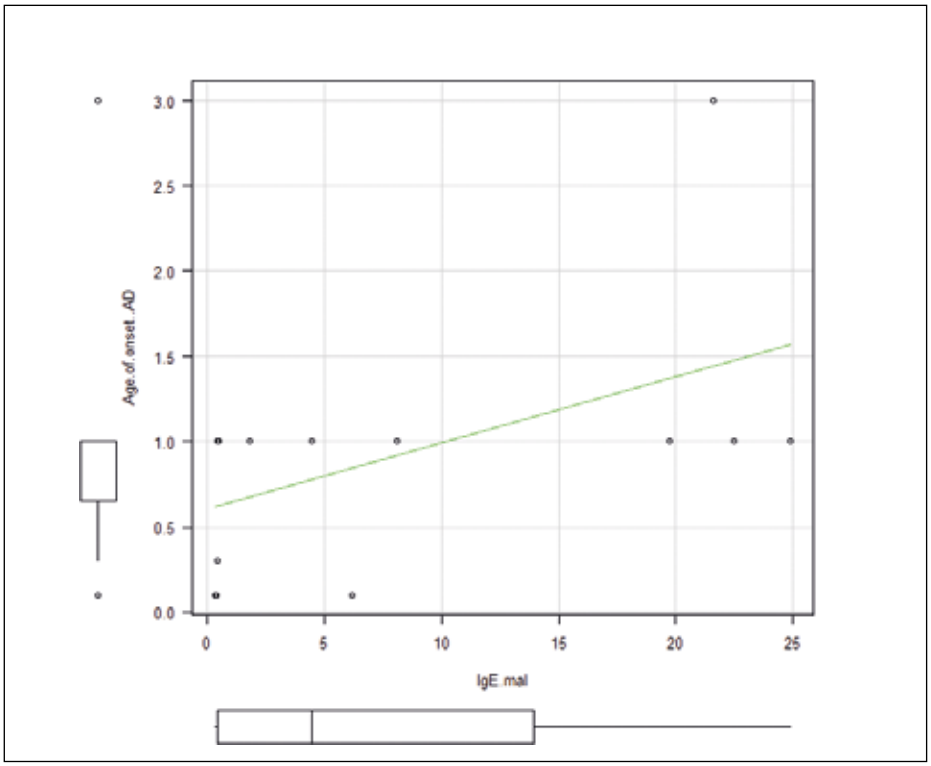

Fig. 3. Correlation of age of onset of AD and Malassezia spp.-specific IgE, p=0,0372.

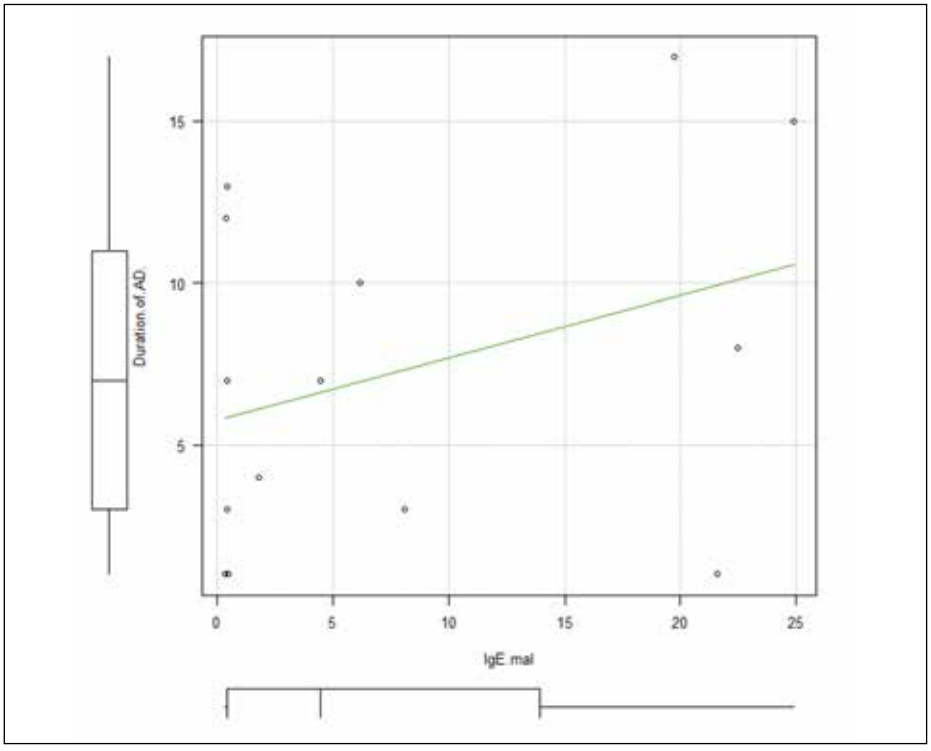

Fig. 4. Correlation of duration of AD and Malassezia spp.-specific IgE, p=0,375.

DISCUSSION

TLRs play the key role in the innate immune system and are directly engaged in the pathogenesis of many skin diseases as they recognize molecules of many pathogens.

The Salpietro C. study identified the overall variant *TLR2* rs4696480 as the most common in children with AD using the candidate gene method in a cohort of 187 children with AD and 150 healthy controls [11]. SNP rs4696480 in *TLR2* is located near an evolutionarily conserved sequence as well as several transcription factor binding sites, including retinoid receptors, NF-κB, and the interferon regulatory factor [12]. The presence of multiple transcription factor binding sites in an evolutionarily conserved sequence indicates that this region is transcriptionally relevant and potentially is genetically or transcriptionally reflected. The Oh D.Y. study reported an increase in the incidence of A-allele at position

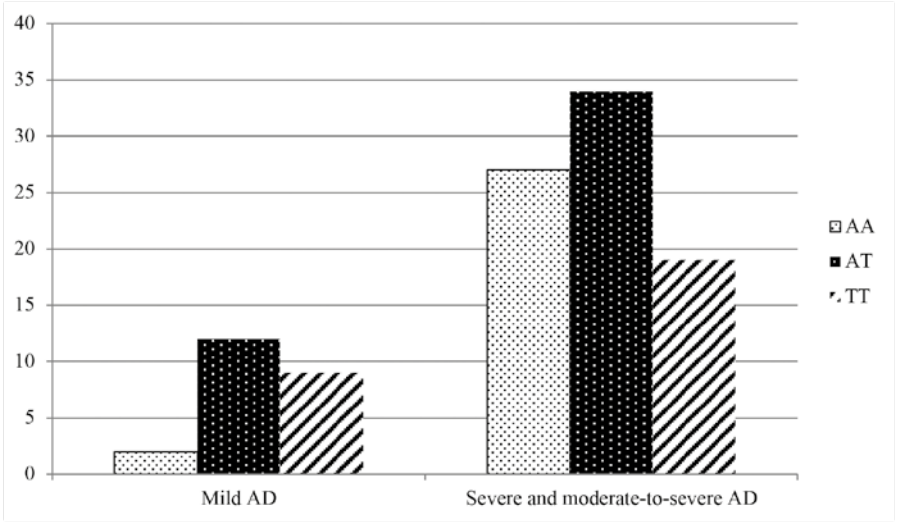

Fig. 5. TLR2 rs4696480 and severity of AD according to SCORAD

rs4696480 of the *TLR2* gene among German adult patients with severe AD (SCOAD> 50) as compared to patients with mild-to-moderate AD (SCORAD ~ 50) [12]. Eder et al. [13] reported an association between the *TLR2* rs4696480 SNP gene and asthma, wheezing, atopy, or symptoms of allergic rhinitis in children of farmers. It has been suggested that the T allele in the promoter region of the *TLR2* gene has a protective effect against these diseases. Other research groups have found an inverse association between polymorphism and AD severity: Polymorphism in *TLR2* rs4696480 was associated with SCORAD severity, asthma, allergic conjunctivitis, or family history of atopy in patients with AD with serum IgE ≥106 IU / ml, but not in those with IgE <106 IU / ml [14]. Our study has not revealed difference in genotype distribution among Ukrainian children with eczema and healthy controls. Therefore, the influence of polymorphism rs4696480 on AD susceptibility can be population-dependent.

Among clinical features, the severity of AD was related to the genotype. AA-genotype was significantly more frequent among patients with increased severe and moderate-to-severe AD (OR=6.395 (1.240-32.991). TLRs are suggested to mediate the interaction between Malassezia cells (or their immunogenic proteins) and human cells. It is not fully understood if Malassezia sensitization can be mediated via TLR2, and how functional SNPs can contribute to the process of sensitization. Selander C. et al. determined that *M. sympodialis* can activate mast cells, enhance the mast cell IgE response, modulate MAPK activation, and by signaling through the TLR2/MyD88 pathway alter IL-6 production in a dose-dependent manner [15]. In our study genotype did not correlate with Malassezia spp.-sIgE, but the study group was small.

CONCLUSIONS

Malassezia spp. plays an important role in AD, as it can interact with the skin immune system. The impaired skin barrier of atopic individuals and sensitisation to Malassezia spp. correlates with the severity of AD. AA variant of *TLR2* rs4696480 polymorphism predisposes to severe phenotype of AD.

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The Authors declare no conflicts of interest.

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ORIGINAL ARTICLE

IMPACT OF NUTRITIONAL CORRECTION OF PROTEIN METABOLISM DISORDERS ON THE CLINICAL COURSE OF PULMONARY TUBERCULOSIS

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ABSTRACT

The aim: To study the impact of nutritional correction of protein metabolism disorders on the clinical course of pulmonary tuberculosis.

Materials and methods: The study involved 67 patients with pulmonary tuberculosis, which were divided into two groups: group I – 35 patients who underwent nutritional correction of protein metabolism disorders against the background of antimycobacterial therapy (AMBT) and group II – 32 patients who received standard AMBT. An assessment of clinical indicators and the condition of protein metabolism (PM) was conducted by determining the concentration of individual non-essential, essential amino acids and their total amount.

Results: The proposed correction scheme includes food products containing essential nutrients and biologically active compounds that have a positive impact on the corresponding links of pathogenesis and can be used throughout all phases of treatment. Its application had a positive impact on the indicators of PM (significant ($p<0.05$) increase in total amount of essential amino acids (TAEAA), total amount of non-essential amino acids (TANEAA) and total amount of amino acids (TAAA) in blood serum and the concentration of individual essential and non-essential amino acids (significantly reached the level of indicators in healthy individuals) and clinical course of tuberculosis (intoxication syndrome disappeared earlier by 10.8 ± 0.97 days, and respiratory one by 8.95 ± 1.68 days), there was an increase in the frequency of healing of decay cavities at the time of completion of treatment by 34.0% and a significant ($p<0.05$) reduction in the average duration of treatment by 21.1 ± 2.91 days.

Conclusions: The application of nutritional correction of protein metabolism in the complex treatment of patients with pulmonary tuberculosis made it possible to obtain a pronounced positive impact on the clinical course of the disease and the condition of protein metabolism, which contributed to an increase in the effectiveness of treatment and rehabilitation.

KEY WORDS: amino acid composition of blood serum, nutrients, complex treatment of tuberculosis

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INTRODUCTION

Ukraine is in second place in the European region by the incidence rate of tuberculosis (TB), about 65.0% of new cases of the disease occur in vulnerable and marginalized groups of the population. The high prevalence of TB is due to the presence of a number of challenges that have negatively affected the health of the population. Most of the population is on the verge of poverty, does not have the opportunity to eat a rationally and balanced, accordingly, does not receive the needfull amount of proteins, the structural elements of which are amino acids [1-3]. TB leads to significant disorders of tissue metabolism, there was a tendency to reduce the overall concentration level of amino acids in the acute phase of the tuberculosis process, not only due to essential amino acids, but also non-essential ones, which was explained by insufficient synthesis and overuse of them for the energy and plastic needs of the body [4-6]. Intensive AMBT, which acts directly on the causative agent of the disease, remains the main and obligatory component of the modern approach to the treatment of this pathology. Pathogenetic therapy in TB patients is aimed at correcting metabolic processes and dysfunctions of various organs and systems, at normalizing existing metabolic disorders [7-9].

Imbalance in the diet of TB patients before the onset of the disease leads to a deficiency of the most biologically active nutrients, which contributes to the development of the pathological process and creates the basis for a complicated course of the disease [10-12]. Today, there are no modern dietary guidelines, available and understandable recommendations for the nutrition of TB patients, which can be used throughout all phases of treatment and will meet the physiological needs of patients and offer a list of food products, containing biologically active compounds which, in turn, have a positive impact on reducing inflammation, normalizing metabolic disorders caused by inflammation and long-term AMBT, on the activation of reparative mechanisms, the correction of psycho-emotional status.

THE AIM

Study of the impact of nutritional correction of protein metabolism disorders (NCPMD) on the clinical course of pulmonary tuberculosis.

MATERIALS AND METHODS

The studies were conducted in accordance with the principles of bioethics in compliance with the WHO regulations, World Medical Association Declaration of Helsinki. The study protocol was approved by the Bioethics commission of the Bogomolets National Medical University. Informed consent was obtained from all study participants. The study involved 67 patients with newly diagnosed pulmonary tuberculosis. Among them there were 53 men (79.1%), 14 women (20.9%). The average age of patients is 38.4±1.8 years. All patients were divided into two groups: group I – 35 patients who underwent NCPMD on the background of AMBT and Group II – 32 patients receiving standard AMBT, no statistically significant difference between groups by sex and age ($p > 0.05$). Within 5 days after hospitalization a multipurpose evaluation was conducted in accordance with diagnostic examination plan, required for persons with pulmonary pathology. The criteria for exclusion from the study were diseases of the gastrointestinal tract, hepatobiliary disease, diabetes mellitus, HIV infection, viral hepatitis, under 18 years of age.

Before the start of treatment, 32 (91.4%) persons of group I and 29 (90.6%) ones of group II had intoxication syndrome (IS). Respiratory syndrome (RS) was detected in 31 (88.6%) patients of group I and 29 (90.6%) patients of group II. Weight loss was determined in 21 (70.0%) patients of group I and 26 (70.2%) patients of group II. In 23 (76.7%) patients of group I and 29 (78.4%) ones of group II, the tuberculous process occupied more than three lungs segments, decay cavities were present in 24 (80.0%) patients of group I and 23 (82.1%) ones of group II. Bacterial excretion was present in 29 (82.9%) patients of group I and in 27 (84.4%) patients of group II. It should be noted that patients with massive bacterial excretion prevailed in both groups: in 16 (45.7%) patients of group I and in 15 (46.9%) patients of group II.

For study the condition of protein metabolism (BU) the concentration of individual non-essential amino acids (NEAA) (ornithine, aspartic acid, serine, glutamic acid, proline, glycine, alanine, cysteine, tyrosine, and glutamine), essential amino acids (EAA) (lysine, histidine, arginine, threonine, valine, methionine, isoleucine, phenylalanine, and leucine) and their total amount (TAAA) (mg per 100 ml of blood serum) were determined. The studies were carried out on an empty stomach. The material was venous blood; precipitation of protein samples was carried out by the method of deproteinization of samples with sulfosalicylic acid. The studies were carried out on an automatic analyzer of amino acids AAA-339-T, by the method of ion-exchange column chromatography on the basis of the laboratory of technology of biological products (chromatography group) of O. V. Palladin Institute of Biochemistry.

Before to the start of treatment, patients of both groups had PM disorders, manifested by a decrease in the total amount of essential amino acids (TAEAA) by 1.2 times (group I up to 8.5 ±0.5 mg and group II up to 8.8 ±0.4 mg per 100 ml of blood serum) compared with the control group (10.9 ±0.7 mg per 100 ml of blood serum). Also, in patients of both groups, the level of the total amount of non-essential amino acids (TANEAA) was reduced by 1.2 times (group I to 15.9±0.4 mg and group II to 15.9±0.4 mg per 100 ml of blood serum) compared with the control group (19.7±0.9 mg per 100 ml of blood serum). Which led to a decrease in TAAA in patients of both groups by 1.2 times (group I to 24.4±0.5 mg and group II to 24.7±0.8 mg in 100 ml of blood serum) compared with the control group (30.6±2.4 mg in 100 ml of blood serum). The control group consisted of 30 healthy individuals aged 18 to 55 years, men – 16 (53.0%), women – 14 (47.0%).

Etiotropic AMBT in both groups was performed according to current guidelines. The treatment regimen in the intensive phase included the use of isoniazid, rifampicin, pyrazinamide, ethambutol for 2 months (60 doses). The drugs in all studied groups of patients were administered once in a daily dose under the supervision of medical personnel in accordance with the prescribed treatment regimen.

An individual approach was used in the design of the diet and differentiation was carried out taking into account the phase of development of the tuberculosis process and the general condition of the body, NCPMD was produced by enriching the diets of patients with the appropriate products listed in Table I.

Statistical data analysis was performed using Statistica 10.0 and Microsoft Excel. Data are given as arithmetic mean ± standard deviation (M±SD) with normal distribution of variables. The significance of the difference in indicators was calculated by Student's t-test with a normal distribution of values. The results of comparisons were considered reliable if the error probability was less than $p<0.05$.

RESULTS

At the end of the intensive phase of treatment it was found the disappearance of IS during the first month of treatment was observed in 26 (81.3%) patients of group I and only in 17 (58.6%) patients of group II. At 2 months of treatment, IS disappeared in 5 (15.6%) patients of group I and in 7 (24.1%) patients of group II. Sustained normalization of body temperature, improvement in appetite, the disappearance of night sweats was observed on average after 19.75±3.2 days in patients of I group and 30.55±4.1 days in patients of group II after the start of treatment ($p<0.05$). After 1 month of treatment, disappearance of RS was observed in 17 (54.8%) patients of group I and only in 12 (41.4%) patients of group II, at 2 months of treatment RS disappeared in 11 (35.5%) patients of group I and in 11 (37.9%) patients of group II. The cessation of coughing, a significant decrease in shortness of breath from the start of treatment in patients of group I was observed on aver-

Table I. Pathogenetic nutritional correction of the diet for patients with newly diagnosed pulmonary tuberculosis

№	Links of pathogenesis	Biologically active compounds	Products nutrition
1	2	3	4
1.	Reduction of inflammation		
	- activation of immunometabolic processes	Protein	Sour-milk, dairy products, meat, eggs
	- decreased expression of anti-inflammatory cytokines, increased activity of phagocytes	Vitamin D	Sea fish, eggs
	- protection of mucous membranes from bacteria, activation of cellular antibacterial immunity	Secretory immunoglobulin A Lactobacillus acidophilus	Dairy products – prebiotics. Acidophilus
	- interleukin synthesis	PUFAs W-3	Sea fish, walnuts
	- tissue antioxidant protection	Vitamins and provitamins	
		Ascorbic acid	Citrus fruits, cabbage, green onions, parsley, dill, currants, horseradish, wild rose
		α-Tocopherol	Unrefined vegetable oils, nuts, legumes
		Retinol	Beef liver, whole milk, eggs
		Alpha-, beta-, gamma-carotenes	Carrots, pumpkin, persimmon, oranges
		Trace elements	
		Selenium	Garlic, seafood
		Copper	Fish, marine aquatic organisms
		Magnesium	Groats, almonds
		Zinc	Meat, pumpkin seeds
		Cobalt	Meat, seafood
		Manganese	Cereals
		Plant antioxidants	
		Ubiquinone	Pistachios, sesame
		Anthocyanins	Red grapes, cranberries, blueberries, red cabbage
		Catechins	Green and black tea, blueberry, sea buckthorn
		Coumarins	Cinnamon, mint, green tea, blueberries
		Chlorophils	Green parts of plants, garden greens
		Polyphenols	Green tea, red grapes, onions, apples, strawberries, raspberries
	- antiseptic action	Bioflavonoids, quercetin, rutin	Plums, cherries, blueberries, apples, apricots, red peppers, green tea
		Salicylates Ascorbic acid	Cherry, raspberry Citrus fruits, cabbage, green onions, parsley, dill, currants, horseradish, wild rose
		Malic acid Cinnamic acid Phytoncides	Apples, dogwood Cinnamon Onion, garlic, horseradish, currant, citrus
		Terpenes Hydroquinone	Dill, coriander, mint, cumin Lingonberry, pear, wild strawberry, cranberry, blueberry
		Benzoic acid Benzaldehyde Eugenol	Cranberry, lingonberry Elderberry, almond Clove, basil
	- anti-inflammatory, desensitizing effect	Calcium	Sour-milk, dairy products
	- specific bacteriostatic action	Essential oils	Thyme, mint, cloves
2.	Normalization of metabolic disorders caused by inflammation and long-term chemotherapy		
	- increase in appetite	Choleretic effect	Cherries, apples, cabbage, onions, parsley, celery, dried fruits, chicory, mint, wild rose
	- enzyme inducers	Synthesis of liver benzpyrene hydroxylase, intestinal and liver monooxygenases	White cabbage, Brussels sprouts, cauliflower, spinach
	- prevention of the negative impact of specific therapy	B vitamins	Beef liver, poultry, fish, whole grain bread, wheat bran
3.	Completion of inflammation, activation of reparative mechanisms		
	- acceleration of epithelization	Vitamin A	Beef liver, whole milk, eggs
		Calcium	Dairy products
	- rebuilding the gut microbiota ecosystem	Vitamins B1, B2, B6, B12, PP	Natural yogurt
4	Correction of psycho-emotional status		
		Vegetative phyto- regulators	Lemons, oranges, vanilla, cinnamon, bananas
		Probiotics	Natural yogurt

Table II. Indicators of the concentration of essential amino acids in blood serum in patients of groups I and II in the dynamics and in the control group (x ± SD)

Amino acid (mg in 100 ml of blood serum)	Control group (healthy individuals) n= 30	Group I (n= 35)	Group 2 (n= 32)
Lysine	2,2±0,2	2,1±0,022	1,7±0,1
Histidine	1,1±0,1	1,0±0,022	0,8±0,11,2
Arginine	1,2±0,1	1,1±0,022	1,0±0,031,2
Threonine	1,2±0,1	1,2±0,12	1,0±0,031,2
Valine	1,9 ±0,2	1,9 ±0,03	1,9±0,1
Methionine	0,4±0,04	0,3±0,02	0,3±0,021
Isoleucine	0,7±0,1	0,7±0,03	0,7±0,04
Phenylalanine	0,7±0,04	0,7±0,022	0,6±0,031
Leucine	1,2±0,1	1,2±0,1	1,2±0,07
The total amount of essential amino acids	10,9±0,7	10,1±0,12	9,1±0,21,2

Note. 1 - p<0,05 when comparing with indicators of healthy individuals;
2 - p<0,05 when comparing I and II groups of patients

Table III. The concentration of non-essential amino acids in blood serum in patients of groups I and II in dynamics and in the control group (x ± SD)

Amino acid (mg in 100 ml of blood serum)	Control group (healthy individuals) n= 30	Group I (n= 35)	Group 2 (n= 32)
Ornithine	0,7±0,1	0,7±0,02	0,7±0,02
Aspartic acid	0,1±0,01	0,1±0,01	0,1±0,01
Serine	0,9±0,1	1,1±0,052	0,9±0,01
Glutamic acid	0,7±0,1	0,8±0,022	0,5±0,021,2
Proline	1,8 ±0,2	1,7 ±0,02	1,7±0,1
Glycine	1,5±0,1	1,6±0,12	1,3±0,04
Alanine	3,3±0,3	3,1±0,3	3,0±0,1
Cysteine	0,8±0,1	0,8±0,1	0,8±0,1
Tyrosine	1,5±0,1	1,5±0,03	1,5±0,1
Glutamine	8,5±0,8	8,3±0,052	7,6±0,1
The total amount of non-essential amino acids	19,7±0,9	19,8±0,12	18,1±0,2

Note. 1 - p<0,05 when comparing with indicators of healthy individuals;
2 - p<0,05 when comparing I and II groups of patients

age after 37.24±5.12 days and in group II after 46.19±3.44 days. Indicators of the termination of bacterial excretion did not differ statistically in both studied groups (group I – 17 (58.6%) patients, group II – 14 (51.9%) ones). The frequency of healing of decay cavities in both study groups differed from each other, in favor of group I – 10 (31.25%) patients versus 4 (13.3%) ones.

After 2 months of treatment assay of the dynamics of PM indicators showed that patients of group I have a significantly (p <0.05) higher concentration of individual EAA and, accordingly, a higher concentration level of TAEAA compared to indicators in group II. Significantly (p <0.05) higher concentration of such EAA as: lysine, histidine, arginine, threonine in patients of group I compared with the corresponding indicators in group II. And also, significantly (p <0.05) higher TAEAA in patients of group I (10.1±0.1 mg compared with the corresponding indicator in group II 9.1±0.2 mg in 100 ml of blood serum) and it is significantly did not differ from that in the control group (Table II).

At the same time, in patients of group II, there is a significantly lower concentration of such amino acids as histidine (1.4 times), arginine (1.2 times), threonine (1.2 times), methionine (1.3 times), phenylalanine (1.2 times) compared with the corresponding indicators in the control group. Therefore, a decrease in the concentration of individual EAA led to a significant (p<0.05) decrease (1.2 times) in TAEAA compared with the corresponding indicator in the control group 10.9±0.68 mg per 100 ml of blood serum.

Analyzing the concentration of individual NEAA and their total amount in patients of groups I and II in dynamics and in the control group after 2 months of treatment, it should be noted that in patients of group I, compared with the corresponding indicators in group II, there is a signifi-

cantly ($p<0.05$) higher the concentration of such NEAA as: serine, glutamic acid, glycine, glutamine, and TANEAA was 19.8±0.10 mg, which is significantly ($p<0.05$) higher compared to the corresponding indicator of 18.1±0.20 mg in 100 ml of blood serum in patients of group II (Table III).

This indicates that in patients of group I there was a normalization of the indicators of the concentration of NEAA, and they did not significantly differ from those in the control group. At the same time, in patients of group II, there is an unreliable, but significantly lower concentration of some NEAA and, accordingly, lower TANEAA 18.1±0.20 mg per 100 ml compared to the corresponding indicator in the control group 19.7±0.90 mg per 100 ml blood serum. In patients of group I, there is a significantly ($p<0.05$) higher concentration level of TAAA 29.9±0.20 mg compared with the corresponding indicators in group II 27.2±0.50 mg per 100 ml of blood serum and it does not significantly differ from indicator in the control group.

DISCUSSION

The changes in the amino acid spectrum of blood serum in patients with TB before the start of treatment that we have identified represent PM disorders in general and can be considered an integral consequence of various causes. They have a negative impact on the metabolic processes of the body in totaly and the clinical course of TB, which is manifested by prolonged IS and RS, the possible development of complications, and a lengthening of the rehabilitation period. Our hypothesis that the use of AMBT alone will not be enough for the full normalization of PM indicators (achieving the indicators of healthy individuals) have been confirmed, this is indicated by an amino acid imbalance, a decrease in TAAA and individual NEAA and EAA in blood serum [8,9]. The obtained data allowed us to determine the priority clinical indicators for the inclusion of NCPMD in the complex treatment of patients with TB: – the presence of risk factors in the patient (socially vulnerable patients, the unemployed, retired employees, homeless people, released from prison); – long-term development of the disease, accompanied by prolonged IS and RS, which contributed to the emaciation of the body and the development of metabolic disorders; – loss of body weight; – lesion of large parts of lung tissue by the pathological process accompanied by its decay; – bacterial excretion; – signs of protein metabolism disorders[8,9,13,14]. The proposed correction scheme includes food products containing essential nutrients and biologically active compounds that have a positive impact on the corresponding links of pathogenesis (reduction of inflammation, normalization of metabolic disorders caused by inflammation and long-term AMBT, activation of reparative mechanisms, correction of psycho-emotional status) and can be used throughout all phases of treatment. Which had a positive impact on the PM indicators (significant ($p<0.05$) increase in blood serum TAEAA, TANEAA and TAAA blood serum and the concentration of individual EAA and NEAA (significantly reached the level of indicators in healthy individuals) and the clinical course of TB. There was a positive trend in the disappearance of IS (disappeared faster by 10.8±0.97 days) and RS (disappeared faster by 8.95±1.68 days), an increase in the frequency of healing of decay cavities at the time of completion of treatment by 34.0% and a significant reduction in the average duration of treatment by 21.1±2.91 days in these patients ($p<0.05$). Further studies to improve the NCPD scheme in the complex treatment of patients with TB are promising, since the method can provide a significant additional therapeutic and preventive potential without drug overload of patients, promote the level of social rehabilitation of TB patients.

CONCLUSIONS

The inclusion of nutritional correction of protein metabolism disorders in the standard regimen of treatment with antimycobacterial drugs made it possible to obtain a pronounced positive impact on the clinical course of the disease and the condition of protein metabolism, which contributed to an increase in the effectiveness of treatment and rehabilitation of patients with pulmonary tuberculosis.

Conflicts of Interest: authors have no conflict of interest to declare.

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ORIGINAL ARTICLE

FEATURES OF CEREBRAL HEMODYNAMICS IN PATIENTS AFTER STROKE DEPENDING ON THE VARIABILITY OF BLOOD PRESSURE AND THEIR QUALITY OF LIFE

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ABSTRACT

The aim: To study cerebral hemodynamics in patients after ischemic stroke (IS) depending on the variability of blood pressure (BP) and to assess the quality of life (QOL).

Materials and methods: The study included 90 patients of SIS «RSCPC» SAD aged 33 to 72 years: The 1st (main) group consisted of 30 patients with ischemic stroke (IS) on the background of hypertension (HTN) with mild neurological deficits; 2nd – 30 patients who have been suffering from HTN for more than 10 years and have manifestations of dyscirculatory encephalopathy of I-II stage.; 3rd group – 30 patients who did not suffer from HTN.

Results: Variability of blood pressure in patients with ischemic stroke with mild neurological deficits on the background of hypertension (hypertension) did not differ significantly from that in patients with hypertension with more than 10 years of experience, but their cerebral blood flow rate was significantly lower. Neurological functions, cognitive and psycho-emotional statuses and, as a consequence, quality of life were also significantly worse in patients after stroke.

Conclusions: cerebral disorders and quality of life in patients after stroke are associated with decreased cerebral blood flow, regardless of the variability of blood pressure.

KEY WORDS: hypertension, stroke, blood pressure variability, cerebral circulation, quality of life

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INTRODUCTION

Arterial hypertension (HTN) is one of the leading factors in the deterioration of quality and life expectancy worldwide. According to the World Health Organization (2013), the number of people with hypertension in the world is> 1 billion. The dynamics of statistical indicators of health of the population of Ukraine indicates an uncontrollable increase in the prevalence of hypertension. According to the Center for Medical Statistics of the Ministry of Health, there are> 12 million patients with hypertension in Ukraine, which is about ⅓ adult population (30 and 36% in urban and rural areas, respectively) (Ministry of Health of Ukraine, 2012).

Hypertension is considered to be the most common risk factor for stroke, and the risk of stroke is directly related to high blood pressure, both systolic and diastolic [1]. A systematic analysis of stroke factors in 188 countries between 1990 and 2013 identified high systolic blood pressure (SBP) as the main (64.1% of cases) of the five leading modified factors affecting stroke [2].

Blood pressure variability (BPV) and heart rate variability negatively affect the course of both hypertension and the severity of its complications, namely cerebrovascular [3].

It was found that spontaneous fluctuations in blood pressure during the day play an important role in the development of endothelial dysfunction and atherosclerosis, which was demonstrated in experimental models. Accurate analysis of blood pressure variability during the day is of undeniable pathophysiological importance for understanding the mechanisms involved in homeostatic control of blood pressure in healthy individuals and in diseases such as essential and secondary hypertension, congestive heart failure, diabetes and chronic kidney disease. This indicator allows us to judge the damage to target organs due to high blood pressure and the progression of changes over time. An independent association between high blood pressure variability and clinical outcomes has also been found in epidemiological studies [4].

All these indicators of variability are calculated by the value of the standard deviation (SD) from the corresponding blood pressure measurements. More sophisticated methods of analysis are also used, which include the calculation of the coefficient of variation (ratio between SD and mean blood pressure) and the calculation of «true mean blood pressure variability» (ARV24), which is perhaps the most accurate way. This index averages the absolute difference in blood pressure levels between successive measurements and thus takes into account the sequence in which the measurements were performed. The use of these techniques allows to exclude from the analysis of the stratification of the circadian rhythm and to make more accurate the calculation of the variability of blood pressure. As standards of variability, the criteria are the value of systolic blood

pressure (SBP) – 15/15 mm Hg. Art. (day/night), diastolic blood pressure (BP) – 14/12 mm Hg. Art. (day/night). The patient is assigned to a group with high variability in case of exceeding at least one of the four critical values [5].

The variability of clinical BP, or intervisional variability, is largely due to the complex interaction of different regulatory mechanisms and the body's need to respond to «challenges» of the environment. This is a multicomponent phenomenon that depends on human activity, psychological factors, response to antihypertensive therapy and the state of the nervous and humoral systems. Determinants of BP variability have been studied in several population studies: most often they include age, blood pressure, heart rate (HR), sex and changes in regulation of the central and peripheral nervous system [6]. Humoral mechanisms in the occurrence of blood pressure fluctuations also have an impact, first of all such humoral factors as angiotensin, endothelin, nitric oxide, bradykinins, insulin, etc. The association between BP variability and sympathetic activity is discussed. At the same time, target organ damage, arterial rigidity, autonomic nervous system dysfunction and impaired baroreflex activity are predictors of cardiovascular complications and may be the cause of increased BP variability. Therefore, it is believed that this indicator is a marker of existing pathology, rather than an independent predictor of cardiovascular complications [7].

Recently, however, there is growing evidence of inter-visit variability in BP as an independent prognostic factor for cardiovascular risk. The ASCOT study is the first major study to show that inter-visit variability in BP was a stronger predictor of both stroke and coronary events than mean BP. The prognostic significance of SBP inter-visit variability did not depend on heart rate and was not related to the white coat phenomenon [8].

A study by Muntner P. showed that high intervisional variability in blood pressure increases the risk of death during 14 years of follow-up [9]. In the Honolulu Heart Program, SBP intervisit variability was associated with an increased risk of coronary events even after eliminating factors that could influence these outcomes [10]. In addition, inter-visit variability in BP is an independent determinant of the development of cognitive impairment in elderly patients at high risk of cardiovascular complications, as demonstrated in a study by Nagai M. et al., which involved 201 elderly patients at high risk of cardiovascular disease. vascular diseases. In a study by Muntner R. et al. pulse pressure and old age were independently associated with high interbusiness variability of SBP [10]. Lee N. T. et al. conducted studies to identify the relationship between arterial stiffness index and BP variability in patients with hypertension using DBPM. It is established that the variability of blood pressure is an independent factor in increasing the index of arterial rigidity [6]. There was a statistically significant inverse relationship between the risk of cardiovascular and total death and fluctuations in blood pressure during the day and night. It is shown that the prognostic possibilities of BP variability are much higher compared to the ratio of day and night blood pressure and the average daily value of diastolic blood pressure.

Hypertension (HTN) is one of the most common and significant factors in the reduction of cerebral hemodynamic reserve, which is determined by the possibility of autoregulation of cerebral circulation in pathological conditions. Normally, a stable blood supply to the brain is maintained in a wide range of changes in the parameters of central hemodynamics and provides adaptation to adverse living conditions. Physiological (aging processes) and pathological processes significantly reduce cerebral hemodynamic reserve. First of all, this is reflected in the parameters of systemic blood pressure (BP), within which the stability of the blood supply to the brain is maintained. If normal autoregulation persists within a wide range of changes in systemic systolic blood pressure from 80 to 180 mm hg. art., then in a patient with hypertension, cerebral atherosclerosis and hypertensive angiopathy, the direct dependence of cerebral blood flow on blood pressure occurs at 140-150 mm hg. art. [11]. Mechanisms of autoregulation of cerebral circulation compensate for elevated systemic blood pressure by narrowing of cerebral arteries – vasoconstriction. Decompensation (explosion of vasoconstrictor regulation) leads to passive stretching of arterioles, overflow of the capillary bed under high pressure, impaired microcirculation and small focal brain damage. Hemodynamic loads in the conditions of decompensation gradually form the structural transformation of extra- and intracranial arteries in the form of hypertrophy and hyperplasia of the muscular membrane, changes in the architecture of the vascular bed. Pathological tortuosity of blood vessels, hypertensive micro- and macroangiopathy – signs of structural adjustment of the vascular system, indicating a significant functional decrease in the compensatory capacity of the circulatory system. The basis of morphological and structural reorganization of the vascular bed are two main processes: proliferation (increase in cell mass due to increasing their number) and hypertrophy (increase in cell mass without increasing their number). Critical narrowing of the main arteries creates conditions for circulatory failure in the vascular pool, which can not always be compensated by collateral circulation.

In patients with hypertension, cerebral blood flow is reduced, and a chronic increase in blood pressure leads to cerebral vasospasm and decreased brain perfusion [12]. Maintenance of cerebral blood flow is possible at the proper level only due to compensatory vasodilation of vessels of the microcirculatory tract of the deep parts of the brain.

THE AIM

To study the cerebral circulation in patients after ischemic stroke (II) depending on the variability of blood pressure and to assess the quality of life of the studied group of patients.

MATERIALS AND METHODS

The study included 90 patients of SIS «RSCPC» SAD aged 33 to 72 years: 1st (main) group consisted of 30 patients

Table I. Anthropometric data of the studied patients

Characteristic	Main group, n=30	Control group 1, n=30	Control group 2, n=30	The level of significance of differences between groups, p
Age, years	57,6±7,0*	57,5±7,5*	44,4±7,9	<0,001
Weight, kg	87,1±10,9*	84,3±13,9*	76,4±10,5	0,002
Height, m	173,2±7,6	171,1±7,7	170,4±7,4	0,26
BMI, kg/m2	29±2,9*	28,6±3,6*	26,2±2,6	0,001

Notes: ANOVA was used for comparisons between groups and Sheffe's criterion was used for posterior comparisons (in case of normal distribution law); the Kruskal – Wallis criterion and the Dunn test was used to make posterior comparisons (in the case of a distribution law different from the normal one).
* - the difference from group 3 is statistically significant.

Table II. Complaints of the studied patients

Complaints	Main group, n=30	Control group 1, n=30	Control group 2, n=30	The level of significance of differences between groups, p
Decreased attention and memory	22 (73,4%)*	16 (53,3%)*	0 (0%)#,&	<0,001
Headache (recurrent)	18 (60,0%)*	14 (46,7%)	5 (16,7%)#	0,002
Periodic dizziness	16 (53,3%)*	17 (56,7%)*	0 (0%)#,&	<0,001
Periodic nausea	15 (50,0%)*	12 (40,0%)*	0 (0%)#,&	<0,001
Sleep disorders	22 (73,4%)*	14 (46,7%)*	3 (10,0%)#,&	<0,001
Coordinator violations	18 (60,0%)*,&	2 (9,1%)#	0 (0%)#	<0,001
Weakness in the extremities (mono, or hemiparesis)	9 (30,0%)*,&	0 (0%)#	0 (0%)#	<0,001
Reduced efficiency	24 (80,0%)*	17 (56,7%)*	0 (0%)#,&	<0,001
Rapid fatigue	25 (83,3%)*	19 (63,3%)*	3 (10,0%)#,&	<0,001

Notes: The chi-square test was used for comparisons between groups and the Bonferroni correction was used for posterior comparisons.
- difference from the main group is statistically significant;
& - difference from control group 1 is statistically significant;
* - the difference from control group 2 is statistically significant.

(civil servants) who suffered an ischemic stroke (II) on the background of hypertension (HTN) with lung neurological deficits and returned to work; 2nd – 30 patients (civil servants) who have been suffering from HTN for more than 10 years and have manifestations of dyscirculatory encephalopathy I-II; 3rd group – 30 patients (civil servants) who did not suffer from HTN and sought medical help only in acute cases, without chronic diseases. The average age of patients was 57.6±7.0 years in the main group, .57.5 ± 7.5 years in the first control group, 44.4 ± 7.9 years in the second control group. All patients in the main group had MRI-verified ischemic stroke with mild neurological deficits (NIHSS scale 7.2 ± 2.5 points). All patients of the main and control groups received antihypertensive and antiplatelet therapy.

Research methods used: clinical (clinical and neurological examination of the patient, stroke severity assessment: National Institutes of Health Stroke Scale – NIHSS, neuropsychological testing – short scale of mental status assessment Mini Mental Stale Examination – MMSE, anxiety and depression scale DASS-21), inter-visit measurement of blood pressure, instrumental – ultrasound of the vessels of the head and neck), medical and statistical. Statistical analysis of the results was performed in the statistical package IBM SPSS Statistics Base v.22, as well as using the statistical environment EZR v.1.35 (R statistical software version 3.4.3, R Foundation for Statistical Computing, Vienna, Austria).

To represent quantitative characteristics, the mean and standard deviation of the indicator were calculated, for comparison between groups we used analysis of variance in the case of normal distribution law or Kruskal-Wallis test in case of distribution law different from normal. Their frequency (%) was calculated to represent qualitative features, the chi – square criterion was used for comparison, and the Bonferroni correction was used for pairwise comparison for three or more groups.

Correlation analysis was used to identify the relationship between quantitative indicators, and Spearman's rank correlation index was calculated. In the analysis in all cases, the critical level of significance is assumed to be 0.05.

Measurements of inter-visit office blood pressure were performed with a conventional mechanical tonometer between 08.00 and 11.00 hours before taking antihypertensive drugs three times. The average values of SBP and DBP were taken into account.

Table III. BPV level, indicators of cognitive and psycho-emotional status.

Characteristics	±SD			The level of significance of differences between groups, p
	Main group, n=30	Control group 1, n=30	Control group 2, n=30	
SBP, mm Hg	11,7±2,9*	10,8±3,3*	7±2,1	<0,001
SBP, mm Hg	6,4±2,5*	5,6±2,1	4,6±1,5	0,004
anxiety, points	11±3,6*	9,4±3,9	7,1±2,3	<0,001
depression, scores	14±5,8*	10,8±4,2*	7,8±2,4	<0,001
MMSE, points	27,2±1,2*	27,7±1,3*	28,1±4,6	<0,001

Notes: ANOVA was used for comparisons between groups and Sheffe's criterion was used for posterior comparisons (in case of normal distribution law); the Kruskal – Wallis criterion and the Dunn test was used to make posterior comparisons (in the case of a distribution law different from the normal one).
* - the difference from group 3 is statistically significant.

Table IV. Indicators of linear blood flow velocity in extra- and intracranial arteries in the studied groups (The table presents Me (QI-QIII))

Indicator	Main group, n=30	Control group 1, n=30	Control group 2, n=30	p
Vps_CCAd	82 (67 – 89)2,3	90.5 (82 – 116)1	100 (80 – 117) 1	0.001
VpsCCA_s	81 (73 – 98)3	90.5 (78 – 102)	105 (83 – 130) 1	0.006
VpsVAd	43 (34 – 47)	47 (36 – 54)	47 (43 – 54)	0.189
VpsVAs	44 (40 – 48) 3	43 (36 – 55)	49 (44 – 56) 1	0.034
Vps_MCAd	101 (88 – 123)3	117.5 (89 – 136)	123.5 (103– 142)1	0.049
VpsMCAs	100 (89 – 115)3	114 (92 – 131)	124 (112 – 142) 1	<0.001
Vps_V4d	56.5 (47 – 73)	55 (52 – 66)	64 (53 – 75)	0.571
VpsV4s	54 (45 – 62)	55 (44 – 64)	62.5 (51 – 79)	0.060
VpsBA	53.5 (45 – 65)3	62 (55 – 67)	68.5 (55 – 88) 1	0.001
Ved_CCAd	24 (22 – 27)	25 (22 – 29)	27 (20 – 34)	0.600
VedCCA_s	23.5 (17 – 33)	23 (20 – 27)	24 (22 – 30)	0.621
VedVAd	14 (12 – 20)	16 (13 – 19)	15 (11 – 22)	0.475
VedVAs	14 (12 – 18)3	16.5 (13 – 21)	20 (14 – 23) 1	0.009
Ved_MCAd	41 (29 – 55)	42.5 (33 – 53)	54 (39 – 64)	0.173
VedMCAs	43.5 (33 – 48)	43.5 (34 – 53)	43 (41 – 59)	0.286
Ved_V4d	32 (23 – 34)	24 (19 – 29)	24.5 (22 – 33)	0.101
VedV4s	22 (15 – 30)3	21.5 (16 – 26)3	27.5 (23 – 34) 1,2	0.004
VedBA	26.5 (20 – 35)	23 (21 – 34)	27 (24 – 37)	0.125
KIM_CCAd	1.05 (1 – 1.2) 2,3	0.9 (0.9 – 1) 1,3	0.8 (0.7 – 0.8) 1,2	<0.001
KIM_CCAs	1.1 (1 – 1.1) 2,3	0.9 (0.9 – 1) 1,3	0.8 (0.7 – 0.9) 1,2	<0.001

Notes: Kruskal-Wallis criterion was used in the comparison, posterior comparisons were made according to Dunn's criterion:
1 - the difference from group 1 is statistically significant, p <0.05;
2 - difference from group 2 statistically significant, p <0.05;
3 - the difference from group 3 is statistically significant, p <0.05.

RESULTS

Analysis of the study data showed that in the main group there were 12 (40%) women and 18 (60%) men, in group 2 there were 10 (33.3%) women and 20 (66.7%) men, in group 3 were 17 (56.7%) women and 13 (43.3%) men, no differences were found between groups in the distribution by sex (p = 0.17 by the chi-square criterion). Assessing the subjective complaints of patients who participated in the study, it was found that in the main group of patients the number and severity of complaints were significantly more pronounced than in patients of control groups I and II in all options.

The study found that in patients who suffered an ischemic stroke with mild neurological deficits and returned to work, and in patients who had manifestations of dicirculatory encephalopathy on the background of HTN II, the inter-visit BPV did not differ significantly.

Characteristics of the groups are presented in table I.

The values of BPV indicators, the severity of anxiety and depression, the level of cognitive status are presented in Table III.

BPV level, indicators of cognitive and psycho-emotional status.

Table V. The average assessment of quality of life after in the study groups on the SF-36 scale

Indicator	Main group, n=30	Control group 1, n=30	Control group 2, n=30	p
PFsum	50[2,3] (25 – 60)	80[1] (65 – 85)	72.5[1] (50 – 85)	<0.001
PF_Z	-1.508 [2,3] (-2.600 – -1.071)	-0.198[1] (-0.853 – 0.0208)	-0.525 [1] (-1.508 – 0.0208)	<0.001
RPsum	0 [2,3] (0 – 25)	50 [1] (25 – 100)	50 [1] (25 – 75)	<0.001
RP_Z	-2.403 [2,3] (-2.403 – -1.663)	-0.923[1] (-1.663 – 0.556)	-0.923[1] (-1.663 – -0.183)	<0.001
BPsum	52 [2] (41 – 62)	62[1] (62 – 100)	62 (52 – 84)	0.008
BP_Z	-0.997 [2] (-1.464 – -0.573)	-0.573 [1] (-0.573 – 1.040)	-0.573 (-0.997 – 0.361)	0.008
GHsum	37.5 [2,3] (35 – 45)	51 [1] (40 – 57)	45[1] (40 – 55)	<0.001
GH_Z	-1.721 [2,3] (-1.845 – -1.349)	-1.052 [1] (-1.597 – -0.754)	-1.349 [1] (-1.597 – -0.853)	<0.001
VTsum	32.5 [2,3] (25 – 35)	45 [1] (40 – 55)	40 [1] (35 – 50)	<0.001
VT_Z	-1.368 [2,3] (-1.728 – -1.248)	-0.769 [1] (-1.009 – -0.290)	-1.009 [1] (-1.248 – -0.530)	<0.001
SE	50 [2,3] (37.5 – 62.5)	75 [1] (62.5 – 87.5)	87.5 [1] (75 – 100)	<0.001
SE_Z	-1.501 [2,3] (-2.060 – -0.943)	-0.384 [1] (-0.943 – 0.174)	0.174 [1] (-0.384 – 0.733)	<0.001
REsum	0 [2,3] (0 – 33.333)	33.333 [1] (33.333 – 66.667)	66.667 [1] (33.333 – 66.667)	<0.001
RE_Z	-2.461 [2,3] (-2.461 – -1.452)	-1.452 [1] (-1.452 – -0.443)	-0.443 [1] (-1.452 – -0.443)	<0.001
MHsum	36 [2,3] (32 – 48)	56 [1] (44 – 64)	52 [1] (44 – 60)	<0.001
MH_Z	-2.156 [2,3] (-2.379 – -1.490)	-1.046 [1] (-1.712 – -0.602)	-1.268 [1] (-1.712 – -0.824)	<0.001
PHsum	-0.435 [2,3] (-0.835 – 0.0380)	0.230 [1] (-0.0265 – 0.644)	0.0611 [1] (-0.425 – 0.622)	<0.001
PH	45.647 [2,3] (41.653 – 50.380)	52.300 [1] (49.735 – 56.438)	50.611 [1] (45.748 – 56.220)	<0.001
MHsum	-1.943 [2,3] (-2.277 – -1.404)	-1.113 [1] (-1.817 – -0.468)	-0.907 [1] (-1.283 – -0.465)	<0.001
MHPH	30.573 [2,3] (27.235 – 35.963)	38.872 [1] (31.833 – 45.320)	40.926 [1] (37.173 – 45.352)	<0.001

Notes: Kruskal-Wallis criterion was used in the comparison, posterior comparisons were made according to Dunn's criterion:
[1] - the difference from group 1 is statistically significant, $p < 0.05$;
[2] - difference from group 2 statistically significant, $p < 0.05$;
[3] - the difference from group 3 is statistically significant, $p < 0.05$.

The state of cerebral hemodynamics was assessed using ultrasound duplex scanning of the intra- and ester of cranial vessels of the head and neck. This method allows you to visualize the vessel, its walls and surrounding tissues, blood flow in the vessel, its direction, speed, resistance.

A standardized SF-36 questionnaire was used to determine the quality of life of the patients included in the distribution described above. The standard questions grouped 8 scales: physical functioning (PF), role activity (RA), pain intensity (PI), general health (GH), vital activity (VA), social functioning (SF), emotional state (ES) and mental health (MH) (Table IV).

The patient (in our study, the answers were provided exclusively by patients themselves, without the involvement of guardians) chose the answer to the proposed question. Each answer was evaluated in points. When forming a

scale, these points are added and mathematically processed according to standard formulas. Indicators of each scale have values from 0 to 100, where 100 means complete health (Table V).

DISCUSSION

The analysis of anthropometric data revealed that patients of the main and first control groups were overweight (BMI> 25), while patients of the second control group (almost healthy) had a BMI slightly higher than the reference.

These results indicate the adequacy of rehabilitation measures in the treatment of patients after mild ischemic stroke and the effectiveness of basic antihypertensive, antiplatelet and neuroprotective therapy. At the same time, the severity of cognitive decline, and especially psycho-emotional disorders (levels of anxiety and depression within moderate limits) in patients of the first control group indicates the progression of cerebrovascular complications on the background of HTN. When comparing the above data from studies of patients with primary and first contr. groups with a group of relatively healthy patients (2 contr. gr.), inter-visit BPV (SBP, DBP) was significantly lower in the latter.

It should also be noted that the variability of DBP in the main group was significantly higher than in the control groups, which may be due to the severity of damage to target organs in HTN. The fact that in patients of the main and control groups of BPV is within acceptable limits, is explained by adequate antihypertensive therapy.

Indicators of comprehensive assessment of cognitive and psycho-emotional spheres were performed on the scales of neuropsychological testing – a short scale of assessment of mental status Mini Mental Stale Examination – MMSE, anxiety and depression scale DASS-21. Significant differences between groups were obtained.

In the main and first control groups there were more pronounced indicators of reduced cognitive and psycho-emotional spheres (anxiety and depression), almost equally, compared with the group of relatively healthy patients.

Cognitive deficits were determined by the Short Mental Status Scale (MMSE). Psycho-emotional status was determined by the DASS-21 anxiety and depression scale.

Correlation analysis was used to identify the relationship between blood pressure variability and anxiety, depression and MMSE.

For patients with Gr1, there was a moderate negative correlation of depression with SBP (Spearman correlation = -0.53 at p = 0.003).

For patients with contr.gr1, no association was found between pressure variability and anxiety, depression and MMSE (p> 0.05).

For patients contr.gr2 revealed a moderately positive positive correlation between depression and DBP (Spearman correlation index = +0.40 at p = 0.03).

When comparing the linear blood flow velocity in the extra- and intracranial arteries and the thickness of the intima-media in the main vessels in the studied groups of patients according to Doppler ultrasound, the results are given in table. 4. Significantly, the blood flow rate was slowed in patients after stroke in the left middle cerebral (LMC), right posterior cerebral (RPC) and basilar arteries (BA) compared with patients in the control groups.

Despite the fact that patients of groups I and II did not significantly differentiate between the indicators of inter-visit BPV, the quality of life of patients with stroke was lower than that of PF – physical functioning, SF – social functioning, MH – mental health, total indicators physical and psychological condition (PHsum (PH), MHsum (PH)).

CONCLUSIONS

Intervisional BPV in patients after stroke did not differ significantly from that in patients with DE II degree. on the background of HTN, but was significantly higher than the inter-visit BPV in patients without HTN (p <0,001, p = 0,004).

High BPV in patients with DE IIst. significantly impairs the cognitive and psycho-emotional functions of patients.

In the study of cerebral blood flow, a significant decrease in velocity in the vertebrobasilar and carotid basins was observed in the group of patients who suffered a stroke compared with the group of patients with hypertension and the group of patients without vascular pathology.

The quality of life of patients (civil servants) who suffered a stroke with or without a motor impairment and returned to work was significantly lower in terms of physical functioning, social functioning, mental health, total physical and psychological condition (PHsum).), MHsum (PH)) than in patients with dyscirculatory encephalopathy on the background of long-term hypertension (p <0.01) and patients without vascular pathology.

Given the impact of cerebral hemodynamics on neurological, cognitive and emotional functions and quality of life of patients, it is recommended to optimize drug and non-drug treatments for hypertension and its cerebrovascular complications that lead to normalization of cerebral blood flow. Adequate antihypertensive, antiplatelet, vascular and neuroprotective therapy in combination with physiotherapeutic and psychotherapeutic methods is meant.

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Research topic: Improving the prevention, treatment and rehabilitation of patients with hypertension and coronary heart disease with comorbid pathology in an outpatient setting (2014-2019, state № registration 0119U001045).

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ORIGINAL ARTICLE

IMPROVING CLINICAL MANAGEMENT OF PATIENTS WITH THYROID CANCER

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ABSTRACT

The aim: Obtaining evidence for an interdisciplinary approach to the clinical management of patients with thyroid cancer, identifying weak areas and justifying opportunities for improvement.

Materials and methods: Data from 410 medical records of inpatients with thyroid cancer and 17 units of formalized documents of the health care facility where the study was conducted. Methods: statistical, graphic, comparative analysis, descriptive modeling, generalization.

Results: Patients' need for interdisciplinary care were determined by cancer itself and by the presence of 234 cases of accompanying pathologies and complications in 147 (35.9%) patients. Interdisciplinary interaction is positioned as the provision of medical care by the medical staff of the unit where the patient stays and receives expert care. Treatment planning is carried out through the advisory participation of physicians of different specialties, rather than multidisciplinary consensus. Clinical management of the patient and discharge are carried out by the attending physician. Clinical pathways are designed for the department where the patient is hospitalized. Opportunities for pre- and postoperative rehabilitation are not used. Interaction with primary and secondary care facilities is limited.

Conclusions: The key directions of improving the clinical management of patients with thyroid cancer are identified: to improve the patient's clinical path, to strengthen interdisciplinary interaction of specialists through the use of digital technologies, to make clinical decision through the multidisciplinary consensus.

KEY WORDS: interdisciplinary approach, multidisciplinary team, clinical path, consensus, patient

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INTRODUCTION

The positive outcome for malignant neoplasms treatment depends on many factors: type, location, stage of the pathological process, comorbidities, and care organisation. The complexity of tasks facing health care and society in the fight against cancer conditioned developing interdisciplinary approach to their solution. It began to spread actively only in recent years, with the introduction of the principle of patient-centered care as a component of its quality. At present there is a global tendency in health care towards multidisciplinarity in place of advisory and board tools for clinical decision-making concerning cancer patients [1].

The correctness of choice in favour of multidisciplinary teams of professionals has already been proven, considering that a multidisciplinary team is a mobile functional unit for coordinating work and providing safe and effective care. However, activities organisation, participation in clinical decision-making, psychosocial support and lifelong management of a cancer patient differ significantly depending on a health care institution, and it requires further research [2, 3].

The relevance of the topic is growing considering the need for assessing the team functioning quality during the clinical support of the patient. This refers to the quality of communication among multidisciplinary team members in which clinical information is transmitted. Ineffective communication can lead to both negative consequences for the patient, reduced job satisfaction and increased turnover of medical staff [4, 5].

Of particular importance on this issue is the prospects of research on the development and implementation of standardization for cancer care using such a technology as clinical pathway, which is considered by researchers to be an important tool for supporting interdisciplinary processes [6]. The use of medical information systems and technologies by multidisciplinary teams remains insufficiently studied [7].

THE AIM

Obtaining evidence for an interdisciplinary approach in the clinical management of the patient with thyroid cancer in a highly specialized health care facility, identifying weak areas and justifying opportunities for further improvement.

MATERIALS AND METHODS

Materials were selected according to criteria that would ensure the achievement of research objectives. Primary data confirming management decisions to implement and maintain an interdisciplinary approach in the institution (orders, regulations, job descriptions, local medical proto-

Table I. Ways of Admission of Patients with Thyroid Cancer to the Hospital (2019)

Referral	Absolute number of patients	Percentage of total hospitalized (%)
By the general practitioner, family doctor	16	3,9
By the endocrinologist	183	44,6
By other specialists	-	-
Self-motivated medical care seeking	211	51,5
Total	410	100,0

cols, clinical pathways, a total of 17 units) were subjected to qualitative analysis followed by assessment of their compliance with modern world scientifically sound recommendations on the chosen topic.

Medical records data of thyroid cancer patients were used to determine the needs of patients for multidisciplinary care. In total, 410 inpatient medical records were subjected to medical and statistical analysis, that is 93.2% out of 440 operative interventions conducted in 2019 in the research site Municipal Non-Profit Enterprise "Kyiv City Clinical Endocrinology Center". Calculations of relative (percentage) and mean (M) values, standard deviation (σ), significance of differences (T-test at $p \leq 0.05$) were determined using licensed statistical software package Microsoft Office Excel 10. Conducted qualitative analysis of medical records showed using in real clinical practice technologies of interdisciplinary teams, which was further comlemented by comparison with world models of interdisciplinary management of cancer patients.

Possibilities of improving teamwork with the help of generalization and modeling methods are presented in the descriptive version; statistical data – graphically (in the form of tables).

Ethics commission Shupik National Healthcare University of Ukraine, Kyiv, Ukraine.

concluded the study complies with the current standards and principles of the "Code of Ethics of the Ukrainian Doctor", current regulations of Ukraine and the requirements of the Declaration of Helsinki (07.02.2022 protocol of Ethics commission No 2).

RESULTS

The need for multidisciplinary treatment is due to their state of health. Changes in health and pathological symptoms force patients to seek the advice of medical doctors of various specialties for the first time, which begins their clinical path. However, the data of the study materials showed that the majority of patients were admitted to the surgical hospital without any contribution of primary or secondary care specialists (Table I).

In general 320 (78.0 ± 2.0%) city residents and 90 (22.0 ± 2.0)% rural residents were hospitalized. All 410 cancer patients were admitted to the hospital in a planned manner. For the first time 381 (92.9%) patients were hospitalized, and 29 (7.1%) patients were readmitted.

The duration of the disease ranged from several months – in 281 (68.5 ± 2.3)% of patients – up to one year and more – in 96 (23.4 ± 2.1)% of patients; 33 (8.0 ± 1.3)% of patients were diagnosed with thyroid cancer for the first time during surgery.

According to age and gender characteristics, the sample of patients was as follows: there were 62 (15.1 ± 1.8%) male and 348 (84.9 ± 1.8%) female. The average age of male and female patients was 45.9 ± 13.6 years, and 48.6 ± 12.8 years respectively; no significant difference between the age characteristics of male and female patients was found ($t = 0.769277345$ at $p \leq 0.05$).

In addition to the main diagnosis of thyroid cancer, the management of which required an interdisciplinary approach, 147 (35.9%) patients were diagnosed with 234 cases of comorbidities and complications of the underlying disease.

Of the total number of cancer patients with concomitant diseases and complications of the underlying disease, 89 persons, or 60.5%, had one disease and / or complication of the underlying pathology, 32 persons, or 21.8% – two, 18 persons, or 12.3%, – three, 8 persons, or 5.4% had more than three diseases and / or complications of the underlying disease. That is, a significant proportion of patients had polymorbid pathology, which increased the need for appropriate interdisciplinary care.

It is established that the use of the multidisciplinary approach is justified in the research site in terms of staffing: in 2019 the staff consisted of 101 medical doctors and 165 mid-level practitioners. The medical doctors included 37 endocrinologists, 13 surgeons, 8 anesthesiologists, 6 ultrasound diagnosticians, 5 neurologists, 4 ophthalmologists, a radiologist, and 5 health care organizers. Laboratory diagnostics was provided by four laboratory physicians.

The composition of the mid-level staff is formed by 150 nurses, 11 laboratory assistants, a laboratory assistant for X-ray examinations, and medical statisticians.

Thyroid cancer patients are admitted to the Department of Endocrine Surgery, but the patient's clinical pathway involves several units throughout the institution. The first such structure is the outpatient department, where the patient undergoes diagnostic tests and consultative examination by an endocrinologist before hospitalization.

Routine tests, such as general blood tests, general urine tests, blood glucose levels, fecal tests for worm eggs in all self-reported patients were performed in the outpatient department of a specialized health care facility. A significant proportion of patients, namely 149 persons, or 74.9% of those referred by an endocrinologist or general practitioner, also underwent routine pre-hospital exam-

inations after treatment at the facility where the study was performed. not in a family doctor's outpatient clinic or a multidisciplinary secondary care facility.

During pre-hospital assessment medical doctors and diagnosticians – medical doctors of ultrasound, functional diagnostics units (cardiologist), roentgenologists, laboratory doctor – deal with the patient and the biological material, diagnostics test data. The duration of prehospital assessment may vary from one to three days. Assessment outcomes are entered into inpatient case history and with data visualization transmitted through a local information system to the Department of Endocrine Surgery.

The next step in the clinical pathway is preoperative management of the patient in the Department of Endocrine Surgery – which includes examination by the attending physician, endocrinologist, anesthesiologist, and head of the department. All patients with concomitant diseases and complications of the underlying disease are further consulted by medical specialists, depending on the nature of the patient's comorbidity. Consultations are conducted independently by professionals involved in this clinical case. Together with the patient or official representatives, the tactics of treatment and pain management is developed, as evidenced by the informed voluntary consent to diagnostics and treatment, including surgery and anesthesia. The duration of the preoperative period varies from one to three days.

Preparation for surgery, intensive care and postoperative supervision during the operating day are carried out in the department of anesthesiology with intensive care beds, surgery is carried out in the operating room. This component of clinical management of the patient involves surgeons, anesthesiologists, mid-level medical staff, pathologists who conducts intraoperative diagnostic examination of biological material.

Surgical treatment is carried out on the second-fourth day after hospitalization, depending on the duration of preoperative preparation and the clinical condition of the patient.

Postoperative management of the patient takes place in the department of endocrine surgery. It involves daily observation of the patient by the attending physician, and by the physician on duty on weekends and out of working hours of the attending physician. Intensive and planned treatment, postoperative wound care are provided by the attending physician and the nurse for the next nine days. Final histopathological examination data are used to establish the final diagnosis.

The final stage of the patient's clinical pathway is the discharge by the attending physician for the outpatient supervision of an endocrinologist and an oncologist. The recommendations of specialists regarding the observation of not only the underlying but also concomitant diseases and complications of the underlying disease are taken into account.

It was found that the clinical pathway of the patient is typical for all patients treated in the department of endocrine surgery in 2019, it designed for clinical management of patients with thyroid cancer and pathology of other endocrine organs The clinical pathway being developed not on the basis of nosology, but on the basis of unit of patient's stay in the hospital.

The local clinical protocol for patients with thyroid cancer contains the steps of patient route and the mechanisms of staff interaction, similar to those presented in the clinical pathway. Multidisciplinary teams as health care providers are positioned as the staff of departments with whom the patient interacts during his clinical pathway.

Job descriptions define functions of medical doctors with a focus on the specialty; at the same time it is mentioned that a medical doctor has the right for involving additional specialists for taking medical and diagnostic activities and is obliged to work in close contact with related specialists and offices. The doctor determines the indications for hospitalization according to the profile of the disease, the tactics of conservative and surgical treatment, taking into account the patient's condition and the need for preoperative preparation.

Medical technological documents (local medical care protocol, patient clinical pathway) and job descriptions are approved for use by the head of the institution.

DISCUSSION

The research data and primary material testified the introduction of a multidisciplinary care model in the research site, as a lot of medical doctors of various specialties and mid-level medical staff take part in the management of the patient with thyroid cancer. However, the mechanisms and degree of interaction are somewhat different from the approaches to clinical management of cancer patients already adopted in the world medical practice since the end of the last century.

Thus, the prehospital stage is characterized in most cases by performing atypical functions by a highly specialized endocrinology care institution, in particular routine examinations of patients seeking for medical care, representing 51.5% of the total number of hospitalized, as well as of those referred by primary or specialized care professionals. This indicates a low level of communication between primary and highly specialized medical care, between patients, general practitioners-family doctors and endocrinologists of outpatient facilities. The current state of affairs is confirmed by the practice of discharge of patients: none of them was given recommendations for further supervision by a general practitioner-family doctor. Thus, the principles of patient orientation and continuity of medical care as components of its quality are violated. Lack of effective coordination and teamwork in public health systems is common in many countries around the world [8], and the health care facility where the study was conducted appears to belong to such a system.

The preoperative stage, according to the data obtained, is a consultative examination of the patient on admission to the hospital by the main staff of professionals: surgeon, anesthesiologist, endocrinologist, head of the department.

In the future, surgery is performed by a surgeon, anesthesia is provided by an anesthesiologist. During postoperative period management is carried out by the attending physician, who also provides recommendations for discharge. That is, the composition of specialists is gradually limited, and only if necessary, other medical doctors are involved as consultants.

Thus, the constant interaction, exchange of observations, experience and knowledge among physicians involved in the treatment of the patient are not introduced, as well as constant communication with the patient throughout the clinical pathway, especially when the clinical situation changes. Traditionally the attending physician, not a multidisciplinary team, is responsible for the patient, as accepted in the world practice. The clinical decision is made by the attending physician alone, taking into account the advisory opinions of other specialists, and not by the interdisciplinary consensus [9].

At the stage of preoperative preparation rehabilitation care is stipulated by local medical protocols and patient clinical pathways. In practice the patient is examined in the rehabilitation department at this stage, which can be conducted on an outpatient basis. Global studies show that pre-surgery rehabilitation measures for cancer patients can improve physical and / or psychological outcomes and help patients function better throughout the treatment period, rehabilitation programs should include exercise, psychological support and components of therapeutic diet [10]. Psychological care for cancer patients is not practiced in the research site, as shown by the absence of psychologist among the staff member, although it is highly important at all stages of treatment.

Rehabilitation care for cancer patients is to be continued after discharge, which requires close cooperation of the multidisciplinary team of inpatient facility with medical doctors of outpatient facility, under whose supervision the patient is referred [11]. The study showed that recommendations are provided by the attending physician and are limited.

In order to improve the clinical management of cancer patients in the research site, it is proposed to take a number of measures to improve the technology of clinical management of patients. They can be based on:

1) further improving the standardized clinical process by developing and implementing clinical pathways of the patient on a nosological basis;

2) supplementing local care protocols for patients with thyroid cancer with targeted diagnostic, therapeutic and rehabilitation measures at each stage of the patient's stay in the hospital;

3) implementing the above-mentioned measures by multidisciplinary teams that are adaptive in terms of composition and technical capabilities for communication, and are formed in accordance with the patient's needs at each step of the patient's clinical pathway;

4) adapting multidisciplinary teams functions and authorities depending on the tasks during the patient's clinical pathway;

5) using modern digital technologies to ensure constant interaction, experience and knowledge exchange, required real-time communication frequency among multidisciplinary team members, the patient, primary and secondary care professionals concerning hospitalization, clinical management and rehabilitation during the whole life of the patient.

CONCLUSIONS

The research outcomes showed development areas as regards clinical management of thyroid cancer patients. Improving the clinical pathway of the patient and strengthening the interdisciplinary interaction of specialists in time and space should be the core of innovations.

Multidisciplinary teams should become a permanent communicative and functional structure of the health care institution, which accompanies the patient with cancer throughout the clinical pathway in the hospital and determines the content by consensus, plans and provides inpatient diagnostics & treatment, provides recommendations for further outpatient management after discharge and, if necessary, before the planned hospitalization.

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ORIGINAL ARTICLE

WAYS TO IMPROVE THE RESULTS OF SURGICAL TREATMENT OF PATIENTS WITH ATYPICAL FORMS OF ACUTE APPENDICITIS

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ABSTRACT

The aim: To search for new and improvement of known methods of diagnosis and surgical treatment of atypical forms of acute appendicitis.

Materials and methods: There were analyzed the results of diagnosis and surgical treatment of 852 patients with atypical course of acute appendicitis, which amounted to 25.3% of the total number of patients in this category. Depending on the chosen diagnostic and treatment tactics, patients with acute atypical appendicitis were divided into two groups: control (n=423) and main (n=429).

Results: It was found that among atypical forms of acute appendicitis retrocecal location of the appendix is 61.2% of cases, pelvic – 24.3%, medial – 11.2%, subhepatic – 3.4%. Destructive forms of atypical acute appendicitis occurred in a total of 92.5% of cases, 77.7% of patients had various types of peritonitis.

Conclusions: Authors improved and tested a number of diagnostic (rectal thermometry, ethanol test) and operative methods for destructive forms of acute appendicitis complicated by typhoid (including laparoscopic). The proposed diagnostic and treatment algorithm allowed to optimize the treatment tactics of this category of patients and reduce the incidence of complications in the early postoperative period from 9.9% to 3.5% ($p<0.001$).

KEY WORDS: acute appendicitis, atypical course, diagnosis, surgical treatment

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INTRODUCTION

Acute appendicitis remains the most common acute surgical disease of the abdominal cavity, which requires emergency surgery [1]. Features of the clinical picture of atypical forms of acute appendicitis are widely discussed today and are reduced to the differential diagnosis with a variety of acute and chronic processes that develop in the abdominal cavity [2]. The difficulty of diagnostics acute atypical appendicitis is evidenced by the significant frequency of unreasonable surgical interventions, which reaches 20-39% [3], and the high percentage of postoperative complications (20-40%) due to late treatment of patients, prolonged time comprehensive examination of them in the hospital [4]. The number of appendectomies in the absence of histologically proven inflammation in the appendix reaches 17-47% [5]. Diagnostic errors in this case cause a lot, as for acute appendicitis, mortality – 0.1-0.3% [6]. The frequency of diagnostic errors in the use of modern instrumental techniques in patients with suspected acute appendicitis (ultrasonography, CT, laparocentesis, laparoscopy) reaches 35.5% [7]. Even during laparocentesis it is not always possible to visually assess the nature of the contents of the abdominal cavity, microscopic examination of the fluid, in addition to the study of the native drug, is quite long. And so far there is no express method that has allowed to differentiate the exudate from the transudate.

THE AIM

To find new and improve known methods of diagnosis and surgical treatment of atypical forms of acute appendicitis.

MATERIALS AND METHODS

There were treated 3370 patients with acute appendicitis in the clinic of the Department of Surgery №2 of the Bogomolets National Medical University from 2010 to 2020. Atypical forms were found in 852 patients (25.3%), of which the retrocecal location of the appendix is 61.2% of cases, pelvic – 24.3%, medial – 11.2%, subhepatic – 3.4%. Depending on the chosen diagnostic and treatment tactics, patients with acute atypical appendicitis were divided into two groups: control and main. The comparison group included patients (423 people) operated on during 2010-2015 (first observation period) for acute appendicitis, who used standard approaches in diagnosis and treatment. The main group included 429 patients, in the treatment of which we used our improved diagnostic and therapeutic methods (II period of observation – 2016-2020). There were 324 men (38.03%) and 528 women (61.97%). The age of patients ranged from 21 to 85 years, the average age was 37.2±1.2 years. The vast majority of patients in both groups were people of working age (90.7% and 91.02%, respectively). Groups of patients are comparable in age and sex.

Destructive forms of atypical acute appendicitis occurred in a total of 92.5% of cases. Different types of peritonitis

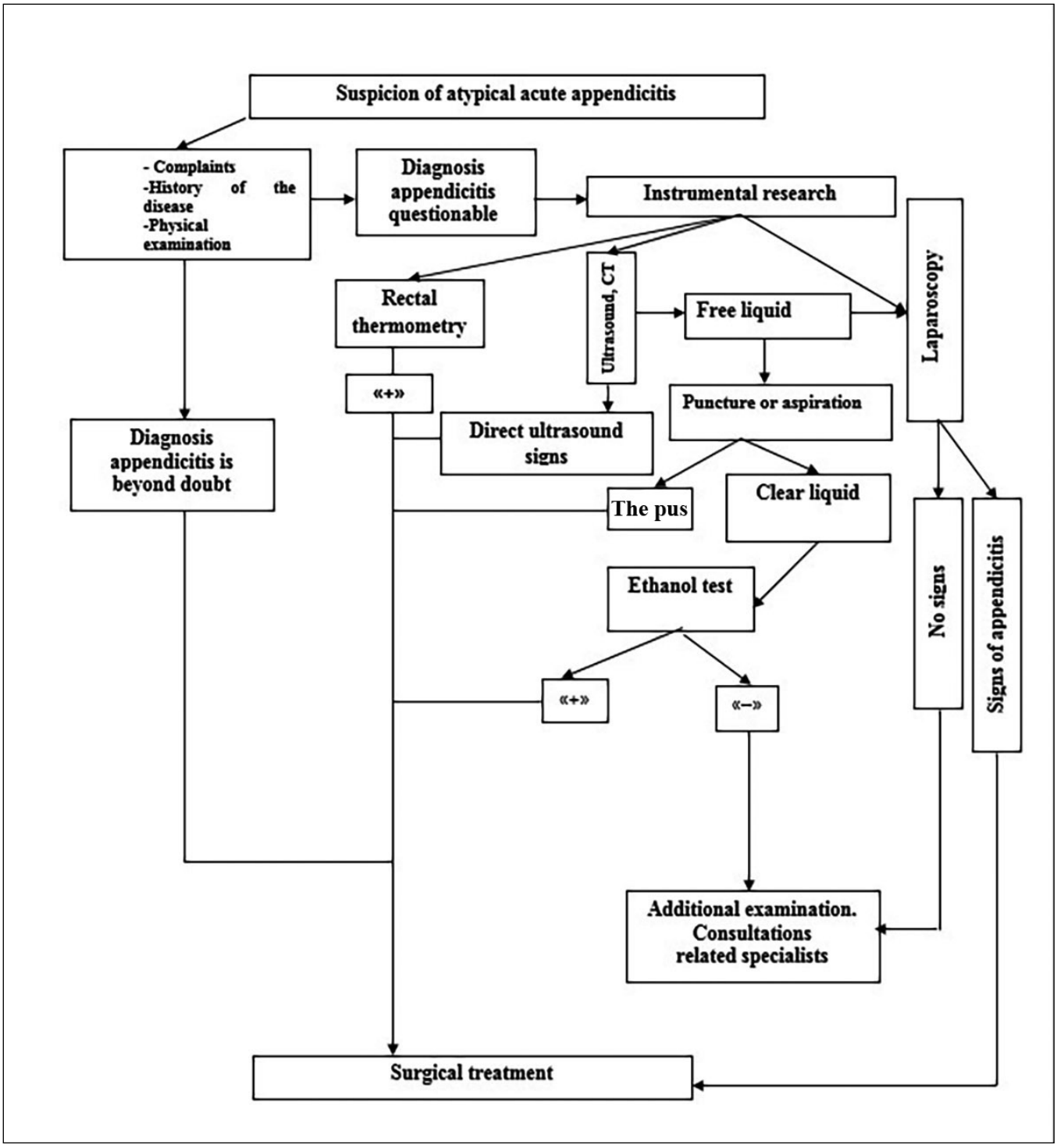

Fig 1. Diagnostic and treatment algorithm

were found in 662 patients (77.7%). A significant proportion of patients in both groups (37.1% and 36.1%) with acute appendicitis with an atypical course were admitted to the hospital a day after the onset of the disease. Concomitant diseases were diagnosed in 274 patients (32.2%).

In patients with suspected acute atypical appendicitis, a thorough collection of complaints, medical history, physical, laboratory, and, if necessary, instrumental examination was performed. When pelvic location of acute appendicitis was suspected, the temperature of various parts of the rectum was recorded at a depth of 10 cm with a portable digital high-temperature moisture-resistant thermometer. With the pelvic location of the inflamed appendix, the temperature reaction (above 37.6° C) will be local, that is, it will be determined at the point of contact of the rectum with the inflamed appendix. An increase in temperature in several parts of the rectum, in the absence of a clinical picture of acute peritonitis, indicates in favor

Table I. Structure of pathomorphological forms of acute appendicitis with atypical course

Pathomorphological forms	Total (%)	Groups of patients				P
		Main		Comparison		
		n	%	n	%	
Catarrhal	64 (7,5)	43	10,02	21	4,96	<0,01
Phlegmonous	580 (68,08)	289	67,4	291	68,8	>0,05
Gangrenous	208 (24,4)	97	22,6	111	26,3	>0,05
Total	852	429	100	423	100	

Table II. The nature of early postoperative complications in patients with acute appendicitis with atypical course

Postoperative complications	Groups of patients		
	Main	Comparison	Total
Postoperative wound suppuration	9 (60%)	19 (45,2%)	28 (49,1%)
Early connective intestinal obstruction	1 (6,7%)	5 (11,9%)	6 (10,5%)
Postoperative peritonitis	–	2 (4,8%)	2 (3,5%)
Abdominal abscess	–	3 (7,1%)	3 (5,3%)
External intestinal fistula	–	6 (14,3%)	6 (10,5%)
Postoperative scar infiltrate	5 (33,3%)	7 (16,7%)	12 (21,1%)
Total	15 (3,5%)	42 (9,9%)	57 (6,7%)

of acute gastroenterocolitis or inflammation of the uterine appendages in women.

When free fluid was detected in the abdominal cavity, one of the available instrumental methods was used to take it and visually evaluate it. In difficult cases for clinical diagnosis, an ethanol test was performed: 50% ethanol solution was added to the test fluid – in the presence of exudate, fibrin monomer was polymerized to form a gel.

All patients underwent surgery. Given that during the second period of observation in the diagnosis of acute atypical appendicitis laparoscopy was widely used, in case of confirmation of the diagnosis it was completed by laparoscopic appendectomy (171 patients (39.9%). In conditions of severe destruction of the appendix, when the appendix is involved in the inflammatory process and it is impossible to make a standard cover of the stump of the appendix with their own tissues, used advanced appendectomy techniques, when peritonization of the stump of the appendix was carried out with an adhesive plate laparoscopic surgery – everted peritoneal flap.

STATISTICS

Statistical analysis was performed using Statistica 10 (Serial Number: STA999K347150-W) and MEDCALC® (open-access website, https://www.medcalc.org/calc/). Data distribution normality was checked using the Shapiro-Uilk criterion. Comparison of the data between the groups was carried out using the paired Student's t-criterion for unrelated samples. Comparison of the indicators in dynamics was carried out using Student's t-criterion for related samples. No abnormal distribution was observed in the study. The confidence intervals given in the article were constructed for the confidence level of 95%.

RESULTS

When acute appendicitis with an atypical course was suspected, we relied on the diagnostic and treatment algorithm developed by us (Figure 1). In cases where the clinic of acute appendicitis was in doubt, instrumental methods of studying patients were used. Positive results of rectal thermometry and ethanol test were an indication for emergency surgery. The use of this diagnostic and therapeutic algorithm in the atypical course of acute appendicitis allowed to increase the proportion of persons operated on for its non-destructive forms. The structure of pathomorphological forms of acute appendicitis with an atypical course is shown in Table I.

There is also a tendency to reduce the number of patients with gangrenous forms of appendicitis ($p>0.05$), but their significant percentage in both groups and the lack of significant difference in frequency indicates other factors than the atypical location of the appendix, which affect these indicators, primarily the age of patients and their late treatment.

Analyzing the results of treatment of patients with acute appendicitis with atypical course, it should be noted that during the first observation period the frequency of discrepancies between clinical and pathological diagnoses was 18.2% versus 4.9% in the second period ($p<0.001$), and in the second period not at all cases of chronic forms of the disease were registered (against 1.3% in the first), and the percentage of subacute forms decreased from 12.96% to 1.9% ($p<0.001$).

Analyzing the frequency of postoperative complications, it should be noted that in the early postoperative period their frequency was 6.7% (57 people): in patients of the main group – 3.5% (15 people), and in the comparison

group – 9.9% (42 people) (p<0.001). The nature of early postoperative complications in patients with acute appendicitis with atypical course are shown in Table II.

Analyzing the structure of postoperative complications, it should be noted that in the atypical course of acute appendicitis, the frequency of postoperative purulent complications is not clearly dependent on the degree of destruction of the appendix, as noted in typical acute appendicitis. The frequency of postoperative complications in catarrhal appendicitis in patients of the comparison group was (19.05%), in phlegmonous – 6.9%, gangrenous forms – 27.03% (in patients of the main group 4.7%, 5.9%, 26, 8% respectively). Thus, both cases of postoperative peritonitis in patients of the comparison group were associated with the progression of acute gynecological pathology of the uterine appendages (initially patients were operated on for catarrhal appendicitis). Patients were re-operated, during the operation the cause of peritonitis was eliminated, intubation of the small intestine, lavage and drainage of the abdominal cavity were performed.

A total of 8 patients with atypical acute appendicitis were reoperated (0.9%), one person in the main group underwent laparoscopic surgery (0.2%) and 7 people in the comparison group underwent relaparotomy (1.7%). No cases of death of patients with acute appendicitis were observed during this observation period.

DISCUSSION

In case of untimely diagnosed acute appendicitis due to the destruction of the appendix, the inflammatory process spreads to the surrounding anatomical structures (cecum, peritoneum, blood vessels) [8]. This in turn can lead to the development of severe purulent-septic complications (peritonitis, abscesses, typhlitis, pyelonephritis, etc.) [9]. Performing standard variants of appendectomy in the conditions of infiltration of the cecum can be a dangerous development of the failure of the sutures with the occurrence of intestinal fistula, which requires a long stay in the hospital [10]. The use of laparoscopic techniques in destructive forms of acute appendicitis on the background of purulent-inflammatory complications is discussed [11].

The use of our improved method of rectal thermometry in case of suspicion of acute pelvic appendicitis (sensitivity of the method was 93.1%, specificity – 82.8%) allowed to reduce the frequency of gangrenous forms from 33.3% to 15.2% (p <0,01) due to a significant reduction in the follow-up of patients (by 1.4±0.3 days), and, as a consequence, reduce the number of periapendicular abscesses in this localization of appendicitis from 38.9% to 18.9% (p<0,01).

The high diagnostic value of the ethanol test (sensitivity of the method was 95.8%, specificity – 83.3%) allowed to remove emergency indications for surgical treatment (ie to avoid unreasonable appendectomy) in 21.2% of patients with further dynamic monitoring and follow-up another pathology of the abdominal cavity was found, which is subject to conservative treatment (mesadenitis, toxicoinfection, chronic gynecological pathology, etc.).

Improving the technology of surgical interventions in destructive forms of acute appendicitis complicated by typhlitis has reduced the incidence of complications in the early postoperative period from 9.9% to 3.5% (p<0.001).

CONCLUSIONS

1. At an atypical location of acute appendicitis its retrocecal localization prevails (60,99%), the pelvic form meets in 24,1% of cases. This group is dominated by destructive forms of the disease (92.5%), which are complicated by various forms of peritonitis (77.7%).
2. The introduction of the proposed diagnostic and treatment algorithm in patients with acute appendicitis with atypical course allowed to reduce the frequency of discrepancies between clinical and pathological diagnoses from 18.2% to 4.9% (p <0.001), moreover, in patients of the main group no case of chronic forms of the disease was registered (against 1.3% in the control), and the percentage of subacute forms decreased from 12.96% to 1.9% (p<0.001).
3. The use of an improved method of rectal thermometry in case of suspicion of acute pelvic appendicitis (sensitivity of the method – 93.1%, specificity – 82.8%) allowed to reduce the frequency of gangrenous forms from 33.3% to 15.2% (p<0,01) due to a significant reduction in the follow-up of patients (by 1.4±0.3 days), and, as a consequence, reduce the number of periapendicular abscesses in this localization of appendicitis from 38.9% to 18.9% (p<0,01) .
4. The application of the proposed method for the diagnosis of peritonitis in difficult cases for clinical verification allowed to remove emergency indications for surgical treatment (that is, to avoid unreasonable appendectomy) in 21.2% of patients in whom subsequent dynamic monitoring and follow-up revealed other pathology of the abdominal cavity, which is amenable to conservative treatment (mesadenitis, toxicoinfection, chronic gynecological pathology, etc.).
5. Introduction of advanced diagnostic technologies and surgical interventions, including laparoscopic, in destructive forms of acute appendicitis complicated by typhlitis, reduced the incidence of complications in the early postoperative period from 9.9% to 3.5% (p<0.001).

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ORIGINAL ARTICLE

USE OF EVIDENCE-BASED MEDICINE BY DENTISTS

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ABSTRACT

The aim: To investigate how dentists use evidence-based medicine in clinical practice. Objectives: to determine how dentists understand the role of evidence-based medicine to ensure the quality of dental care; what sources of evidence are used; what are the barriers to the use of evidence and the possibility of removing it.

Materials and methods: Methods of semi-structured in-depth interview, thematic analysis, graphic, generalization were used. Materials: records of respondents' answers.

Results: Dentists have identified the benefits of evidence: a positive treatment outcome; protection against doctor's mistakes; safety of dental interventions, maintaining the level of professional knowledge. Dentists use online evidence resources, training materials, advertising of medical devices and filling materials. Barriers to the use of evidence-based medicine are the lack of sectoral clinical protocols, lack of personal time and low English proficiency, according to dentists. Not all evidence-based medicines and medical devices are approved for use in Ukraine. Removing barriers will ensure more active use of evidence in dental practice.

Conclusions: Dentists are aware of the role of evidence-based medicine in ensuring the quality of dental care, know the sources of evidence. Barriers are the lack of national clinical protocols, their incomplete provision of resources, the lack of dentists' own time and the low level of English language proficiency. The results of the study can be used in the formation of sectoral and local policies for the standardization of health care and continuing education of dentists.

KEY WORDS: clinical recommendations; resource; clinic; barriers; quality of dental care

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INTRODUCTION

Evidence-based medicine has had a significant impact on improving the quality of care. It combined the results of reliable research, the experience of the health worker and the clinical needs of the patient. This allows the doctor to make the right clinical decision, using modern reliable evidence to choose methods of diagnosis, treatment and rehabilitation of a particular patient [1]. However, scientific studies show that evidence-based knowledge has not yet become widespread in the clinical practice of physicians of various specialties [2, 3]. In particular, this topic is relevant for dentists. However, patients' requests for the best treatment results, saturated market of dental services require the use of dentists reliable clinical technology on the principles of evidence-based medicine [4, 5]. There is no national adaptation of clinical guidelines in Ukraine. This task is delegated to health facilities. Therefore, information about the use of evidence-based medicine in dental practice from dentists can show the real situation.

THE AIM

To investigate how dentists introduce and use evidence in clinical practice. Objectives: to identify what dentists see the role of evidence-based medicine in ensuring the quality of dental care; what sources of evidence are used; what barriers and / or facilitations exist for the ongoing use of evidence; which can help dentists make more active use of international clinical guidelines.

MATERIALS AND METHODS

Research methods: semistructured in-depth interviews, which are the most common source of qualitative, reliable data on important issues, in particular, in health care [6, 7]; thematic analysis; graphic; generalization. Research materials: records of respondents' answers to the questions identified by the research objectives. Respondents were 10 out of 51 doctors of the dental clinic in Chernihiv. Doctors of the clinic provide all types of dental services to the population of Chernihiv region. The clinic has the highest accreditation category and a certificate of conformity of the quality management system to the national standard – analogous to the international standard for quality management systems [8].

The group of respondents included 6 women and 4 men; age – 34 – 65 years, duration of professional activity – from 10 to 40 years. The same specialty, but different sex, age, duration of professional activity allowed to obtain the homogeneity of the group and at the same time different points of view on the problem.

The data were collected by the interviewer, the author of the study, the Master of Health Management and the Doctor of Philosophy. The author has experience in sociological research, the results of which are published in professional scientific journals. The interviewer was not personally acquainted with the respondents. This precluded previous arrangements to affect the results.

The study was conducted 10 working days, one interview

Table I. Topics, categories and subcategories based on in-depth interviews with dentists

№	Topics, categories and subcategories	Number of physicians who provided answers (abs.,%)
1	What do you see the role of evidence-based medicine in ensuring the quality of dental care?	
1.1	Benefits for the patient:	
	- positive treatment result	10 (100,0)
	- protection against doctor's mistakes	3 (30,0)
	- safety of dental interventions	6 (60,0)
1.2	Benefits for the doctor:	
	- protection against wrongdoing	8 (80,0)
	- reducing the probability of an unexpected result	6 (60,0)
	- constant support of professional knowledge level	7 (70,0)
2	What evidence sources do you use?	
2.1	Obtained actively from:	
	Internet resources (articles with systematic reviews, clinical recommendations)	2 (20,0)
2.2	Obtained passively from:	
	educational materials (lectures, webinars, scientific and practical conferences)	10 (100,0)
	drug forms	9 (90,0)
	local protocols for dental care	6 (60,0)
	advertising materials for medical devices and filling materials	10 (100,0)
3	What barriers and / or facilitations exist for the ongoing use of evidence?	
3.1	Barriers objective:	
	- there are no sectoral clinical protocols for dental care based on international clinical guidelines	8 (80,0)
	- not all medicines and medical devices are approved for use in Ukraine	2 (20,0)
3.2	Barriers subjective:	
	- lack of own time	2 (20,0)
	- low level of English language proficiency	2 (20,0)
4	What can help you to make more active use of international clinical guidelines?	
4.1	Ministry of Health:	
	- development and implementation of branch clinical protocols of high-evidence dental care	8 (80,0)
	- quality educational materials in programs of continuous professional development	3 (30,0)
4.2	Dental Clinic Administration:	
	- adaptation of branch clinical protocols of dental care to the conditions of the institution (translation, provision of medical devices, medicines, filling materials, training of physicians)	9 (90,0)

lasted 40-50 minutes after the end of the dentist's work shift in a separate room of the clinic with good lighting and low noise. The procedure included getting the researcher acquainted with the respondent, obtaining informed written consent for the interview, explaining the purpose of the study, and conducting the interview.

According to the researcher's budget, the answers were recorded by hand with key phrases and the most important parts of phrases. The researcher's assistant helped record, but did not participate in the interview. All entries were transferred to separate Microsoft Office Word documents marked with conditional numbering of respondents. The notation was transcribed on the same day and the free part of the next day, before the next interview. All responses that were memorized but not recorded were also used to minimize distortion.

The researcher developed a questionnaire for the interview. This was a list of open-ended questions. The researcher could ask additional questions as needed.

Thematic analysis of the results was carried out by carefully studying the texts of the answers, the primary processing of textual data (elimination of word-parasites, emotional exclamations, repetitions, slang words). Iterative open coding was performed by dividing the texts into smaller parts. Frequently repeated words or short phrases were used as code markers. The search was performed

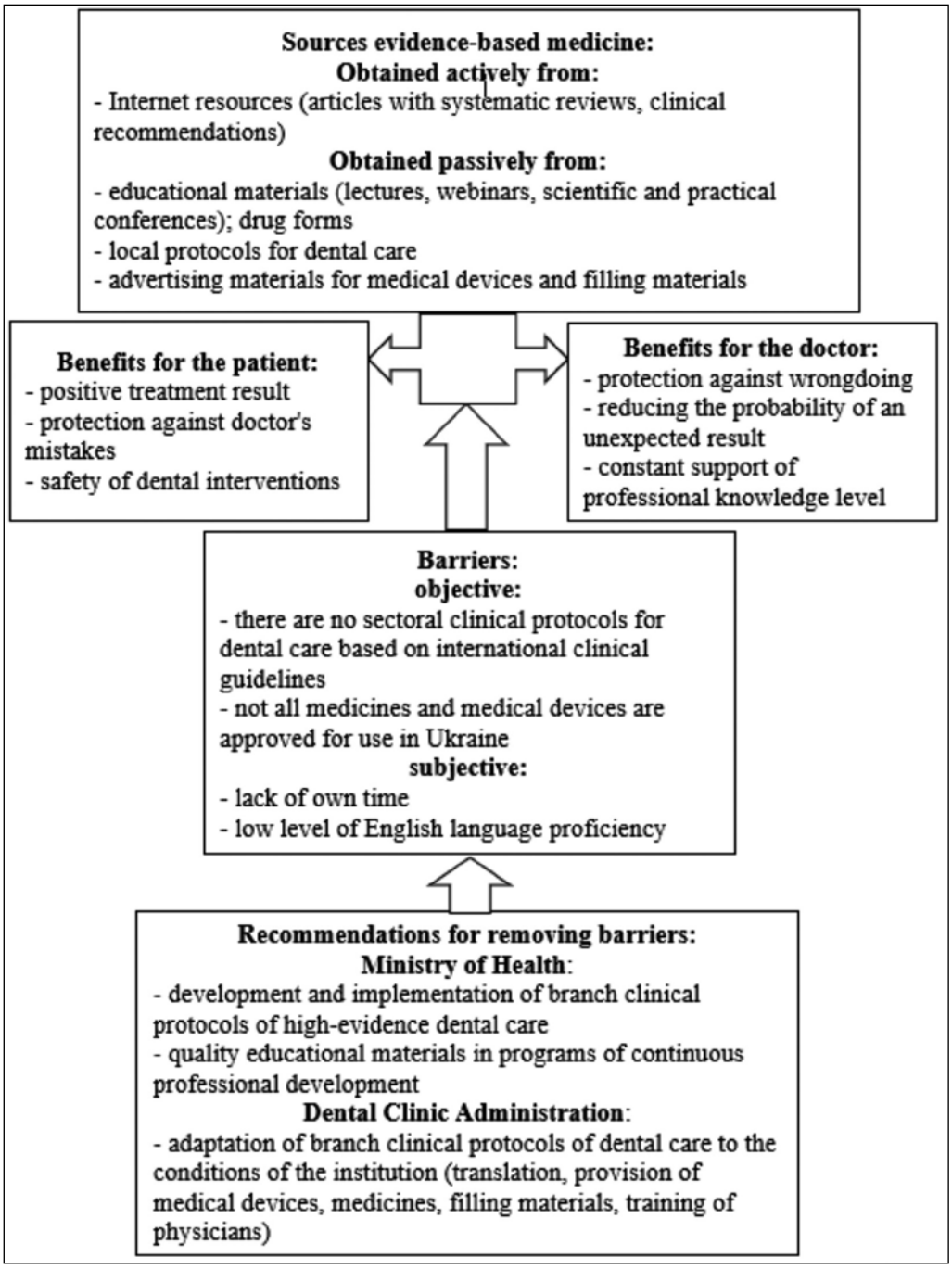

Fig. 1. Scheme of the benefits of evidence in dental care for parents and physicians, barriers to their use and recommendations for removing barriers

using MX EXCELL software. Open source was grouped into separate categories and subcategories to relate them. The coding results with topics, categories and subcategories are presented in Table I.

Triangulation of the data was chosen by the method of increasing the reliability of the results. Sources of scientific literature with data similar on a subject, but with quantitative researches are used. Examples are given in the discussion of the results. The reliability of the results was also confirmed by the interviewer's careful adherence to the research protocol, ethical standards and the use of additional questions.

Ethics commission Shupik National Healthcare University of Ukraine, Kyiv, Ukraine.

Concluded the study complies with the current standards and principles of the "Code of Ethics of the Ukrainian Doctor", current regulations of Ukraine and the requirements of the Declaration of Helsinki (07.02.2022 protocol of Ethics commission No 2).

RESULTS

The coding of the answers to the first question revealed two categories: dentists recognize the role of evidence-based medicine for the patient and for the physician. The dominant advantage for the patient, all doctors considered the possibility of a positive outcome of treatment. "Clinical protocols are based on international clinical guidelines.

They are the standards of health care, and compliance with the standards ensures quality and positive results for the patient in most cases" (physician 7).

The protection of the patient from the doctor's mistakes is presented in the following statement: "Evidence-based medicine is necessary for young doctors with short experience, they can make mistakes and harm the patient. The use of protocols reduces the likelihood of physician errors, so the patient can be sure of the right treatment" (physician 3). The safety of dental interventions has been linked to the idea of medicines: "Clinical protocols and drug lists contain the names of safe and effective drugs. It is necessary to know the patient's allergy history to avoid mistakes" (physician 6).

The following answers related to the role of evidence for physicians: "If you follow the protocol, you will not be prosecuted in case of a negative treatment outcome. A negative result may be associated with individual characteristics of the organism and atypical course of the disease" (physician 5). The probability of an unexpected result is reduced: "The physician is more confident that the result of treatment will be positive" (physician 3). Evidence allows physicians to maintain a level of professional knowledge: "You do not need to read a lot of literature, all the data is in the protocol, you can quickly find" (physician 2).

According to the interviews, physicians receive sources of evidence in an active and passive way: independently from Internet resources, training materials and advertising. "I use the PUBMED or NICE database and search for articles by keywords. I translate the text with the help of an interpreter on the Internet. But it takes a long time" (physician 9). "I search for the information I need through Google, from scientific sources, but not very often" (physician 10). "We are currently studying refresher courses every year. We attend seminars, lectures, conferences, they are conducted by professors" (physician 4). "Every year a branch list of medicines is published. We use it in our work. The list includes medicines that are registered in Ukraine, they are safe and effective" (physician 5). "We hear information about promotional materials at our meeting. Medical devices and filling materials are modern, many of them are produced abroad, there is data on their clinical effectiveness, we are told about this during training" (physician 3).

Doctors reported the use of dental care protocols developed by domestic experts: "I use local domestic protocols because they are allowed by order of the chief physician" (physician 8). "I have been using local protocols for a long time, it does not harm patients, and we also use new drugs and filling materials" (physician 2).

Doctors pointed to objective and subjective reasons for barriers to the use of evidence. "National clinical protocols have been developed before. Now this work has been stopped, and I believe that it needs to be resumed" (physician 4). "Not all international clinical guidelines can be applied in Ukraine. Not all foreign drugs and medical devices are allowed" (physician 7).

Doctors called the lack of their own time a subjective barrier: "I need a lot of time to find and translate original sources. I am not sure about the quality of my translation. It is expensive for me to pay for a specialist's translation" (doctor 9); "I understand the general content of the text in English, but a detailed translation with a dictionary takes a long time" (physician 10).

Physicians responded to the question "What can help to use international clinical guidelines more actively" as follows: "Protocols of evidence-based clinical practice should be developed by the Ministry of Health. Dental clinics should provide dental care (physician 3). "If each dental clinic develops its own protocols, there is no guarantee that they will be correct. The guidelines for developing clinical protocols for health facilities are difficult to understand" (physician 1).

Physicians noted the importance of the quality of educational materials: "Information in training cycles and scientific conferences should be more up-to-date and contain more practical component" (physician 4).

Physicians believed that the clinic's administration should promote the availability of evidence. "Clinic management can pay for the translation of international clinical guidelines. Training for doctors can be conducted on the basis of our clinic, the head can invite teachers from medical schools. It can be an intermittent workout to make it convenient for everyone" (physician 1).

DISCUSSION

The results of the study showed that the goals of the study were achieved, the answers to the questions were received. Dentists are aware of the importance of evidence to provide quality care. According to the respondents, the evidence not only determines the high probability of a clinical outcome for the patient, but also helps the dentist to choose the right treatment, prevents his mistakes.

At the same time, the availability of evidence is partial for dentists, and its quality is not always high, because physicians use low-level evidence protocols and promotional products. Physicians believe that barriers to the use of high-quality evidence are the lack of sectoral documents developed on the basis of international clinical guidelines, and the impossibility of their use in Ukraine in full. Dentists do not have enough time and a low level of English language skills to search and translate evidence on their own.

Physicians believe that the barriers can be overcome with the help of the Ministry of Health and the management of the dental clinic. Dental clinics need adapted clinical protocols to national conditions and educational activities in clinics with the provision of quality training materials.

Scheme of the benefits of evidence in dental care for patients and physicians, barriers to their use and recommendations for removing barriers are shown in Figure 1.

The reliability of our results is confirmed by similar but quantitative studies. Canadian dentists prefer low-level evidence, considering the lack of time a barrier to the use of evidence-based medicine. They want to learn evidence in the workplace [9].

Most Davangeri dentists in Karnataka, India, knew about evidence-based medicine (94.8%), and 77% of physicians received this information during scientific conferences. Only 38.5% knew about the different levels of evidence of medical knowledge. At the same time, in complex clinical cases, only 37.0% of dentists used electronic databases of evidence-based medicine [10].

A large-scale sociological survey of dentists in France, Georgia, Poland, Portugal, Slovakia and Turkey showed that more than a third (32.8%) of respondents knew about evidence-based medicine in dentistry, 32.1% of doctors use clinical recommendations. The majority of respondents (89.1%) considered the use of evidence-based medicine appropriate, but 60.0% indicated a lack of time, knowledge and limited data availability [11].

Potential methodological limitations of our study are the interviews of doctors of one specialty, which does not allow to spread the results to other professional groups of physicians. Improving reliability could be achieved through expert evaluation of results.

As such research is practically not conducted in Ukraine, we can recommend this research method as promising for obtaining quality information directly from health professionals about current issues of medical practice.

CONCLUSIONS

It is established that dentists are aware of the role of evidence-based medicine in ensuring the quality of medical care, informed about the sources of evidence. Barriers to their availability for use in clinical practice have been identified: lack of national clinical protocols, certain medical equipment and registration of certain drugs in Ukraine; lack of personal time and low level of English language proficiency. The results of the study can be used in the formation of sectoral and local policies for the standardization of health care and continuous training of dentists.

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ORIGINAL ARTICLE

COMPARATIVE PHARMACOECONOMIC ANALYSIS OF SELF-CONTROL OF DIABETES MELLITUS USING GLUCOMETERS

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ABSTRACT

The aim: To pharmacoeconomic analysis of direct medical costs for self-control of diabetes in Ukraine, Moldova and Georgia. Our observational, cross-sectional study aims at finding out the real costs of covering expenses in order to make decisions on the reimbursement of self-control means.

Materials and methods: 1) International and national clinical guidelines for diabetes; 2) information about the prices of glucometers, test strips from online pharmacy services. Systematization, generalization and pharmacoeconomic analysis of direct medical costs were used in the study.

Results: Based on the generalization of recommendations on the frequency of blood glucose control, 3 scenarios were identified, according to which the costs were calculated: Type 1 diabetes; Type 2 diabetes (insulin therapy); Type 2 diabetes (oral hypoglycemic therapy). The authors conducted pharmacoeconomic analysis of direct medical costs for self-control of DM for PWD in Ukraine, Moldova and Georgia. The study shows that the lowest cost of self-control is provided in Ukraine, in addition, Ukraine has a wider choice of glucometers and test strips. It was revealed that the pharmaceutical markets for glycometers in the three countries depends on the import of equipment.

Conclusions: It is advisable to introduce in Ukraine the reimbursement of self-control devices, namely, glucometers and test strips for all categories of PWD, which will contribute to self-control and, as a result, will be able to prevent the development of complications. Certification of continuous glucose monitoring systems will increase access to new technologies that are already widely used in many countries.

KEY WORDS: Medical direct costs; diabetes mellitus; self-control; people with diabetes

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INTRODUCTION

The prevalence of diabetes mellitus (DM) continues to rise, and the treatment of complications of diabetes becomes a significant burden on the healthcare budget [1]. It is expected that the global economic burden of DM will increase from 1.3 trillion. dollars to 2.5 trillion dollars in the period 2015-2030 [2]. The WHO Resolution WHA74/A74 (May 2021) notes the need to reduce the burden of non-communicable diseases by strengthening the prevention and control of diabetes, since the prevention of complications through glycemic control is recognized as an effective measure of reducing the cost for diabetes treatment.

Hyperglycemia and frequent hypoglycemia (glycemic variability) provoke complications at the level of the cardiovascular system, retinopathy, nephropathy, neuropathy and other acute and chronic complications [3].

International studies have confirmed the dependence of the frequency and severity of complications in diabetes on glycemic control [4]. Conducting intensive regular self-monitoring of glycemia can improve blood glucose levels and achieve a stable level of glycemia due to the timely correction of hypoglycemic therapy and changes in the eating behavior of PWD [5, 6].

Currently, there are many new technologies for measuring the level of glucose concentration in the blood. The results of self-control allow people with diabetes (PWD) to evaluate the effectiveness of therapy, diet, physical activity, make decisions on treatment correction with additional training of PWD. However, despite the fact that self-monitoring is widely used in the treatment of DM, many PWD do not perform tests with the required frequency due to various factors: inconvenience, pain and invasiveness of the testing procedure; cost of tests. Therefore, a significant number of PWD do not achieve optimal treatment outcomes [1, 7].

The importance of self-monitoring remains an issue, so assessing the true costs of self-monitoring can encourage governments to adopt modern economic methods to cover the costs of self-monitoring, and PWD to invest in their health to prevent complications.

According to the IDF Atlas 2021, the prevalence of DM in Ukraine is 7.1%, Moldova – 6.7%, and Georgia – 6.8% [1]. According to the official data of 2017, there were 1.27 million PWD in Ukraine, but since 2017, statistics on deaths from diabetes have been canceled, so there are no confirmed data about diabetes [8]. In 2020, there were about 123,000 PWD in Moldova, and every ninth death in the country was due to com-

plications of DM [9]. In Georgia, according to the 10th edition of the IDF Atlas, there are 190.6 (172.3 – 246.4) thousand PWD [1] and the largest burden of mortality in Georgia is associated with non-communicable chronic diseases, including diabetes [10]. Republic of Moldova, the first of the post-Soviet countries, that have introduced reimbursement system (expenditure on insulin) and insurance medicine since 2004, and Ukraine has reimbursement since 2016 (expenditure on insulin).

THE AIM

Pharmacoeconomic analysis of the direct medical costs for self-control for diabetes in Ukraine, Moldova and Georgia.

MATERIALS AND METHODS

1) international and national clinical guidelines for diabetes; 2) information on the prices of glucometers, test strips from online pharmacy services in Moldova (ff.md, felicia.md); Ukraine (www.tabletki.ua, www.liki24.com); Georgia (https://psp.ge/, https://www.aversi.ge, https://gpchealth.ge); as of January 24, 2022. Systematization, generalization and budget-impact analysis (BIA) were used in the study.

The analysis was carried out taking into account the stages of cost calculation during pharmacoeconomic studies [11] (fig. 1).

RESULTS

At the first stage of the study, pharmaceutical categories were identified that ensure self-control of DM. In the vast majority of cases, in Ukraine, Moldova, Georgia, invasive glucometers are used – both in the preferential provision of PWD. The advantage of glucometers is not only in savings, these devices are simple and understandable to most of the PWD, which reduces the risk of emergency medical situations [12]. At the time of the study, there are no certified means of continuous monitoring of blood glucose in Ukraine and Moldova. FreeStyle Libre continuous blood glucose monitoring system has been certified in Georgia. Therefore, glucometers and consumables (test strips, lancets) were chosen for pharmacoeconomic analysis of the costs of self-monitoring of diabetes. At this stage, lancets were not included in the study, as PWDs can use both disposable lancets and lancing device lancets.

At the second stage of the study, based on the analysis of national and international standards and recommendations, the frequency of blood glucose tests per day was determined depending on the type of DM and hypoglycemic therapy. The goal of PWD treatment is to achieve the target level of glycemia (fasting blood glucose – 4-8 mmol/l; postprandial – up to 10 mmol/l), reducing glucose variability and minimizing the risk of developing complications of diabetes [13]. Self-monitoring of glucose levels significantly improves glycemic control [14]. Inadequate adherence to test frequency is associated with poor long-term outcomes. Increasing the level of blood glucose control in PWD is an important task, so the standards for the treatment of diabetes recommend the frequency of control depending on the type of diabetes and disease therapy.

There are no national guidelines in Georgia on the frequency of self-monitoring, but the Diabetes Centers in Georgia have their own recommendations, which are based on recommendations from ADA, NHS/UK, ISPAD, and ESC/EASD.

Table I. Recommendations on the frequency of blood glucose monitoring depending on the type of diabetes and disease therapy.

Type of diabetes, therapy	Frequency of self-monitoring	Organization, normative document
Diabetes Type 1 (T1D)	3 - 4 times a day	International Diabetes Federation [15].
	4 - 10 times a day	National Institute for Health and Care Excellence (NICE) [16].
	6 - 10 times (or more) a day	American Diabetes Association [17, 18].
	at least 4 times a day	National clinical protocol diabetes T 1 of Ukraine [13]. National guidelines of medical care of diabetes of Russia [21].
	5 times a day (children, teenagers) 3 times a day (adults)	National Diabetes Plan of Moldova [19].
	5 - 6 times a day	National clinical protocol of Moldova [20].
Diabetes Type 2 (T2D) (insulin therapy)	3 times a day	International Diabetes Federation [22].
	3 or more a day	National clinical protocol diabetes T 2 of Ukraine [23].
	3 tests a day	National Diabetes Plan of Moldova [19].
	at least 4 times a day	National guidelines of medical care of diabetes of Russia [21].
	3 - 4 times a day	National clinical protocol of Moldova[20].
Diabetes Type 2 (T2D) (oral antidiabetic treatment)	3 times a week	International Diabetes Federation [22, 24, 25].
	3 - 4 times a day	National clinical protocol of Moldova[20].
	1 time per day at different times + 1 glycemic profile (at least 3 times per day) per week	National guidelines of medical care of diabetes of Russia [21].

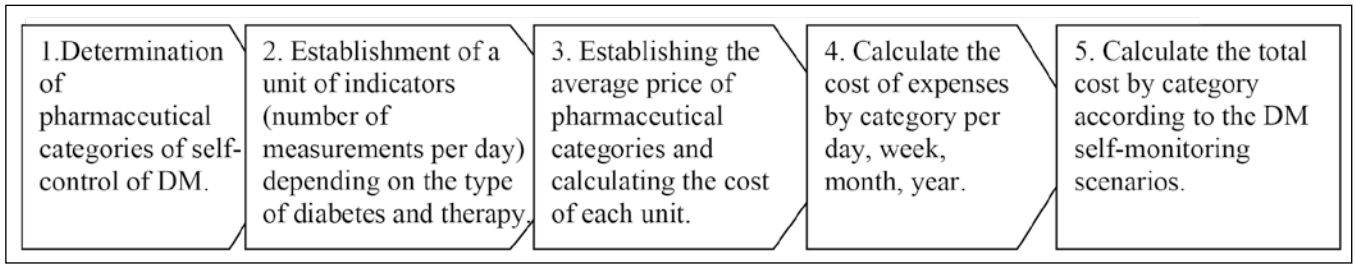

Fig. 1. Stages of the methodology

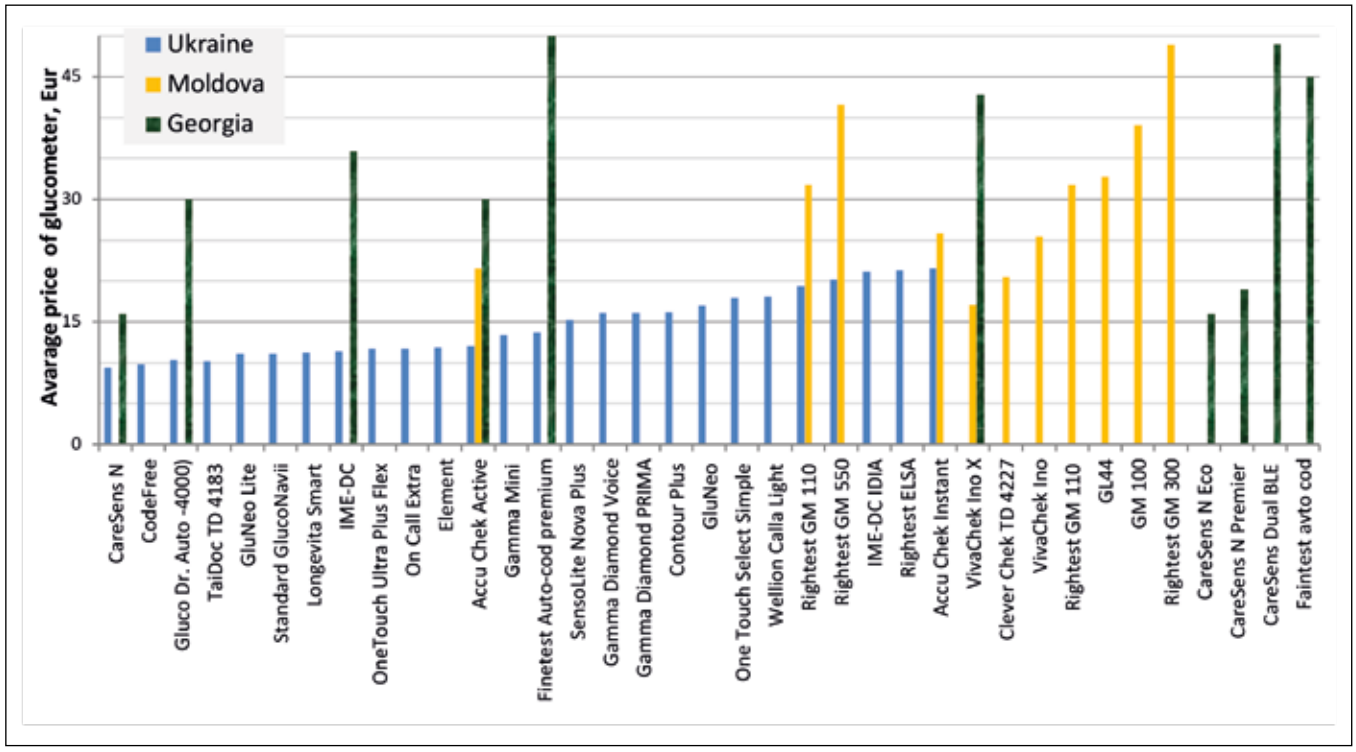

Fig. 2. Glucometers on the pharmaceutical market of Ukraine, Moldova, Georgia with indication of the retail price (Eur).

Based on the generalized information (table I), 3 scenarios were identified, according to which the costs of self-control were calculated for: 1) T1D, it is recommended to measure blood glucose – 4 times a day; 2) T2D on insulin therapy – 3 times a day; 3) T2D on oral hypoglycemic therapy – 1 time per day at different times and plus 1 glycemic profile (at least 4 times a day), that is, 10 times a week. The study did not take into account additional measurements that may be required in some situations (sports, travel, symptoms of hypoglycemia), because these are individual needs, depending on lifestyle, course of the disease, etc.

At the next stage, we analyzed the offers of glucometers and test strips in the pharmaceutical markets of Ukraine, Moldova, Georgia and determined the most popular models of devices, taking into account the availability of test strips for the corresponding glucometers. We set average retail prices for pharmaceutical categories (glucometers and test strips) and calculated the cost of each unit. Since the majority of PWD purchases glucometers and test strips in pharmacies at their own expense, retail prices were applied.

The study included 26 models of glucometers that are in Ukraine and 10 models each – in Moldova and Georgia. It has been established that the markets of glycometers in the three countries depends on the import of equipment.

In Ukraine there are glucometers whose brands are registered in Switzerland, Germany, Hungary, South Korea, China, Taiwan; in Moldova – Switzerland, Germany, China, Taiwan; and in Georgia – South Korea, USA, Germany. Only one model of the Accu Chek Active blood glucose meter is available in the pharmaceutical markets of all three countries.

It has been established that glucometers in Ukraine are cheaper than in Moldova and Georgia, and the average salary in these countries is approximately the same (the average salary in Moldova is 426.27 Eur, in Ukraine – 446.31 Eur, and in Georgia – 392.62 Eur). In Ukraine, the price range is from 9.36 to 21.56 Eur, and half of the popular assortment is sold in pharmacies at a price of up to 15 Eur, in Moldova – 17.12 – 48.91 Eur, with 2 glucometers up to 25 Eur; in Georgia 16.0 – 50.0, and 3 glucometers at a price of up to 20 Eur.

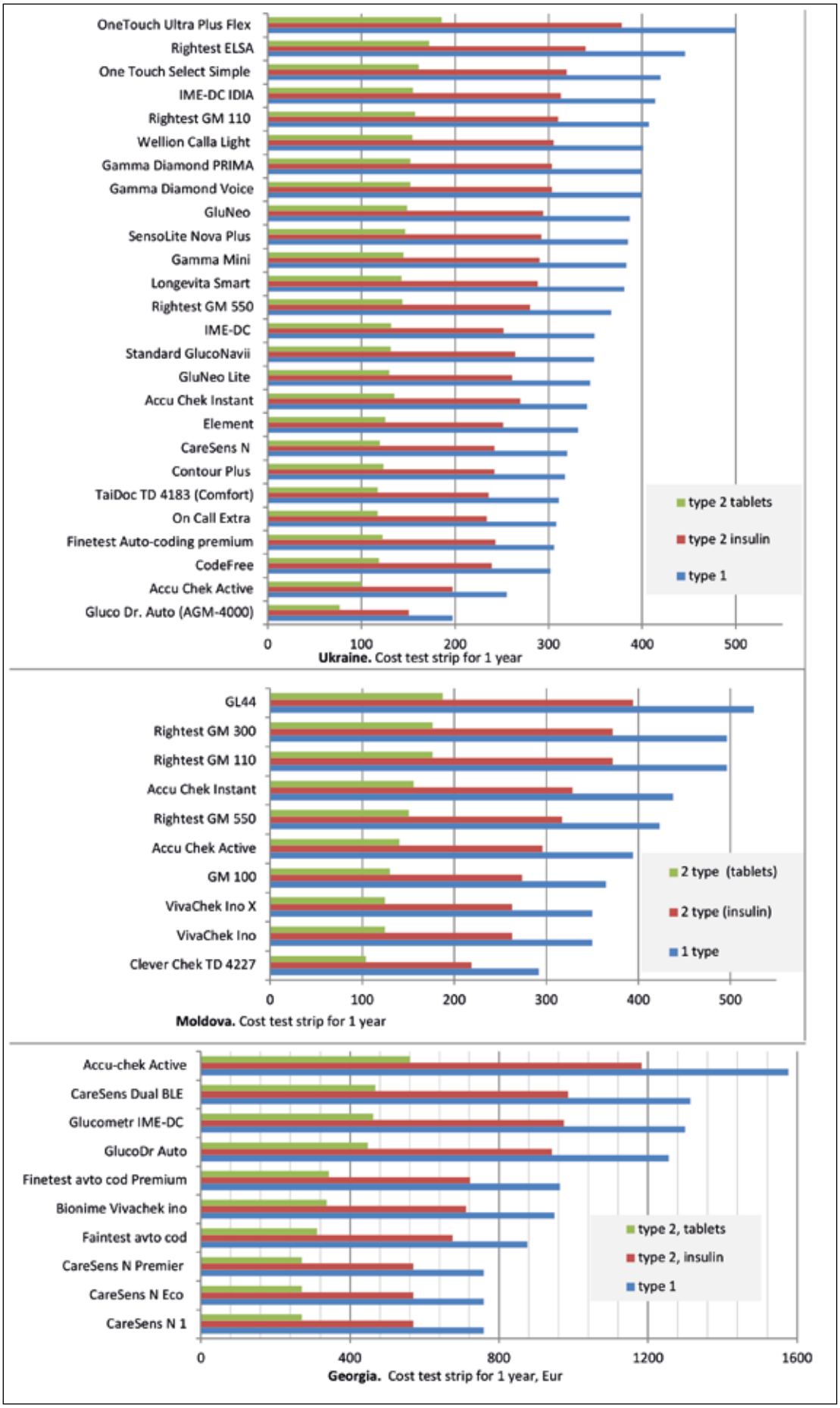

Fig. 3. Cost for test strips for 1 year in dependence of type DM and therapy (Ukraine, Moldova, Georgia)

Test strips for glucometers are presented No. 25, No. 50, No. 100. The cost of one test strip for different models of glucometers in Ukraine is 0.13 – 0.29 Eur, in Moldova – 0.24 – 0.36 Eur, and in Georgia – 0.52 – 1.08 Eur.

Figure 2 is a graphical representation of the cost of consumables calculated under 3 self-monitoring scenarios for three countries. Our research shows that the range of costs for test strips for different models of glucometers for 1 year separately for three countries is:

in Ukraine 1) T1D – 197.43 to 445.63 Eur; 2) T2D (insulin therapy) – 150.67 to 339.53 Eur; 3) T2D (oral antidiabetic treatment) – 77.00 to 172.44 Eur.

in Moldova 1) T1D – 292.00 to 525.60 Eur; 2) T2D (insulin therapy) – 219.00 to 394.20 Eur; 3) T2D (oral antidiabetic treatment) – 104.00 to 187.20 Eur.

in Georgia 1) T1D – 759.20 to 1576.80 Eur; 2) T2D (insulin therapy) – 569.40 to 1182.60 Eur; 3) T2D (oral antidiabetic treatment) – 270.40 to 561.60 Eur.

Lower costs for self-control (at retail prices) in Ukraine are provided by glucometers: Gluco Dr. Auto (AGM-4000) and Accu Chek Active; in Moldova – VivaChek Ino and GM 100, although the last glucometer does not have the lowest price, and in Georgia – CareSens N 1, CareSens N Eco, CareSens N Premier, which have the lowest price.

Glycometers which have the lowest price are not always those which have the lowest price for associated test strips. Therefore, when choosing a device for self-control, PWD needs to focus not only on the price of a glucometer, but also on the price of test strips or total price of ownership and use).

The cost of self-monitoring for 1 year consists of the cost of a glucometer and consumables – test strips for 1 year. But considering that glucometers are used for more than 1 year, and even more so, the manufacturer provides a guarantee of at least 5 years or an indefinite period, when calculating the costs for a longer period (3 years), this must be taken into account, and the discount factor is also taken into account.

DISCUSSION

The cost of self-control can be attributed to relevant, because self-control of diabetes affects the outcome of treatment and prevents complications. And according to the requirements of ISPOR, relevant expenses include expenses that are important for the person from whose perspective the analysis is carried out or the purpose of the study is set [26].

In many European countries, the costs of self-monitoring of DM are covered (in whole or in part) by the state or the insurance fund, which contributes to its implementation and the achievement of the PWD of treatment targets [27].

Some studies show that increased level of government procurement of glucometers for self-monitoring of blood glucose levels to the level of regulatory support for PWD receiving insulin therapy brings economic benefits to the state that significantly exceed the necessary costs for self-monitoring [28].

Reimbursement programs and reference pricing are powerful tools in the process of setting prices for important medicines/medical devices and reduce mortality rates, improve the quality of life of patients and allow the implementation of effective treatment [29].

In Moldova the system of reimbursement covers insulin. According to the National Diabetes Plan in Moldova, the state provides glucometers and test strips, but not in full. From 2022, it is planned to include glucometers and consumables in the reimbursement system, which is already operating in the country since 2004.

In Georgia, a program of universal health coverage was introduced in 2013, aimed at expanding the rights of citizens to a package of state-guaranteed health services. Today, the state provides glucometers and test strips for T1D patients under 18 years free of charge, and T1D patients over 18 years, glucometers are free of charge, but patients cover consumables on their own. From 2022, in Georgia, the state will provide a permanent monitoring system (FreeStyle Libre) to 1200 children and adolescents under 18 years with T1D.

In Ukraine, the system of reimbursement is already in place, and PWD receive insulin and some oral antidiabetic drugs. The level of provision with tools for self-control, purchased from public funds in Ukraine, is insufficient and significantly below the standard level. The state provides glucometers and consumables for some categories of PWD (children, pregnant women), but most categories of PWD cover these costs from their own budget, which is a barrier to self-monitoring and can lead to the development of complications of diabetes.

It is advisable to introduce in Ukraine a reimbursement (full or partial) of the costs of self-control devices, glucometers and test strips for all categories of PWD. This will help stimulate patients to self-control and, as a result, lead to better control of diabetes. This can prevent the development of complications, which is an effective means of reducing the burden of diabetes for the PWD's and the costs for diabetes for society at large.

CONCLUSIONS

The authors conducted pharmacoeconomic analysis of direct medical costs for self-control of DM for PWD in Ukraine, Moldova and Georgia. It is shown that the lowest cost for self-control is provided in Ukraine, in addition, Ukraine has a wider choice of glucometers and corresponding test strips. It was revealed that the pharmaceutical markets of glucometers in three countries are import-dependent.

Pharmacoeconomic analysis of the direct medical costs of self-control makes it possible to finding out the real costs of covering expenses. It is advisable to introduce in Ukraine the reimbursement of self-control devices – glucometers and test strips for all categories of PWD, which will contribute to self-control and, as a result, will be able to prevent the development of complications. This is an effective means of reducing the burden of diabetes for the PWD's and the costs for diabetes for society at large.

Certification of continuous glucose monitoring systems would increase the accessibility of PWDs to new technologies that are already widely used in many countries.

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ORIGINAL ARTICLE

THE AVAILABILITY AND QUALITY OF PALLIATIVE AND HOSPICE CARE ENSURING IN THE COVID-19 PANDEMIC CONTEXT

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ABSTRACT

The aim: To study the availability, quality and features of outpatient palliative and hospice care (PHC) to the population, including the elderly, in the COVID-19 pandemic context in order to optimize the PHC-mobile-teams service.

Materials and methods: Domestic and foreign literary sources; sociological research results. The research methods: biblio-semantic, sociological (questionnaires), systemic approach and systemic analysis, conventional medical-statistical methods.

Results: Based on the analysis of international regulatory documents, domestic and foreign literary sources, the socio-medical importance of PHC is shown. In Ukraine, as in other countries, the number of elderly people is constantly growing, which leads to an increase in the PHC need. The results of the sociological survey determine: PHC needs in terms of age showed that in Ukraine almost 78.86% of people in need of PHC were aged 60 and over; the most popular (86.0% of responses) were PHC-mobile-teams and home-based services; about 80% of respondents said that pain limited their ability to work and affected on their psycho-emotional state and their quality of life; 86.3% of respondents reported an pain increased after COVID-19. The results of an online survey showed the effectiveness of PHC-mobile-teams service by improving the availability of PHC.

Conclusions: To ensure high-quality PHC availability it should be integrated at the Health and Social Care Systems. According to the experience of the Kyiv PHC-mobile-teams service, it significantly increases PHC availability, which is especially important in the COVID-19 pandemic context.

KEY WORDS: Health Care System; palliative and hospice care; palliative patients; PHC-mobile-teams service; COVID-19 pandemic

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INTRODUCTION

Today in most leading countries the development of palliative and hospice care (PHC) is one of the priority medical, social and humanitarian tasks of governments and society. This is due to the aging population, the ever-increasing number of patients with chronic incurable progressive diseases, including those with limited life expectancy. The relevance of this problem is growing every year, as almost 80% of patients dying from chronic diseases need PHC. WHO and international professional organizations define PHC as an integral part of the health care system, but today there is a lack of access to PHC in many countries around the world. Only about 10% of palliative patients have access to PHC, and more 80% of them live in developed countries. [1–7].

In 2014, WHO together with the World Palliative Care Alliance (WPCA) prepared and published the World Atlas of Palliative Care at the End of Life, and in 2019 the European Palliative Care Association (EAPC) – the Atlas of Palliative Care in Europe, it is noted that about 30% of people in need of PHC are patients with cancer and the remaining 60% are patients with progressive chronic life-threatening diseases [5; 6]. In the recent years, the COVID-19 pandemic has significantly worsened the availability of palliative patients for PHC, especially in outpatient settings, which is the aim of our study.

THE AIM

To study the availability, quality and features of outpatient PHC to the population, including the elderly, in the COVID-19 pandemic context in order to optimize the outpatient and PHC-mobile-teams service.

MATERIALS AND METHODS

During the study, a literature search was conducted in JAMA, Scholar and PubMed search engines, as well as in domestic and foreign sources, a sociological survey using our questionnaires (546 respondents) and using modern Internet technologies using our questionnaire "A Questionnaire to Measure Reaction to Pain in Chronic Pain Disorders "(139 respondents) [8]. The following research methods were used: biblio-semantic, sociological (questionnaire), systemic approach and systemic analysis. In the statistical processing of materials were used generally accepted medical-statistical methods.

RESULTS

An analysis of international documents and literature shows that today it is the responsibility of all governments to make PHC available to the public. In Ukraine, as in other countries of the world, the number of elderly people is constantly growing, which leads to an increase in the prevalence of severe age-related chronic diseases and, consequently, an increase in the need for PHC. In the modern sense, PHC are seen as a comprehensive system of medical, social, psychological, and spiritual/religious interventions to comprehensively support patients with life-threatening or incurable diseases when the treatment aimed at recovery is ineffective or unpromising. Unlike traditional health care, innovative PHC aim to ensure the most achievable quality of life for palliative patients and their relatives [1-7; 10-13].

The results of our research on the need for PHC in Ukraine in terms of age showed that almost 78.86% of people who needed PHC were aged 60 and older, of which 34.48% were people aged 80 and older [9].

In 2018-2020, the Institute of Gerontology of the National Academy of Medical Sciences of Ukraine conducted a sample sociological research to study the needs of older people in various types of care. It was attended by 546 elderly people (75 years and older) living in Kyiv. Respondents were asked to conduct a self-assessment of their health status and preferred forms of care through a telephone interview. Analysis of the research results showed that 36.8% of them had incurable diseases that caused constant stay within the apartment and needed long-term or palliative care, 59.7% of respondents needed rehabilitation, and only 3.5% said they did not need assistance. (fig.1).

According to the research results, the most popular (86.0% of responses) were mobile-teams and home-based services, which enable elderly people to live in their usual home conditions and at the same time receive quality medical and social services. Respondents who had severe pain and side effects wanted care in hospice (8.2%), 5.8% of respondents expressed a desire to move to a geriatric boarding house. It should be noted that all of them were over 85 years old, lived alone, and had no relatives in the city. (Fig.2).

Over the past two years, the COVID-19 pandemic has significantly worsened the availability of palliative care patients for PHC, especially on an outpatient basis. During 2020, we conducted a survey of the patients using modern Internet technologies using our questionnaire "A Questionnaire to Measure Reaction to Pain in Chronic Pain Disorders" [8]. The study involved 139 respondents (28.1% men and 71.9% women) aged 20 to 89 years, the vast majority of whom were aged 40-59 years – 59.0%, and 60 years and older – 26.8%.

As one of the most important symptoms in palliative patients is severe pain, we focused on the features of the course of the chronic pain syndrome (CPS) in these respondents, 97.1% of whom had relapsed or had COVID-19. The results of the sociological survey showed that 65.2% of respondents experienced pain for more than 3 months, 46.38% noted intense pain (6 or more points on a 10-point Visual-Analog Scale (VAS)) (Fig. 3). 79.9% of respondents said that pain limited their ability to work, 85.6% – physical activity, and 79.1% – social activity (Table I).

Table I. The results of a sociological study of the course of chronic pain in the respondents who relapsed or were ill with COVID-19

CPS among respondents who relapsed with COVID-19	Patients' well-being from their words
65.22%	Felt pain for more than 3 months
46.38%	Felt intense pain (6-10 points for VAS)
79.90%	Pain limited the ability to work
85.60%	Pain limited moving activity
79.10%	Pain limited social activity
74.10%	Felt indifferent to the environment
88.10%	Felt insomnia
66.20%	Feeling ashamed of self condition
78.40%	Feelings of helplessness due to CPS
73.40%	Feelings of despair in their own strength

Table II. The results of a sociological study of the intensity of chronic pain in the respondents who relapsed or were ill with COVID-19

Percentage of respondents who underwent COVID-19 and had an increase in the CPS	Noted an increase in the intensity of the CPS
7.50%	to 30%
27.30%	for 30-39%
21.60%	for 40-49%
9.40%	for 50-59%
10.0%	for 60-100%

Respondents also noted the impact of the CPS on their psycho-emotional state: 74.1% felt indifferent to the environment, 88.1% – insomnia, 78.4% – helplessness due to CPS, and 73.4% – self-loathing (Table I).

86.3% of the respondents noted an increase in the CPS after COVID-19 disease, of which an increase in pain by 30-39% noted 27.3% of the respondents, 40-49% – 21.6% of the respondents, 50-59% – 9.4% and increased pain by 60-100% noted 10.0% of the respondents (Table II). 89.3% of the respondents said that the CPS worsened their quality of life. We would like to draw your attention to the need to take this into account in order to select an adequate regimen and correct the treatment of the CPS in palliative patients with COVID-19.

Since 2020, the mobile palliative care service in Kyiv has registered: 1,317 palliative patients from different cities of Ukraine, including: 780 patients with various stages of cancer (59.2%); 455 patients with acute cerebrovascular disorders and dementia (34.5%); 82 patients with motor motoneuron disease/MND (6.2%).

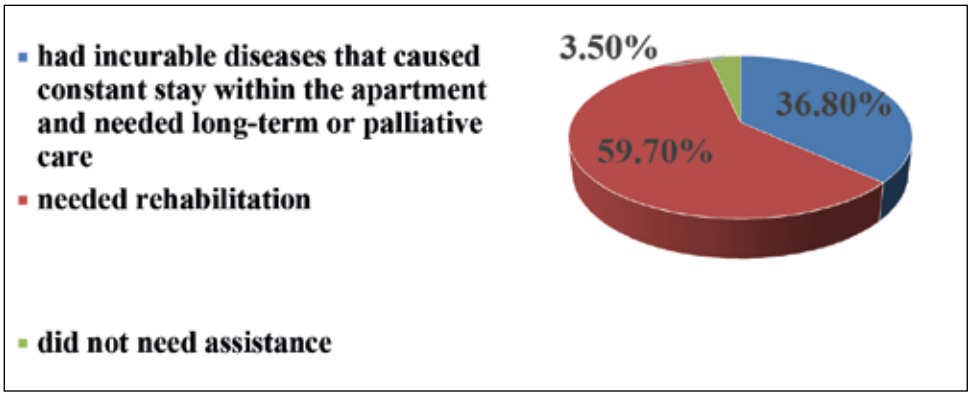

Fig.1. The results of a sociological research to study the needs of older people in various types of care

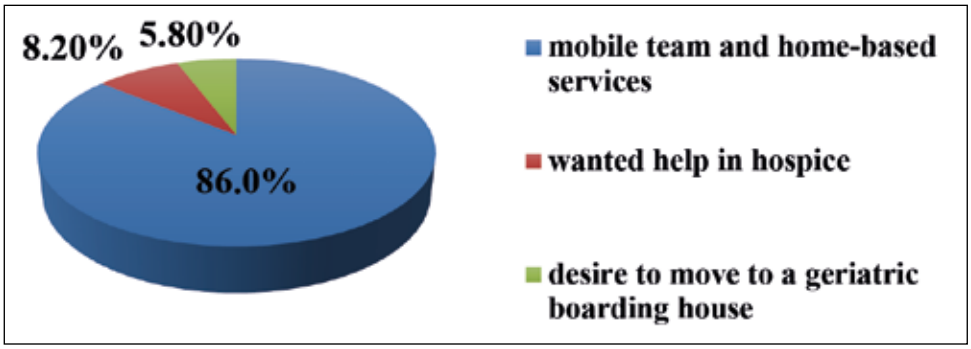

Fig.2. The results of a sociological study of older people to study the desired forms of care

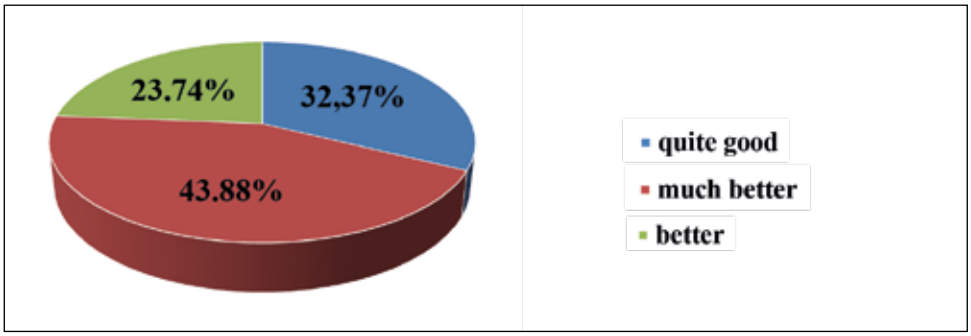

Fig. 3. The results of a sociological study of the course of chronic pain in the respondents who had relapsed or were ill with COVID-19

During the COVID-19 epidemic (for the period from October 1, 2021 to January 31, 2022), specialists of the mobile palliative care service provided 148 consultations to palliative patients and their relatives using means of communication, and 183 palliative patients – on an outpatient basis (of them: primary – 141, secondary – 186, completed episodes – 3). The results of an online survey showed the effectiveness of this form of PHC by improving the availability of this type of care. Thus, 32.37% of the respondents noted the improving of their well-being as "quite good" (improvement was assessed by 70-100%), 43.88% of the respondents – "much better" (40-69%), and 23.74% "better" (up to 40% improvement) (Fig. 4).

DISCUSSION

According to modern international standards and norms: the right to PHC is one of the basic human rights in the modern world; equal access to PHC services should be guaranteed to the population in all countries, according to needs and regardless of income level, cultural and ethnic characteristics of palliative patients; PHC should be available to all patients at the first need, regardless of when and where the need arises; in addition, it should not create excessive financial difficulties, especially for palliative patients from low-income and vulnerable groups [1-7; 10-13].

The increase in the number of elderly people with severe comorbid diseases, whose deaths are caused by severe complications of chronic diseases in addition to cancer, requires PHC and social palliative care services for a long time. These problems are especially relevant in palliative geriatrics, where long-term medical, psychological and social problems prevail, which significantly worsen the development of polymorbidity and reduce the quality of life of palliative patients and their families. [4; 11; 14-21].

Since April 1, 2020, the PHC service was included in the Medical Guarantee Program of the National Health Service of Ukraine (NHSU), which today allowed to increase 8 times the number of health care facilities (HCF) that provide PHC to the population. Thus, if as of January 1, 2020 there were 2 PHC centers, 19 hospices and 71 PHC departments in Ukraine [9], then on April 1, 2021 736 HCF

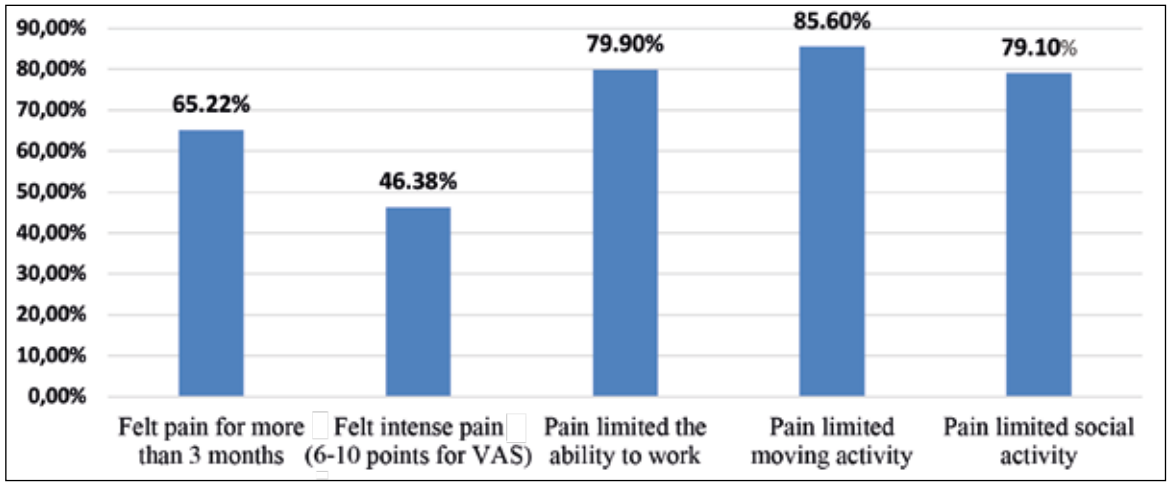

Fig. 4. The results of an online survey of the palliative patients on the effectiveness of the mobile palliative care service in Kyiv

have concluded agreements with the NHSU on providing palliative care to the population: 613 HCF – for the provision of palliative care in the hospital and 486 HCF – for the provision of mobile palliative care. Of course, this will significantly increase the availability of PHC for the population. The introduction of multidisciplinary, interagency and cross-sectoral approaches to ensure the PHC quality is now an important issue.

Today, society is faced with the need to reform the existing of Health Care and Social Care Systems, taking into account the new realities in the demographic structure of the population of Ukraine. The urgency and need for the outpatient and mobile service forms of palliative and long-term care at home is growing every year. Among the PHC organization models in most countries, outpatient forms (day care hospices, outpatient PHC, including PHC at home), which are implemented by multidisciplinary mobile teams prevail. [11; 14-21].

PHC mobile teams/outpatient services, hospice at home and home-based forms of long-term medical and social care should be created at the junction of two organizational forms of medical and social care for the elderly: inpatient or mobile PHC service and social and medical care at home. These multidisciplinary mobile teams (or home care units) provide care for the whole family, not just the individual patient.

The main goal of the hospice at home is to ensure the highest possible quality of life by comprehensively satisfaction of the medical, social, psychological and spiritual/religious needs of palliative patients, including the elderly, and their family members, that are mandatory components of PHC. The multidisciplinary mobile team/PHC department employs/involves doctors of various specialties, including general practitioners-family doctors, nurses, social workers, caregivers, volunteers, priests/medical chaplains, etc.

Thus, the demographic crisis, hostilities in Donbass, migration of young people abroad and within the country lead to an increase in the number of single elderly people in Ukraine, which leads to a growing need for PHC and long-term care for the elderly, including patients with chronic incurable diseases to provide them with a decent quality of life. In Ukraine, as in the rest of the world, it is necessary to introduce training for palliative patient's relatives and caregivers in the methods of caring for seriously ill patients, to organize consultation rooms at PHC HCFs, to conduct trainings and seminars, etc.

CONCLUSIONS

1. The availability of quality PHC is considered today as a global issue. PHC must be an integral part of the Health and Social Care System, as PHC is the most adequate source of the needs and proper quality of life of palliative patients and their relatives, and contribute to the preservation of human dignity at the end of life. Today, the responsibility of all governments to make PHC available to the public.
2. Among the PHC organization models in most countries, outpatient forms (day care hospices, outpatient PHC, including PHC at home), which are implemented by multidisciplinary mobile teams prevail.
3. The results of our research on the need for PHC in Ukraine in terms of age showed that almost 78.86% of people who needed PHC were aged 60 and older, of which 34.48% were seniors aged 80 and over. The urgency and need for the development of outpatient and mobile teams service forms of palliative and long-term care at home is growing every year. The results of our research show that the most popular form of care for the elderly (86.0% of responses) were mobile-teams and home-based care services.
4. The results of a sociological study of the features of CPS in outpatient palliative patients showed that 65.2% of the respondents experienced pain for more than 3 months, 46.38% of the patients reported intense pain (6 or more points on a 10-point VAS), 89.3% of the respondents said that CPS worsened their quality of life.
5. The results of a sociological research of the peculiarities of the course of CPS after COVID-19 disease showed that the strengthening of CPS was noted by 86.3% of the respon-

dents, of which the increase in pain by 40-49% was 21.6% of the respondents, 50-59% – 9.4% the patients, and an increase in pain by 60-100% – 10.0% of the respondents, that must be taken into account for the selection of an adequate scheme and correction of treatment of CPS in palliative patients with COVID-19 disease.

6. According to the experience of the PHC mobile team in Kyiv, this form of PHC service significantly increases its availability, which is especially important in the context of the COVID-19 pandemic.

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ORIGINAL ARTICLE

SIMULATION TRAINING AND VIRTUAL PATIENTS AS A COMPONENT OF CLASSROOM TRAINING OF FUTURE DOCTORS UNDER COVID-19 CONDITIONS

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ABSTRACT

The aim: To present and substantiate the theoretical and applied aspects of the organization of simulation training for higher education applicants in the field of health care based on the analysis and generalization of the experience of the Bogomolets National Medical University.

Materials and methods: To perform the set tasks, the following theoretical and empirical methods of scientific research were used: system analysis; comparison and generalization; bibliosemantic method; the analysis and simulation methods.

Results: The experience of organizing simulation training for higher education students in the field of health care was analyzed and summarized. There have been investigated the functional capabilities of the most common "virtual patient" modeling systems for the formation of the practical component of the future doctors' professional competence. Finally, the features of the organization of the educational process at a medical university in classroom, mixed (classroom-distance) and synchronous (hybrid) forms of education during the period of quarantine restrictions have been described.

Conclusions: A technology for conducting an objective structured practical (clinical) exam has been developed. It helps to standardize the procedure for checking the level formation of the clinical professional competence of a future doctor in accordance with the requirements the standard of higher medical education. It is shown that the use of simulation training and modeling systems "virtual patient" in the preparation of future healthcare professionals increases the effectiveness of training, the interest of students and interns, motivating them to develop the necessary components of the future doctor's professional competence.

KEY WORDS: distance learning, simulation training, virtual patient, objective structured clinical exam (OSCE), special competence

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INTRODUCTION

During the current COVID-19 pandemic, many national medical (pharmaceutical) institutions of higher education (M(Ph)HEI) are facing a number of challenges related to the organization of the educational process under quarantine restrictions and to the need for ensuring the quality and accessibility of higher medical (pharmaceutical) education. The problems of shaping the practical component of the professional competence for future doctors are therefore of particular relevance.

There is the recent normative content of training in terms of learning outcomes, which highlights the list of mandatory general and special competencies of a graduate in the standard of higher education that was approved within the "222 Medicine" specialty for the second (master's) level of higher education [1]. It is noted that students should study clinical disciplines and learn professional competencies at clinical departments of the educational institutions (using simulation methods, diagnostic equipment, etc.) and directly at the patient's bedside.

The system of organization of the educational process and the development of various aspects of the methodology for teaching clinical disciplines to future healthcare professionals is the subject of research by local and foreign teachers. Thus, the paper [2] presents the approaches to organizing training in radiation diagnostics for future doctors using modern cloud services. In the publication [3], the team of authors defines the correct conditions for modern educational environment of a higher medical (pharmaceutical) institution. The paper [4] presents the approaches to organizing teaching biostatistics of future physicians in the context of the introduction of a new curriculum. The works [5, 6] reflect the principles of formation and structure of the simulation training educational and practical center, its role in the assimilation of knowledge and skills in the process of training medical specialists. The papers [7-9] explore the use of "virtual patient" models. The analysis of these works gives grounds for making an assumption about the prospects of using system models as an effective addition to other educational tools in order to consolidate knowledge in clinical disciplines and form the practical skills of a future doctor.

THE AIM

The aim of the article is to present and substantiate the theoretical and applied aspects of the simulation training organization for the applicants for higher education in the

field of health care based on the analysis and generalization of the experience within the Bogomolets National Medical University.

MATERIALS AND METHODS

To accomplish the tasks set, the following theoretical and empirical methods of scientific research were used: system analysis, comparison and generalization for the theoretical substantiation of approaches to the organization of simulation training for future healthcare professionals, bibliosemantic method (for the study of psychological and scientific literature, regulatory documents on the formation of professional competence of future healthcare professionals), empirical methods (interviews with students, interns, and teachers), analysis of the most common "virtual patient" modeling systems for training students of medical HEI, simulation (to develop the structure of the basic concepts of the medical university simulation center).

RESULTS

The organization of the educational process at the Bogomolets National Medical University is undergoing systemic transformations due to implemented quarantine restrictions in March, 2020. Firstly, the university training was carried out distantly, and then – in a mixed (classroom-distance) form of education using the distance learning platform Neuron. Since 2021, it was realized on its own university platform LIKAR_NMU (https://likar.nmuofficial.com/), which is synchronized with automated control system (ACS).

It should be noted that distance learning technologies provide not equal opportunities for forming various components of the professional competence of the future doctors. Most of the difficulties arise in the formation of the practical component of professional competence, namely mastering clinical skills and practicing them on a patient, holding laboratory and instrumental studies, medical manipulations, personal communication with the patient when collecting an anamnesis, etc.

Students are allowed to practice in operating rooms, surgical dressing rooms, manipulation and resuscitation departments of hospitals if they have a document confirming their full course of vaccination or an international, internal, or a foreign certificate confirming vaccination from COVID-19 with a single dose of a two-dose vaccine (yellow certificates), or one dose of a single-dose vaccine or two doses of a two-dose vaccine (green certificates), or a negative polymerase chain reaction test result (valid during 72 hours). If these documents are not available or students are not able to get to the classroom, they have the opportunity to practice their skills in the university simulation center. The specificity of each clinical discipline should be taken into account in the process of developing special competencies, both directly at the patient's bedside and in the conditions of simulation classes at the department and simulation centers.

In the process of studying medical disciplines, it is compulsory to conduct training of clinical skills and constant monitoring of learning special competencies. The latter are defined in the relevant educational and professional programs (EPP) with the involvement of simulation teaching methods for at least 20% of the academic hours allocated in the working curriculum for practical classes during the current academic year. As shown by the authors in work [5], the simulation form of training is optimal for mastering the tactics of providing emergency and urgent medical care with scenario development in the emergency room and the cardiopulmonary resuscitation room.

Summarizing the practical experience and the results of the study of scientific sources, it is possible to define the main tasks of simulation training:

- ensuring the process of forming the practical component of the professional competence of students for higher medical education in simulation centers;
- shaping communication skills, comprehending the sequence of stages of the algorithm for providing medical care;
- formation of principles of work in a team;
- the use of phantoms (imitation models) in order to increase the level of learning theoretical material and mastery of practical skills;
- debriefing — the discussion of implementing scenarios, analysis of the team's actions (communication and interaction in a team, decision-making processes, the role of the leader, distribution of tasks, etc.);
- control of the completed educational material using tests, as well as with the use of computer simulation programs.

At present, one of the promising teaching technologies focused on the formation of practical component of the future doctors' professional competence is a range of modeling systems under the common name "virtual patient".

The results of the analysis of scientific works suggest that "virtual patient" simulators allow modeling the behavioral patterns of a future doctor and providing cognitive activities in several aspects [7]. First, it is an interception, that is the perception of a physiological phenomenon (e.g. symptoms), its interpretation and memorization. The next important aspect is decision making, that is the student's activity in solving a specific case with specific virtual patients and the characteristics of their physical and mental state. Another aspect is the formation the communicative component of the future doctors' professional competence, the perception of the patient's natural speech, understanding and correct interpretation of the doctor's communication with the patient. Moreover, the last but not the least important aspect is the receipt by the system of new knowledge, medical terms and phrases from the user and the formation of a certain ontology, the definition of concepts and their organization.

The example of a modeling system that has a multifunctional didactic potential for use in the process of professional training of future doctors is the *Body Interact* virtual patient simulator [10], running on the Body Interact Studio platform with educational process management capabilities. Using this simulator enables performing a physical examination of a virtual patient, monitoring changes in

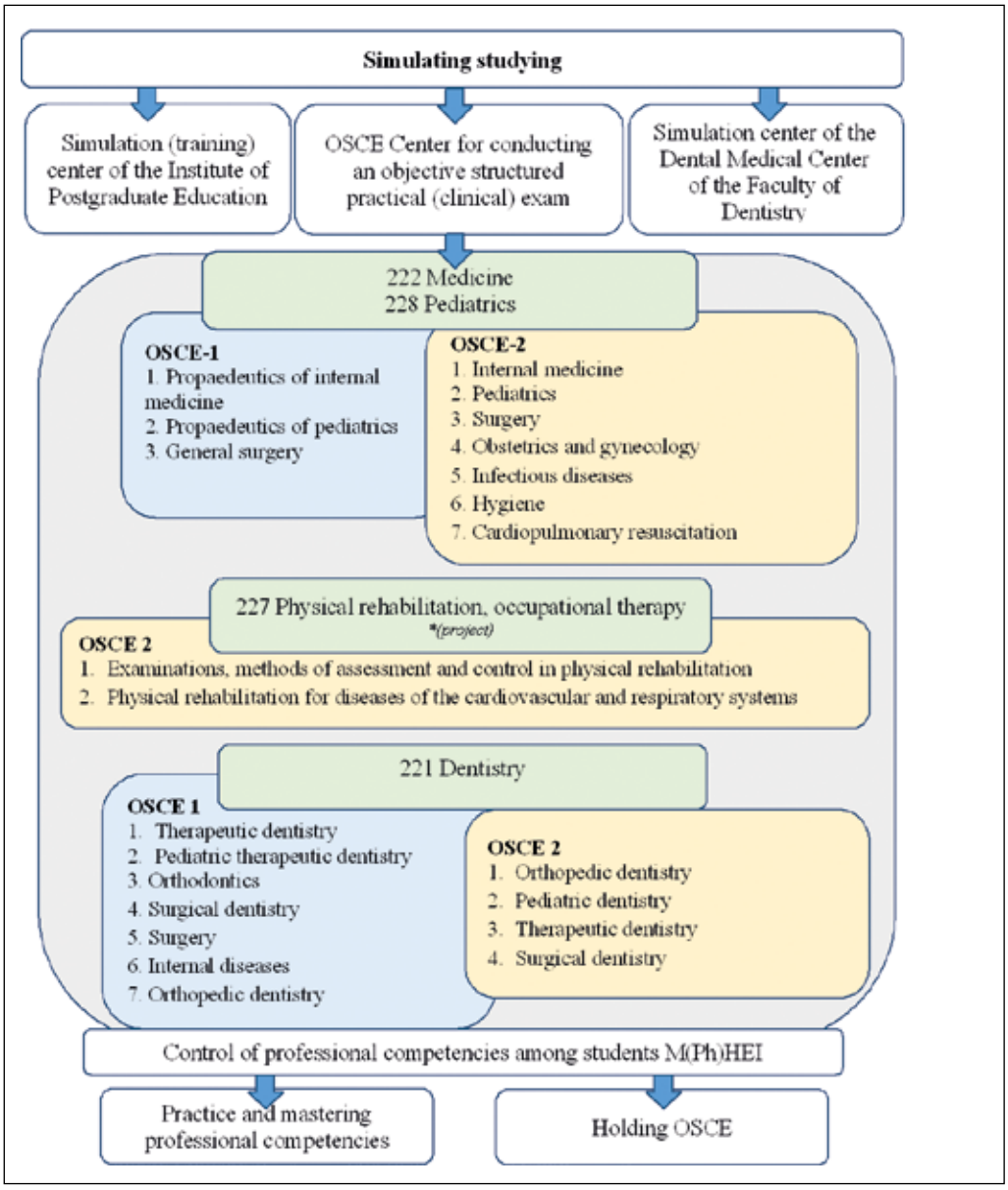

Fig. 1. Scheme of simulation training of Bogomolets National Medical University

their condition in real time, performing medical manipulations, and tracking reactions to treatment, thereby creating opportunities for improving diagnostic skills and decision making in various clinical cases.

Another widespread system for modeling a virtual patient is Academix3D [11] with a detailed description of the classification, pathogenesis, anamnesis, complaints, examination, symptoms, methods of diagnosis and treatment. The system includes the following seven sections: cardiology, pulmonology, nephrology, gastroenterology, endocrinology, rheumatology, and hematology. Similar to the previous simulator, it is possible to perform various manipulations with the patient (laboratory tests, diagnostic procedures, medical manipulations, etc.).

The organization scheme of Bogomolets National Medical University simulation training is shown at the Figure 1. Such organization is implemented in the simulation (training) center of the Institute of Postgraduate Education, the simulation center of the Dental Medical Center of the Faculty of Dentistry and the OSCE Center for conducting an objective structured practical (clinical) exam.

DISCUSSION

Establishing the level of formation of the student's clinical skills in accordance with the requirements of the higher education standard is done on the basis of grades obtained after passing a sequential chain of specially equipped standardized places (stations), where various clinical situations are simulated, allowing to check the individual elements of the practical component of professional competence. For the formation of a comprehensive assessment, the method of objective structured clinical examinations (OSCE) is used, which have been practicing at Bogomolets National Medical University since 2018.

To pass the exam, the students must go through specially equipped places (OSCE stations), where, for a short period of time (5-20 minutes), they have to interact with a clinical

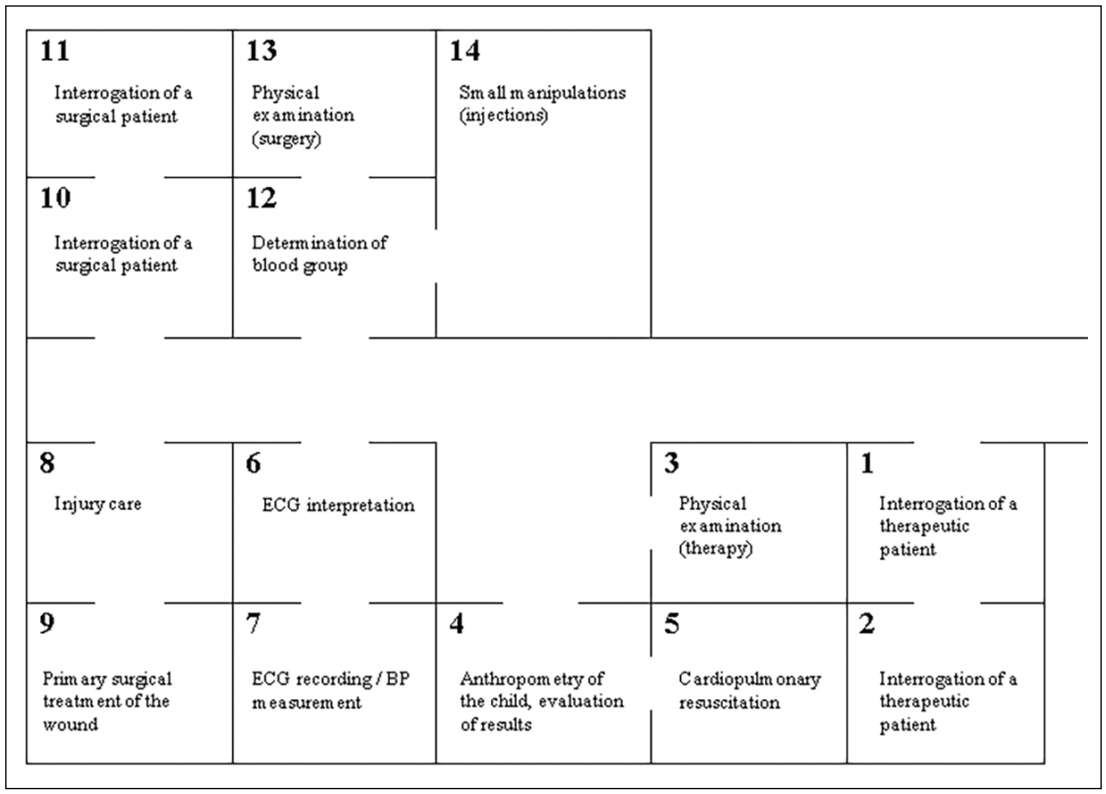

Fig. 2. Scheme of placement of stations for OSCE-1 of 222 medicine and 228 pediatrics specialties

task (OSCE-1) or a clinical situation (OSCE-2) according to a standardized scenario under close to real conditions. Based on the obtained results, the level of formation of the professional competence of the future doctors is assessed. The list of components of professional competence, the verification of which is submitted to OSCE-1 and OSCE-2, is approved at meetings of the relevant cyclic methodological commissions based on the current standards for training specialists and medical care. The departments prepare the methodological support of the OSCE: station passports (containing information about the general format of the station), accommodation and equipment, the process duration, instructions for students, instructions for teachers, instructions for standardized patients, visual materials, algorithm for performing a clinical task, and checklists.

For example, for OSCE-1 (Figure 2), which is based upon third-course students of 222 medicine and 228 pediatrics specialties, 14 rooms are used (where 12 therapeutic, pediatric, and surgical stations will be deployed among them).

Here are these stations in more detail:

THERAPEUTIC PROFILE – 5 STATIONS:

1. Questioning of the patient of therapeutic profile.

2. Physical examination of a therapeutic patient (student demonstrates one of the following professional competencies: pulse study, palpation of apical impulse, determination of relative dullness of the heart, auscultation of the heart, comparative percussion of the lungs, lung auscultation, deep sliding palpation of the sigmoid colon, deep sliding palpation of the liver).

3. ECG registration. Blood pressure measurement.

4. Interpretation of the ECG (student receives one standardized ECG from the following list: sinus tachycardia, sinus bradycardia, atrial fibrillation, atrial flutter, ventricular arrhythmia, atrial extrasystole, atrioventricular first-degree blockade, intranasal blockade, tunicular fibrillation, myocardial infarction).

5. Cardiopulmonary resuscitation.

PEDIATRIC PROFILE – 1 STATION:

1. Anthropometry of the child.

SURGICAL PROFILE – 6 STATIONS:

1. Questioning the patient of surgical profile.

2. Physical examination of a surgical patient (student examines a standardized patient who has one of the following symptoms of clinical situations: pain in the right iliac region, pain in the left iliac region, pain in the epigastric region, or pain in the right hypochondrium).

3. Small manipulations (student demonstrates skills of one of the following manipulations: intravenous, intramuscular, or subcutaneous injection).

4. Determination of blood groups by the AB0 system using coliclons.

5. Primary surgical treatment (PST) of the wound (two options: a cut wound received 2 hours ago or inserting and removing a nodal suture).

6. Injury care (one of the following options: stopping arterial bleeding with a tourniquet, stopping arterial bleeding with finger pressure on the artery, stopping venous bleeding with a bandage, immobilization of the upper and lower extremities with a pneumatic splint, applying a splint bandage in open pneumothorax).

For a student, the minimum percentage of points at each OSCE-1 station to pass the exam is 70%. There are also stations with red flags required to pass the exam, namely "Trauma" and "Cardiopulmonary resuscitation (CPR)". Without

successful completion of these stations, the exam cannot be passed by a student. The OSCE-1 exam is considered passed if a student has successfully gone through more than 9 stations (including two red-flagged ones) out of 12 [12].

The OSCE-2 exam is taken at the end of the 6th year (semester 12) under the conditions that are as close as possible to real clinical situations. Therefore, in the process of doing a therapeutic unit, the students solve tasks from the four stations, where specific clinical situations of a therapeutic kind are imitated. Here is an example of a general instruction that students receive while dealing with a therapeutic unit of the exam.

1. You open the therapeutic unit (consisting of 4 stations) dedicated to one nosological issue.
2. Greet those present.
3. Show an individual letter of passing the OSCE-2 stations.
4. Do not use non-regulated technical means.
5. Interview the patient (station 1).
6. Do a physical examination (using a suggested version of clinical competence), provided that you have previously completed the preparation of hands for the study (washing with soap; if necessary, treat your hands with an antiseptic) and analyze the proposed results of the physical examination (station 2).
7. Interpret the proposed results of laboratory and/or instrumental research methods, establish and formulate a preliminary diagnosis (in written form), select four most informative ones, and minimally necessary laboratory and/or instrumental research methods in order to confirm the diagnosis in a specific clinical situation (station 3).
8. Write a treatment plan for a patient according to the proposed clinical diagnosis with the definition of tactics, the appointment of non-drug and drug therapy (up to four most important drugs): indicate the group of drugs and write out prescriptions using international (non-proprietary) drug names (in Latin) indicating doses, ways in multiplicity reception, and (if necessary) the duration of treatment (station 4).
9. Finish each station at the sound signal.

The clinical situation, the variant of which deployed in the therapeutic unit, changes after two examination cycles (4 examination cycles take place in one day, each of them involves 13 students). This system helps to avoid disclosing information about the exam situations. The passing of one station takes 5 minutes (a unit contains from one to four stations), which allows to pass all the exam stations during a single 75-minute exam cycle,

CONCLUSIONS

Based on the generalization of experience, the main tasks of simulation training have been established. They are to ensure the process of forming the practical component of the future doctors' professional competence. Next, the technology for conducting an objective structured practical (clinical) exam has been developed. It helps to standardize the procedure for checking the level formation of the future doctors' clinical professional competence in accordance with the standard requirements to higher medical education.

The analysis of the didactic potential of "virtual patient" modeling systems and respective approaches to the organization of the educational process was carried out. It was demonstrated that the use of simulation training and "virtual patient" modeling systems increases the effectiveness of training, the interest of students and interns during their preparation as future healthcare professionals. Thus, it motivates them to develop necessary components of their professional competence as future doctors.

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ORIGINAL ARTICLE

NATIONAL EXPERIENCE OF CREATING AND IMPLEMENTING MEDICAL STANDARDS IN CASE EVIDENCE APPEARS «LATER» (DURING THE COVID-19 CORONAVIRUS DISEASE PANDEMIC)

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ABSTRACT

The aim: Identification of methodological processes to accelerate the development of clinical guidelines in an emergency situation (in particular, coronavirus disease COVID-19), analysis of the practice of implementing clinical guidelines and clinical pathway.

Materials and methods: The processes of developing COVID-19 clinical guidelines are described on the websites of the developers. Implementing the patient's own clinical pathway. Survey of 117 health professionals involved in medical care at COVID-19 on management information. A retrospective pragmatic study of organizational and clinical aspects of medical care for 9,259 patients over 18 years with COVID-19 from March 18, 2020 to March 31, 2021.

Results: Acceleration of the methodology of clinical guidelines, changes in legislation have contributed to the improvement of medical care for patients with COVID-19. Clinical pathway (CPw) professionals surveyed: 88.2% satisfied with the structure of CPw, 91.0% were in favor of local instructions and explanations, templates of registration forms, 72.7% needed on-the-job training, 78.1% needed training on medical features, 74.5% noted the positive impact of remote interaction, 61.6% required standard operating procedures. 9259 patients with suspected COVID-19 confirmed PCR in 55.2%. Among those checked, 31.2% of chest computed tomography confirmed pneumonia in 95.7% of CT; 9.3% were hospitalized; fatalities 5.5% of hospitalized or 0.5% of verified.

Conclusions: Changes in the methodology of clinical guidelines, changes in legislation, education based on clinical guidelines have contributed to improving the results of management in COVID-19.

KEY WORDS: Clinical guidelines, clinical pathway

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INTRODUCTION

In emergency cause by COVID-19 primary and hospital care physicians awaited scientific advice on effective treatment for rapid response. Instead of the traditional duration (12 to 36 months) of creating a clinical guideline, there is an urgent need to develop clinical guidelines and standards of care for COVID-19 to save lives and restore human health.

In Ukraine, the development of standards of medical care on the basis of evidence-based medicine was introduced as a result of the European Union's TACIS Program «Support to the development of medical standards in Ukraine» EUROPEAID–NICARE No. 2003/065-429 [1] taking into account the recommendations of the Council of Europe on the methodology of clinical guidelines on best medical practice [2].

THE AIM

Study and apply methodological processes to accelerate the development of clinical guidelines and medical standards in emergency situations, analysis of the practice of their implementation through clinical pathways.

MATERIALS AND METHODS

Carried an analysis of methodological approaches to accelerate the development of clinical guidelines described on the websites of organizations – developers of clinical guidelines and recommendations on coronavirus COVID-19, namely: World Health Organization [3], European Center for Disease Control and Prevention [4], NICE, UK https://www.nice.org.uk/covid-19 [5], SIGN, UK [6], US CDC [7], US FDA [8], US National Institutes of Health [9].

The applied approaches to the development of clinical guidelines and standards for COVID-19 in health care in Ukraine are analyzed, the results of accelerated development and implementation of regulations in the field of health care, including the clinical pathway, on the example of the State Institution of Science «Research and Practical Center of Preventive and Clinical Medicine» State Administrative Department, a Multidisciplinary Research and Practice of Health Care (MRPHC) intensive care.

The views of health professionals directly involved in health care on the implementation of the clinical pathway as part of management documented information have been studied. Of the 117 specialists involved, 110 agreed to answer the questions, including 46 (41.8%) doctors and

64 (58.2%) nurses. The questionnaire included questions about the importance and satisfaction of the medical staff with organizational measures in clinical pathway, satisfaction with the level of current knowledge and the importance of some forms of training. Data were collected and evaluated according to the method of two-dimensional analysis «importance – performance»; the degree of importance of the component was assessed on a 5-point scale.

Pragmatic retrospective study of organizational and clinical aspects of medical care for 9259 adult patients (over 18 years) who sought medical care from the MRPHC for the period from March 18, 2020 to March 31, 2021. Relative rates of hospitalization, calculated mortality, application of methods diagnostics. Medical interventions were performed with written informed consent. Data on medical care are included with the permission of patients / their legal representatives. Confirmation of the diagnosis of coronavirus disease and elimination of the virus in convalescents was obtained by testing for SARS-CoV-2 by PCR using the VD MAX diagnostic system. Computed tomography of the chest was performed at the discretion of the attending physician on the basis of clinical evaluation on the device «SOMATOM go Top». The Ethics Commission agreed on all interventions and calculations.

RESULTS

The COVID-19 emergency prompted organizations to develop clinical guidelines in a short time and to maintain proper quality [3, 5-9]. Most of the recommendations were based on previous epidemic experience and expert opinions.

With the first cases of COVID-19 in Ukraine, the approaches used by institutions of various states and international organizations to justify decisions in the field of health care. According to the results of such a study in Ukraine, «legislation has been changed, approaches to planning the transformation of the health care system to strengthen its resilience to epidemics of infectious diseases, quarantine restrictions and other measures have been justified, and standards of medical and pharmaceutical care have been formulated, identified priority areas for harmonization of health care practices with the best world approaches»[10]. The first medical regulations in January-February 2020 were prepared on the basis of WHO technical recommendations. In the first half of 2020, national standards for coronavirus disease (COVID-19) were updated several times a month (Table I). The 16th version is already in force at the time of writing; over time, the pace of revision of standards has slowed significantly.

The issue of treatment of patients with COVID-19, in particular with a severe and critical course, became acute. In Ukraine, by harmonizing approaches to international medical interventions, the use of unregistered and registered drugs is allowed for indications not specified in the instructions for medical use. [11-13]. Changes in legislation have opened access to medicines for patients.

As in most countries, Ukraine has a living clinical guideline «Clinical management of patients with COVID-19 (2021)» [14], developed almost a year after the national standards. The implementation of clinical guidelines in the MRPHC began with the assessment of its methodological quality using the AGREE II [15] (Table II).

At the national level, three documents were used: clinical guidelines, medical standard and protocol for prescribing drugs, in a health care facility their provisions are combined in a clinical pathway (CPw), in MRPHC supplemented by internal instructions, regulations and more [16,17]. CPw is updated in accordance with the orders of the Ministry of Health of Ukraine and scientific data (Table I). CPw determines the movement of the patient in contact with medical staff, includes coordination and organizational elements: institutional arrangement of the medical institution COVID-19, organizes anti-epidemic measures, informs doctors and nurses.Clinical decision support is structured as "advice", such as "COVID-19 Coronavirus Prevention Guide for Healthy and Contact Persons", "COVID-19 Case Detection", "SARS-CoV-2 Sampling and Transport Test Materials», «Determination of tactics of treatment of patients», «Procedure for dressing and removal of personal protective equipment», «Instructions for mobile medical team» and others. CPw COVID-19 together with national standards, also served as a basis for training medical staff of MRPZ and other medical institutions that joined the program of methodological support for implementation and clinical evaluation.

According to the results of the CPw survey, 97 (88.2%) people were satisfied with the structure of the CPW and 100 (91.0%) expressed a desire to use local instructions and clarifications, templates of registration forms. According to 80 (72.7%) training is required before the introduction of CPW. The need for additional training on the features of providing medical care to patients with suspected / confirmed COVID-19 was noted by 86 (78.1%) respondents. Remote interaction, namely: telemedicine counseling, obtaining results by the patient, receiving results from the patient, self-assessment of the patient according to the «Letter of Self-Control», was positively recognized by 82 (74.5%) respondents, including 68 (61.6%) standard operating procedures, such as patient care, inpatient monitoring, case registration and registration, etc.

During the period from March 18, 2020 to March 31, 2021, 9,259 patients with suspected COVID-19 applied to the MRPHC. During medical care, they performed 17087 tests for SARS-CoV-2 by PCR, ie 1.8 per patient with suspicion. Confirmation of PCR infection was obtained in 5,108 patients (55.2%). Patients with verified infection underwent repeated PCR testing for clinical signs of recovery to verify remediation.

Among patients with verified COVID-19, clinicians prescribed computed tomography of the chest to 1,594 (31.2%) patients, confirming pneumonia in 1,525 people (95.7% of CT scans). The share of CT scans surveyed among all those suspected of COVID-19 was 17.2%.

Due to the severe and critical course of coronavirus disease, 474 patients (9.3%) were hospitalized, 26 people died (5.5% of patients or 0.5% of those with verified COVID-19).

Table I. Parallels in the chronology of development and updating of regulations for medical care in coronavirus disease (details according to the official websites of the Ministry of Health of Ukraine https://moz.gov.ua/article/ministry-mandates/ and the register of medical and technological documents https://www.dec.gov.ua/mtd/home/)

Year, month	National standards number, decree number	Protocol of use of medicines number, decree number	Clinical pathway of the health care facility (own data)
	state level documents		
2020			
January	Jan 24 № 185		
February	Feb 25 № 552		
March	March 13 № 663		
	March 28 № 772		
April		Apr 02 № 762	
	Apr 09 № 827	Apr 10 № 852	
	Apr 23 № 953		
	Apr 24 № 961		v 1 Apr 24
	Apr 30 № 994		
May	May 12 № 1109		
	May 20 № 1227		v 2 May 22
June	June 16 № 1411		v 3 June 21
July		July 21 № 1653	
September	Sept17 № 2122	Sept 17 № 2116	v 4 Sept 25
October	Oct 27 № 2438		
November	Nov 09 № 2557	Nov 11 № 2583	v 5 Nov 11
		Nov 20 № 2693	
December	Dec 10 № 2869	Dec 31 № 3094	
2021			
January	Jan 07 № 10		v 6 Jan 12
			v 7 Jan 26
April			v 8 Apr 16
May		May 13 № 930	
	May 30 № 1056		
June			v 9 June 18
September	Sept 08 № 1907	Sept 20 № 1979	
	Sept 24 № 2057		
November	Nov16 № 2530	Nov 11 № 2495	

Table II. Results of the evaluation of the living clinical guideline "Clinical management of patients with COVID-19 (2021)" to AGREE II

Number of experts	Domains / Standardized score					
	Domain 1. Scope and Purpose	Domain 2. Stakeholder Involvement	Domain 3. Rigour of Development	Domain 4. Clarity of Presentation	Domain 5. Applicability	Domain 6. Editorial Independence
8	67,36%	54,86%	47,40%	60,42%	41,67%	18,75%

DISCUSSION

Our analysis of changes in the methodology of leading organizations for the development of clinical guidelines in the context of the COVID-19 pandemic showed primarily a significant reduction in development time to 2-3 months compared to the previously declared 12-36 months. It is recognized that with a constant desire to ensure the reliability of clinical guidelines and transparency of their development Rapid guideline methodology is possible if the acceleration or reduction of individual processes. A characteristic feature of the «rapid» clinical guidelines was the consensus between the scientific evidence base

and expert assessment as opposed to the previously common practice: there is no strict evidence base – no clinical guidelines. The need for flexible methodological techniques in an extreme pandemic emergency was also recognized. The main feature of the development of clinical guidelines and medical standards during the pandemic was the forced consensus of evidence-based medicine and expert method, which allowed to provide health professionals with best practices for a certain period of time to care for patients with COVID-19. The process of developing clinical guidelines has been accelerated by shortening, skipping, reorienting or parallel stages of work, while the «art of compromise» has limits, such as NICE: maintaining proper quality and safety of care through multidisciplinary development, systematic search and review evidence by several experts, constant updating of evidence, transparency of decision-making and meticulous reporting and analysis of the facts of medical care [5].

A certain sequence of development of documents from clinical recommendations and medical standard at the national level to the clinical path or other types of documented information (local protocol, standard work procedure) of the health care institution in accordance with DSTU ISO 9001: 2015. reflects the strategy of implementing coordinated approaches to health care [2]. In Ukraine, the development of health care standards based on evidence-based medicine and the SIGN 50 methodology has been implemented since 2006 as a pilot project, and since 2009 on a regular basis. The development procedure included stages: 1) search and selection of recommendations for adaptation with the evaluation of the prototype AGREE II, 2) translation and adaptation of clinical guidelines, 3) development of standard or unified clinical protocol, 4) external review, public discussion, 5) approval, 6) performance in health care facilities. The duration from the plan to the completion of development ranged from 24 to 48 months. In adapting the clinical guidelines, the developers identified drugs, diagnostic methods that could not be included in the standards for use in the health care system due to lack of authorization for use. In the first 2-3 months after the announcement of the pandemic, there was a heated discussion on the development of guidelines for physicians based on the expert opinion of experts, based on practical experience in the absence of rigorous scientific data. However, discussions in scientific and medical circles have concluded that expecting strong scientific evidence to develop a medical standard will do much more harm to patients' health and lives than using treatment recommendations that are largely based on positive experiences with certain technologies. And scientific data on this issue is gradually but steadily increasing, which has led to a rapid update of the governing documents, which have been updated up to 16 times in 18 months.

In turn, the use of recomendations set out in the clinical guidelines, adapted to local conditions, mastered by medical staff in the process of providing medical care with monitoring of their implementation, significantly improves the results of medical care. This statement is supported by a comparison of endpoints, such as mortality rates (0.5% of cases) among healthcare patients with a commitment to the local CPw and the national average (2.0%): in Ukraine as of March 31, 2021 according to the Ministry of Health of Ukraine https://www.kmu.gov.ua/news/operativna-informaciya-pro-poshirennya-koronavirusnoyi-infekciyi-2019-ncov-1-4-21 1691737 people fell ill with COVID-19, 33246 (2.0%) deaths were registered.

The importance of clinical guidelines and medical standards and supporting their further implementation through CPW. Our practice has proved that CPw is needed for continuous interdisciplinary integrated medical care, taking into account the staffing and resource conditions of the institution, coordination of interventions of medical professionals who provide primary, emergency and specialized (highly specialized) medical care. The difference from the previous experience before the pandemic was the dynamism, rapid constant updating of new scientific data of clinical guidelines and standards, as well as the use to raise awareness of such a relatively «narrow» issue – infectious disease management for medical staff of various specialties. The educational role of national clinical guidelines and medical standards has significantly increased. The staff of medical facilitys increased the demand not only for clinical guidelines, but also for organizational recommendations on anti-epidemic measures to protect health care workers and patients from COVID-19 infection, instructions on infectious safety and epidemic response directly in the medical facility.The results of the pragmatic study of some outcomes of CPw-based care not only confirmed the benefits of «documented» management, but also showed the need to maintain the availability of equipment for laboratory diagnostics, including PCR testing, adequate capacity per 2 tests per patient, equipment for special X-ray examination of the lungs, including computed tomography, based on the need for examination up to 20% of the population.

CONCLUSIONS

1. In the context of the medical and biological emergency caused by the COVID-19 coronavirus pandemic, there have been changes in the methodological approaches to the development of clinical guidelines and standards of care, in particular:

a) accelerate development by reducing, skipping or parallel implementation of individual stages, accelerating certain processes and methods,

b) the predominance of electronic «live» publications for dynamic updates, rapid changes in accordance with data updates.

2. A characteristic feature of the Clinical Guidelines for COVID-19 in a pandemic was the consensus of

evidence-based medicine and expert opinion, the priority of official recommendations of practical medicine for the diagnosis and treatment of diseases by consensus over their absence. before high-quality scientific evidence.

3. The compromise between evidence and expertise remained multidisciplinary and even increased the number of members of the working group to increase the reliability of clinical recommendations by accelerating the work of large forces in contrast to the methodological approach, which reduces individual stages of development. Confirmation of the recommendations remains unchanged as soon as evidence emerges from a systematic review of sources to identify and critically evaluate the evidence.
4. The need for timely, affordable and effective medical care for a large number of coronavirus patients in Ukraine has led to changes in legislation aimed at aligning with the world's best approaches to increase resilience to COVID-19: «emergency» drug use and flexible methodological approaches to development living clinical guidelines and medical standards.
5. National health recommendations and standards, local standards in the context of limited data contribute to improving health management outcomes through educational functions.
6. The implementation of recommendations and standards requires the development of clinical pathways in health care facilities and a detailed description of their implementation through internal instructions and regulations.

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ORIGINAL ARTICLE

DEVELOPMENT OF THE PUBLIC HEALTH SYSTEM IN THE CONDITIONS OF CURRENT CHALLENGES AND THREATS

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ABSTRACT

The aim: Analysis of the development and optimization of the public health system in the face of current challenges and threats.

Materials and methods: Bibliographic, information-analytical, statistical methods and content analysis were used in the study. An analysis of the regulatory framework for the development of the public health system, including WHO strategic documents and national legislation was conducted. A critical assessment of the pre-existing public health system under the Semashko model was provided. The main stages of development of the new public health system of Ukraine, it's structural, financial and economic, organizational and managerial, scientific and educational, information and communication aspects are described. Reporting materials of the Public Health Center of the Ministry of Health of Ukraine and regional health centers, the state institution «Center for Medical Statistics of the Ministry of Health of Ukraine» and state institutions «Laboratory Centers of Ukraine» were analyzed.

Results: The development of the national public health system in Ukraine is carried out in accordance with the main directions of state policy, recommendations of the WHO and other international organizations in health care and aims to ensure health and well-being, prevent and minimize the negative consequences of current challenges and threats to population health. The public health development strategy is defined and enshrined in the legal framework. Structural development includes the creation of a national, 23 regional public health centers, a network of local structures, their staffing, the formation of a network of training institutions and their continuous development. The organizational and managerial strategy provides coordination of activities, intersectoral and intersectoral cooperation, improvement of technological and resource provision of institutions and institutions of the public health system. Financial and economic activities include multi-channel financing of structures and public health activities. Information and analytical activities provide effective monitoring of health and well-being, obtaining organizational and managerial and government structures objective information for making sound management decisions.

Conclusions: Development of the national public health system in Ukraine and its optimization is carried out in accordance with the main directions of state policy, recommendations of the WHO and other international organizations in health care and aims to ensure health and well-being, prevent and minimize the negative consequences of modern challenges and threats to population health. Optimization of the public health system includes a number of measures of functional-structural, organizational-administrative, regulatory, financial-economic, scientific-educational, information-analytical nature, aimed at ensuring the implementation of the main operational functions of public health.

KEY WORDS: public health, functional and structural development, organizational and managerial, financial and economic, information and communication aspects

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INTRODUCTION

The strategic goal of health care systems is to ensure a high level of health and well-being of the population, which is reflected in a number of strategic documents at the international and national levels. To achieve this goal, it is necessary to understand and take into account the multifactorial nature of health, its perception as a result of complex dynamic influences generated by numerous determinants, awareness of health dependence on socio-economic, epidemiological, environmental context, etc.

Modern global processes show that health care systems face many complex challenges and new health challenges in the process. Healthcare systems should solve many difficult problems and face many complex challenges for public health, the answers to which must be substantiated and scientifically proven. Current healthcare challenges are manifesting at various levels, including global (COVID-19 pandemic, climate change, armed conflicts), regional (European aging, non-communicable disease epidemics, migration, etc.), national and local. However, many determinants of health are often beyond the control of the health sector, which can be influenced only by integrated direction of the various similar sectors.

The need for new approaches to health, new partnerships, strategies, mechanisms of action is growing in proportion to the growing interdependence of health and leading determinants in a complex health landscape. At the same time, the validity of development strategies and the sequence of their implementation determine the prospects for successful human development in the global, regional, national and local dimensions. In view of the above, the world community has outlined the trajectory of social development in the Sustainable Development Goals as part of the Development Agenda until 2030 [1,2].

It is known that only in the field of coordinated organized actions taken by government agencies and collective action of society as a whole, it is possible to achieve effective disease prevention, prolong life and improve public health. This approach to strengthening, preserving and protecting public health is implemented through public health services, which have been operating successfully for decades in many countries around the world.

In accordance with the world guidelines, Ukraine has developed a national Strategy for Sustainable Development until 2030, which is consistent with the global document and the Strategy for Sustainable Development «Ukraine – 2020» and the Renewed Strategy for Sustainable Development of the European Union. This document identifies strategic directions for long-term development for Ukraine and promotes the integration of sustainable development goals into national plans, strategies and programs. The strategy includes 17 goals. The goal 3 «Good health and well-being» contains a number of important objectives, including stopping the HIV/AIDS and tuberculosis epidemics, reducing premature deaths from non-communicable diseases, ensuring general quality immunization of the population, reducing tobacco consumption, etc [3].

The strategic European document «Health 2020. A European policy framework and strategy for the 21st century» mains the priority of public health development. Investments in the institutional structure of public health and strengthening organizational and stuff resources, improving health care, health promotion, and disease prevention are recognized as important aims. Traditional approaches include public health analysis, epidemiological surveillance, health promotion, prevention, communicable disease control, environmental protection and sanitation, disaster preparedness and response, health hygiene, etc. Modern approaches include social determinants, social health gradient and strategic management of health [4].

The European capacity building plan and public health services contain a forward-looking vision for public service in the 21st century and a base for action [5].

THE AIM

Analysis of the development and optimization of the public health system in the face of current challenges and threats.

MATERIAL AND METHODS

Bibliographic, information-analytical, statistical methods and content analysis were used in the study. An analysis of the regulatory framework for the development of the public health system, including WHO strategic documents and national legislation was conducted. A critical assessment of the pre-existing public health system under the Semashko model was provided. The main stages of development of the new public health system of Ukraine, it's structural, financial and economic, organizational and managerial, scientific and educational, information and communication aspects are described. Reporting materials of the Public Health Center of the Ministry of Health of Ukraine and regional health centers, the state institution «Center for Medical Statistics of the Ministry of Health of Ukraine» and state institutions «Laboratory Centers of Ukraine» were analyzed.

RESULTS

The analysis of normative and legal documents of the national level on the development of the public health system allowed to determine the strategic guidelines and tactical steps for the development of a new important area, their compliance with global and European trends.

According to legal documents, together with the State Sanitary and Epidemiological Service, public health functions were performed by other central executive bodies and local self-government bodies, including the Ministry of Education, Agrarian Policy, Infrastructure, Regional Development, Youth and Sports. state ecological inspection, state emergency service, etc.

The formation of a modern public health service in the context of reforming Ukraine's health care system take into account WHO recommendations and international experience. In accordance with the principles of Ukraine state policy and international documents signed by Ukraine, the country has begun construction of a new modern European health care system, which includes public health service as an integral part. The process of its formation involves studying and taking into account the positive experience of other countries and WHO recommendations. The National Reform Strategy for Ukraine 2015-2020 identified the public health care system development as one of its priorities [6]. The implementation of such important task must be carried out in accordance with the international documents, first of all with «Health 2020. A European policy framework and strategy for the 21st century».

The priority of public health building in Ukraine was enhanced by the adoption of a strategic course of European integration and signing of an association agreement between the EU, the European Atomic Energy Community and their member states. Article 22 «Public Health» of the Association Agreement between Ukraine and the EU provides that all participants will develop cooperation in the health care direction to improve its safety and human health protection as a precondition for sustainable development and economic growth [7].

The analysis of the legal framework showed the compliance of strategic documents at the national level with European and international ones. The implementation of the provisions of global and regional strategic documents in health care field and development of public health services is realized in the Concept of development of the public health system, approved by the Ukrainian government in 2016. The need for public health services development arise because of health condition of population in Ukraine, existing challenges and threats, directions of development strategy for the national health care system and international obligations [8].

The Semashko model's assessment of the existing public health system revealed a number of fundamental shortcomings and inconsistencies with its current challenges. It is known that Semashko model of health care system in Ukraine was characterized by centralization of management, state funding, extensive development of the network institutions. It was aimed at maintaining hospitals, focused mainly on treating patients with insufficient investment in prevention sector. In such conditions, the needs of a healthy population were not taken into account. That did not allow to control and influence on the incidence. The functions of the public healthcare system were divided among various services. The State Sanitary and Epidemiological Service took a key position and focused mainly on the control of infectious diseases by regulating risk factors and providing inspections of sanitary legislation compliance. At the same time, the implementation of epidemiological surveillance did not correspond to modern approaches. There was a lack of technologies to improve the health of the population. Total control of sanitary facilities has led to a deterioration of the business climate in the country and has not helped to reduce the incidence of the population. Insufficient attention has been paid to monitoring, analyzing and assessing the risks to public health. The extensive laboratory network had outdated laboratory equipment without of research quality control systems and standard operating procedures because of insufficient material support.

According to legal documents, together with the State Sanitary and Epidemiological Service, public health functions were performed by other central executive bodies and local self-government bodies, including the Ministry of Education, Agrarian Policy, Infrastructure, Regional Development, Youth and Sports. state ecological inspection, state emergency service, etc.

Public health functions were performed by other central and local executive organizations, including the ministries of education, agrarian policy, infrastructure, regional development, youth and sports, the State Environmental Inspectorate, and the State Emergencies Service together with the State Sanitary Epidemiological Service. However, effective interagency cooperation between State Sanitary Epidemiological Service and the Ministry of Health (MOH) of Ukraine was absent.

Significant problems of preventive services before the reform were the unstructured system of disease reporting; the existence of parallel surveillance systems for individual infectious diseases; lack of information systems for accounting, monitoring of diseases that operate in real time; insufficient funding of institutions; formal involvement of civil society, business entities, public and charitable organizations in the formation and implementation of public health policy; lack of integration of medical science into the world scientific space, etc.

Thus, the need to create a modern public health service in Ukraine was conditioned by the need for the system to be able to withstand the challenges and threats to public health. The Concept of development of the public health system 2016 defined the principles, directions, tasks, mechanisms and deadlines for the development of the public healthcare system. It aims to formulate and implement of effective public policies to maintain and enhance the health of the population, increase life expectancy and improve the quality of life, prevent disease, maintain an working age group and promote a healthy lifestyle in society. The organizational principles of the public health system define legality, intersectoral cooperation and coordination, setting priorities, efficiency, accountability and continuity.

The Concept envisages the creation of a multisectoral public health system with a coordinating role of the Ministry of Health; harmonization of its legal framework with European legislation; introduction of a multisectoral approach to problem solving; ensuring the functioning of the Public Health Center of the Ministry of Health; meeting the health, risk assessment and problem-solving needs of the population at the national and regional levels; ensuring centralization and decentralization; involvement of medical workers in the performance of certain tasks in the field of public health; setting priorities to ensure their priority funding; improvement of analytical and information components of activity, creation of information databases and information exchange system; formation of an interdepartmental coordination council at the Ministry of Health; introduction of mechanisms for financing the public health system, etc.

According to the Concept, the public health system was created as a component of the national health care system.

The organizational structure of the public health system is headed by the Center for Public Health of the Ministry of Health of Ukraine. The Public Institution «Public Health Center of the MOH» was established in 2015. The PHC is a sanitary and preventive health care institution, which main task is to provide active work in the field of public health. It conducts epidemiological surveillance (observation), laboratory activities, performs actions to protect the population from infectious diseases and non-communicable diseases, biosafety and biological protection, performs organizational and methodological functions in the field of public health. The main directions of the activities of the PHC include analytical-informational, laboratory-diagnostic, preventive-educational, organizational-methodical, scientific-practical, scientific, medical practice, research, consulting and publishing [9].

Structurally, the Center includes departments for support of reforms and regional development, development of educational programs and professional competencies, project management and international cooperation, communications and outreach, organization of surveillance, statistics and analysis, information systems, research, antimicrobial resistance and infectious control, coordination of programs for diagnosis and treatment of HIV, tuberculosis, viral hepatitis and opioid dependence, pharmaceutical management and stockpile management, development and monitoring of prevention programs and non-medical support, behavioral risk factors, MSME and emergency response, production and environmental factors work, legal support, as well as a number of reference laboratories, a branch of the Ukrainian Institute of Public Health Research [10].

The Center for Public Health has carried out a significant amount of work on the formation of the regulatory framework of the public health service at various levels of government and the implementation of tasks provided by the Concept of Public Health System Development. With his participation, the National Action Plan on Noncommunicable Diseases to Achieve Global Sustainable Development Goals, the Strategy for Ensuring Biosafety and Biological Protection on the Principle of Single Health for 2025, the National Strategy for Combating HIV / AIDS and Tuberculosis were substantiated and developed. and viral hepatitis until 2030, the National Action Plan for Combating Antimicrobial Resistance, approved at the government level, etc.

Given the epidemiological context, the Center for Public Health initiated and conducted an «Assessment of measures implemented in response to COVID-19». The key objective of the event is to review the health system's ability to respond to the COVID-19 outbreak and to identify practical ways to improve the ongoing response to the COVID-19 outbreak..

In 2021, at the initiative of the Center for Public Health in Ukraine, the Joint External Evaluation (JEE) was launched. It is a voluntary, joint, multisectoral process to assess a country's capacity to prevent, identify and respond quickly to public health risks and emergencies, regardless of their nature.

During 2016-2020, the regional development of the public health system was carried out. At the regional level, 23 public health centers have been established. Monitoring and evaluation departments have been opened in 18 public health centers, and immunoprophylaxis departments in 16 public health centers. The staff of 23 regional public health centers at the end of 2020 was 2153.5 units.

The Center for Public Health has prepared an operational guidance structure for the development and planning of regional public health programs.

At the initiative of regional public health centers, 13 regional programs were created, 5 of which were approved by regional councils. The main areas of regional public health programs are immunoprophylaxis and infection control, combating the spread of HIV / AIDS, combating the spread of hepatitis B and C, prevention of breast cancer among women.

In the framework of the project «Strengthening the implementation of the WHO Framework Convention on Tobacco Control in Ukraine» to improve cross-sectoral cooperation on tobacco control at the regional level and protect the population from the harmful effects of tobacco smoke in two regions approved Strategies and Action Plan for Tobacco Control 2021 – 2025.

Test operation of the Pathogen Control System was launched in three laboratories of the Center for Public Health.

Further steps in building and optimizing the public health system are related to the formation of a network of territorial Centers for Disease Control and Prevention. The creation of a network of territorial CDC began in accordance with the Government resolution and order of the MOH in 2021 [11].

The Chief State Sanitary Doctor of Ukraine, who is the Deputy Minister of Health, heads the management vertical in the public health system according to the draft law of Ukraine «About the Public Health System» [12].

Addressing financial and economic issues has been an important aspect of building a public health system. Given the multifaceted and diverse activities of public health centers at different levels of government, its funding requires significant economic resources. A multi-channel mechanism was used to address funding issues. According to reports from regional public health centers, their funding system is hybrid and in 2020 contained 5 sources of funding, including state budget (55%), regional budget (15%), National Health Service of Ukraine (23%), Global Fund (7%), own revenues (0.001%).

Along with structural, organizational, managerial and financial and economic transformations, considerable attention is paid to the formation of its staffing in the process of building the public health system. The specialty «public health» was included in the list of fields of knowledge and specialties in which higher education students are trained since 2017.

Educational standards for the training of bachelors and masters of public health were developed by working group of the MOH.

Educational standards for the training of masters of public health were approved by the Ministry of Education and Science of Ukraine in 2018. Educational standards for bachelors of public health were approved in 2020. Educational standards for the training of doctors of philosophy in public health are undergoing final examination and were developed in 2021.

Training of bachelors of public health was started in Ukraine since 2018, and training of masters of public health was started since 2019. Bogomolets National Medical University was one of the first educational institution in Ukraine, which received licenses to train bachelors and masters of public health [13,14]. Six higher education institutions had licenses to train bachelors and thirteen education institutions had a license to train masters of public health in 2021.

Some amendments had drafted to the National Classifier of Ukraine «Classifier of professions» to include new professions «environmental and health specialist» and «public health specialist» in order to employ graduates of higher education institutions in the field of public health.

Scientific support for the development and operation of the public health system is provided by scientific institutions subordinated to the Center for Public Health and the Ministry of Health of Ukraine, including state scientific institutions of hygienic and epidemiological profile.

Information and analytical activities of the public health system include the collection and processing of information for the formation of the public health information fund, preparation and publication of periodic reports on health status, sanitary and epidemiological situation and environmental indicators, etc. Data from more than 30

reporting forms are subject to analysis, including on diseases of socially significant and socially dangerous diseases.

To ensure uninterrupted monitoring and analysis, it is necessary to continue subventions from the state budget for regional public health centers and to develop appropriate regulations, taking into account all existing risks.

To improve communication with all stakeholders in public health, the Center has developed a draft Communication Strategy on Priority Public Health, which is in the process of being agreed.

In the context of international cooperation in solving public health problems, close cooperation with international public health organizations and foreign partners is maintained, development and revision of existing regulations in order to harmonize European Union legislation in the field of public health and sanitary legislation. . Attracting international technical and financial assistance for the implementation of priority projects in the field of public health in Ukraine is carried out within the framework of projects of the Global Fund, the European Union, other partners and donors.

DISCUSSION

Analysis of the development and optimization of the public health system in Ukraine shows the progressive nature of development, compliance with strategic documents of international and national levels and validity given the current nature of the challenges and threats to public health. The European Action Plan on Capacity Building and Public Health Services states that public health systems in individual countries of the WHO European Region have significant differences in organizational and structural models, governance, funding, staffing, etc. [5]. Ukraine has formed a national public health system in accordance with internationally recognized strategies, which are reflected in a number of documents of the WHO, WHO / Europe and other international organizations [1,2,4]. The substantiation of the functional-structural model took into account the national features of the health care system, the existing challenges and threats to public health, the possibility of minimizing them. The study and use of foreign experience was important.

As a result of the long process of formation and improvement of the public health system, a functional-structural model was created, which ensures the implementation of the main operational functions of public health, including epidemiological surveillance and assessment of health and well-being of the population, monitoring and response, including in emergencies, protection and promotion of health, prevention of diseases, etc. They are provided by an extensive network of public health institutions at the state, regional and local levels, their optimal organizational structure, multi-channel funding, strategic management, training and continuous development, and more.

Crucial was the formation of the legal framework for public health services at various levels of government. A number of regulations, strategies and programs have been approved at the governmental level. The active work of regional public health centers has contributed to the adoption of important regional programs on topical issues of public health and well-being. The introduction of multi-channel financing helped to solve economic problems during the development of the system. The training of bachelors and masters of public health by universities, along with the use of existing medical and preventive staff, the introduction of training and other forms of continuing professional development have helped to solve staffing problems.

Extensive international cooperation, participation in international projects and support of international organizations play an important role in the processes of optimizing the national public health system.

CONCLUSIONS

The development and optimization of the public health system in Ukraine was based on the socio-economic, epidemiological, environmental context, existing challenges and threats to the health and well-being of the population. The development of the public health system is carried out in accordance with the principles of state policy of Ukraine and international documents signed by Ukraine, taking into account the recommendations of the WHO. The country has defined and approved a strategy for public health development, formed a regulatory framework, built a network of public health institutions at various levels of government, conducts training and research, develops intersectoral cooperation and international cooperation. The system is able to implement the basic operational functions of public health.

Important tasks for the future are further development of the legal framework of the system, improvement of technological and resource provision of public health, adoption of the Law of Ukraine «On Public Health» and implementation of its provisions, development of intersectoral and international cooperation in public health.

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ORIGINAL ARTICLE

CURRENT CHALLENGES FOR THE HEALTH CARE SYSTEM DUE TO THE LACK OF MEDICAL STAFF AND THE CONTINUOUS PROFESSIONAL DEVELOPMENT OF DOCTORS

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ABSTRACT

The aim: Research of the ways of adequate solving of problems with understuffed healthcare system and problems with continuous professional development of doctors.

Materials and methods: We have used a official statistical data for the period from 2009-2020 years. This data was analyzed with usage of systemic approach and statistical epidemiological analysis.

Results: According to the data from Ministry of Health of Ukraine during the first year of the pandemic (2020) the quantity of our doctors has diminished by 6.9 thousands, and quantity of nurses – by 22,5 thousands which is much bigger deficit then in period of 2018-2019 years. The insufficiency of pediatric doctors in Ukraine has reached 1000 vacancies, general physicians – 1700, family doctors – more than 3000 vacancies, surgeons – more than 950 vacancies. It is also important to involve medical experts and medical associations and unions in the process of accreditation and licensing of providers of continuous medical education.

Conclusions: Existing deficit of medical personnel should be replenished by increasing of medical education of students in medical universities and colleges funded by government. Existing system of continuous professional development of doctors requires a lot of changes (additional activities, new technologies) which must be implied with the help of professional medical associations and unions.

KEY WORDS: medical staff, continuous medical education, COVID-19

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INTRODUCTION

There is a great insufficiency of medical personnel in Ukraine due to pandemic of Covid-19, war conflicts and natural disasters. No doubt that such situation has a great influence on people's access to the medical help, especially in countries with low or middle low economy [1, 2]. Emergency care and pediatric healthcare system are suffering most from those factors. According to the WHO analysis, financial investments of the government are crucial for efficiency of healthcare system in case of different emergency situations and pandemic COVID-19 [2].

Also it is important to establish a adequate system of continuous medical education which includes medical and non-medical trainings, communicative and management skills [3, 4]. Such necessity was declared by doctors themselves. But quite often such continuous medical education is limited by insufficient of time or financial resources of doctors in Ukraine [5].

In European countries continuous professional development of doctors (CPD) is strongly supported by government laws. It is important because the quality of CPD has a direct influence on quality and accessibility of medical help in the country.

A positive progress in development of continuous professional development of doctors in Ukraine was in its connection with European accreditational council of continuous medical education (EACCME). Such direction of development of a system of continuous medical education must be discussed with professional medical associations and different unions of Ukrainian medical doctors for creating a common policy for establishment and providing a proper quality of continuous medical education.

THE AIM

Research of the ways of adequate solving of problems with understuffed healthcare system and problems with continuous professional development of doctors.

MATERIALS AND METHODS

We have used a statistical data from Center of medical statistics of Ministry of Health of Ukraine for the period from 2009-2020 years. This data was analyzed with usage of systemic approach and statistical epidemiological analysis.

RESULTS

Ukraine take a 38th place in European region by the level of sufficiency of doctors and nurses in hospitals [6]. This situ-

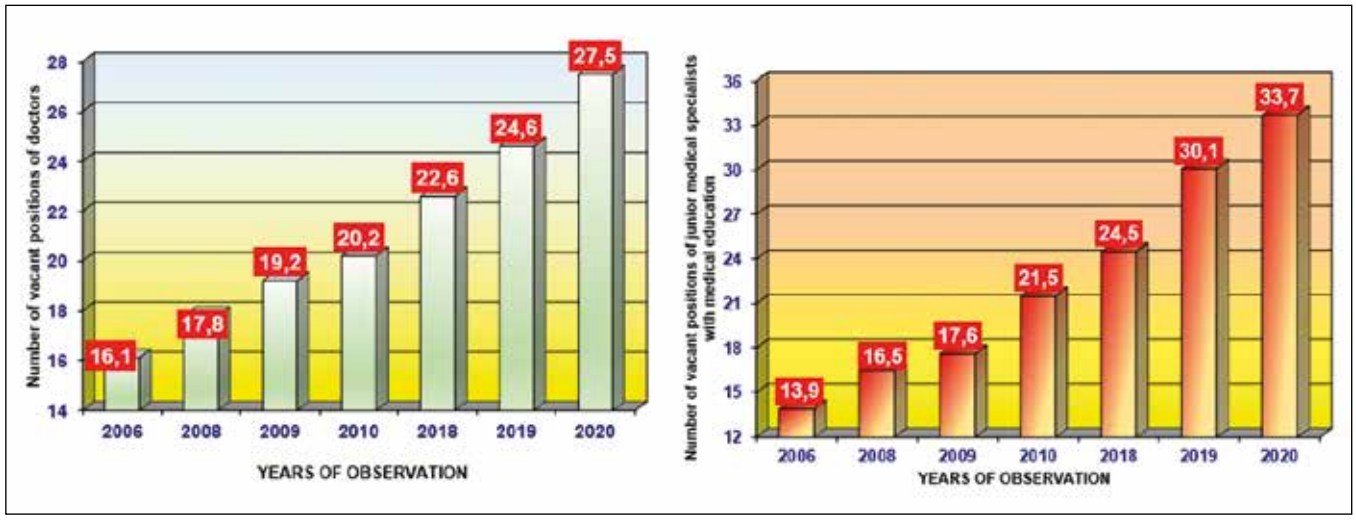

Fig. 1. Increasing of personal deficiency of doctors and nurses in period from 2006 till 2020 (in thousand).

ation is engraved with decreasing of education of medical personnel in medical universities and colleges throughout last 5 years. It is explained by creation of additional difficulties in admission of medical students in universities for so-called «improvement of quality» of future doctors.

According to the data from the center of medical statistics of Ministry of Health of Ukraine on 31.12.2020 we have 147361 doctors and 273526 lower medical personnel working in our healthcare system [7]. But during the first year of the pandemic (2020) the quantity of our doctors has diminished by 6.9 thousands, and quantity of nurses – by 22,5 thousands which is much bigger deficit then in period of 2018-2019 years (pic. 1). Statistical gap between existing vacancies and physically existed working medical workers is 34537 persons. Quantity of medical stuff working additional medical vacancies is 7004, with coefficient 1,1.

The level of sufficiency of medical doctors on 10,000 of population is 35,6, which is decreased on 1.4% in comparison with 2019. The level of sufficiency of nurses in Ukraine is 66.0 on 10,000 of population (in 2019 – 70,9). Sufficience of working medical personnel in Ukrainian hospitals is 81.0% which is less in comparison with data from 2019 (82,7%). This tendency is describing a decreasing of medical personnel in Ukrainian hospitals very clearly. The same tendency also includes decreasing of nurses to 88.5%, which is less for 0,7% in comparison with data from 2019.

The quantity of physicians, who are directly involved in providing of medical care for the population (excluding administration, dentists, statistical workers) was 100436 or 24,3 on 10000 of population (in 2019 – 24.7). Such level of quantity of physicians is quite similar to same level in USA, but lower than the level in Europe. For example at 2017 a quantity of doctors in Sweden and Finland was nearly 33 for 10000 of population, in France and Germany – 34, in Italy – 37, in Norway – 38, in Latvia – 31, in Great Britain – 23 and in Poland – 20 [7].

The insufficiency of pediatric doctors in Ukraine has reached 1000 vacancies, general physicians – 1700, family doctors – more than 3,000 vacancies, dentists – more than 1,000, surgeons – more than 950 vacancies.

The most difficult situation with understuffed hospitals is in the east cities of Ukraine, where still exists a danger of a war conflict. This has led to a decreasing of access and quality of medical care in those cities.

Coefficient of comparison in quantity of doctors and nurses in Ukraine is 1:1,9, which is lower than the same coefficient in European countries (1:2,4). This could be easily explained by decreasing of education of students and migration from cities, ravaged by war.

In 2020 in medical universities of Ukraine were studied 56.4 thousand of students. Only 23.5 thousand of them were sponsored by government and 32,9 thousand were funded by private institutions or persons (mostly dentistry and pharmacy faculties). In 2020 from Ukrainian medical universities where graduated 11.8 thousand of young specialists (in 2019 – 11,3 thousand). In 2021 only 160 students where accepted at the first course of pediatric faculties of Ukrainian medical universities.

In 2020 in specialized medical colleges were studied 49 thousand of students, which is less then in 2019 (52 thousand). In 2020 where graduated only 15.6 thousand of nurses (in 2019 – 16,8 thousand) [7].

DISCUSSION

The direct citation from article "Personnel resources of healthcare system of Ukraine. Systematic analysis. Project USAID": "The reserve of the students of such specialties as "general medicine" and "nursing" is insufficient for sustaining quantity of workers in healthcare system when old doctors will be retired. There is only one currently studying student for three retired doctors. The same situation exists in case of nurses: one student per 4 retired nurses. On other hand, we are observing an increased quantity of nostrification applications in our medical universities for the specialists who has departed in foreign countries [8].

So we can come to conclusion that current status of healthcare system in Ukraine has such features:

- Decreasing quantity of walking doctors and uncontrolled immigration and retirement of medical specialists;

- Decreasing of prestige of medical and nursing specialties;
- Decreased amount of students in medical universities and colleges of Ukraine;
- Decreased amount of doctors and nurses in rural regions;
- Increased imbalance between different medical specialties and quantity of doctors and nurses in big cities and rural regions.

All those problems with additional negative influence from pandemic situation with Covid-19 and war conflict have become a great danger for our state. They should be solved by raising a prestige of medical specialties, increasing salaries of doctors and nurses and proper modern continuous medical education.

According to the data from WHO, general quantity of medical care workers in European region was 12.7 million. Analytical prognosis for 2030 predicts an increasing of this quantity to 16.8 million of medical care workers [9].

Answering the challenges of pandemic situation, some countries from Organization of economic cooperation and development (OECD) already created different policies which allow facilitated migration and accommodation of medical workers from other countries to cover their deficiency in medical personnel. But such policies do not answer the question about functioning of Healthcare systems of countries from where is ongoing emigration of doctors.

Without stabilization of deficiency of medical personnel and increased amount of medical students in medical universities and colleges of Ukraine, we cannot create a proper and accessible medical care for our people. Also it would be very hard to provide proper medical care in case of different pandemics or any other emergency medical situations.

Current pandemic situation due to Covid-19 has created different difficulties for education of medical students because of necessity of distant education, but in the same time it promotes a development and implementation of modern technologies in educational process in medical universities of Ukraine. During the time of pandemic situation with Covid-19 medical universities and colleges have established new technological approach for distant educational process [10]. But level of education of young medical specialists will be quite low without proper medical practice and offline practical lessons [11]. It is unacceptable in our age of modern medical technologies and high expectations of our people for proper adequate medical help.

There are different approaches to continuous medical education throughout the world [5,9,12,13]. In Ukraine and in some other European countries doctors could be accepted for prolongation of their license only after accumulation of necessary quantity of points (credits) of continuous medical education. Search points are received by participation of doctors in different educational activities, medical conferences, educational medical courses etc. All those activities are needed for increasing the proficiency of doctor and his level of competence in his specialty. In Ukraine this process is controlled by the Ministry of Health, while in Europe it relies on professional medical associations and unions.

Modern continuous medical education must be individualized and directed on self-improvement of a doctor. According to the data from Ministry of Health of Ukraine (2019) the doctors where interested mostly in such educational activities as congresses, conferences, seminars, simulation trainings, clinical stages, distant online courses and courses of thematic improvement.

No doubt, that the main part of continuous medical education relies on individual education and self-improvement of a doctor, which must be connected with his own necessities and interests in medical education and acquiring new qualifications and competencies. That's why doctor's feedback is quite important for continuous medical education providers to create a proper medical content [12, 13].

Another part of continuous medical education is connected with necessities of hospitals (opening of new units, acquiring of new medical technologies).

Modern continuous medical education includes a lot of new modern forms of studying such as master-classes, simulation trainings, thematic schools, seminars, discussion clubs, and long educational courses with involvement of distant digital technologies. There is also a possibility to study with the help of internet resources, different web channels, YouTube channels etc [14]. Modern popular educational courses may include technology of modeling of situations [15].

We must admit, that part of this educational activities are funded by doctors themselves which has its own influence on a motivation for participation in such activities of continuous medical education.

We have come to conclusion that the most important thing in continuous medical education is its practical efficiency without necessity for mindless collection of CPD/CME certificates. That's why accreditation and licensing of different providers of continuous medical education is quite necessary.

It is also important to involve medical experts and medical associations and unions in the process of accreditation and licensing of providers of continuous medical education. Plus, such evaluation must include different other factors such as individual self-evaluation, checking of CPD portfolio and examination of practical skills of a doctor.

CONCLUSIONS

1. Existing deficit of medical personnel should be replenished by increasing of medical education of students in medical universities and colleges funded by government.
2. Existing system of continuous professional development of doctors requires a lot of changes (additional activities, new technologies) which must be implied with the help of medical experts and representatives of professional medical associations and unions.

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ORIGINAL ARTICLE

NATIONAL HEALTH EXPENDITURE TRENDS, 2000 TO 2019

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ABSTRACT

The aim: To assess the long-term dynamics of health spending in Ukraine from the standpoint of readiness to make progress in the universal health coverage (UHC)

Materials and methods: Data from the Global Health Expenditure Database, European Health for All database, World Bank Open Data, collected during 2000-2019 were used. The research was conducted using bibliosemantic, historical methods and benchmarking.

Results: All indicators of health spending in Ukraine showed some growth: total and government health spending of % Gross Domestic Product (GDP) by 34% (95% CI 13-55) and 28% (95% CI 8-48), total and government health spending per capita in US $ by 7.1 and 6.5 times and in Purchasing power parity (PPP) – by 4 and 3.8 times. Growth was interrupted during the global (2008) and national (2017-2019) financial crises. Out-of-pocket spending in Ukraine grew and amounted to 51.1% in 2019, which is by 2.1 times more than in the European region – 24.0% (15.5; 36.6). In 2019 Ukraine ranked among 10% of the countries with the worst combination of government health spending per share of GDP and share of OOPS in total health spending.

Conclusions: The study found an unsustainable upward dynamic in health spending. In the last decade, there has been a clear trend towards an increase % OOPS in total health spending against low, aimed at reducing government health spending as % of GDP, which could negatively affect UHC.

KEY WORDS: health spending of % GDP, health spending per capita, % OOPS, universal health coverage

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INTRODUCTION

Universal health coverage (UHC) is being of critical importance for achieving any country's sustainable development goals. A key role in achieving this is played by sustainable funding systems, which, despite all the difficulties, are able to mobilize the necessary health care funds from public and quasi-public sources, reducing the burden of personal costs and thus increasing access to health care, especially for vulnerable groups of people [1].

Achieving UHC requires increasing health funding, especially in low- and middle-income countries [2] and reducing the share of out-of-pocket health payments. (OOPS), which remains the main financial barrier along the way [3]. The UHC problem is even more pressing in the wake of the COVID-19 pandemic, which has been the worst economic shock in decades [4].

The last long-term analysis of health spending in Ukraine.was completed in 2013 [5]. More recent studies of this kind have not been conducted in the country.

THE AIM

To assess the long-term dynamics of health spending in Ukraine from the standpoint of readiness to make progress in the universal health coverage.

MATERIALS AND METHODS

This study accessed health spending data that were pre-collected and pre-summarized by the WHO in the Global Health Expenditure Database (https://apps.who.int/nha/database). This accessed database contained materials representing comparable data for 192 countries over 20 years (2000-2019), each of which, according to the World Bank, is classified into specific income group – with high, upper-middle, lower-middle and low incomes. Ukraine's Health Expenditure profile (https://apps.who.int/nha/database/country_profile/Index/en) was also analyzed to describe the situation in detail. The information base of the study was supplemented by the materials of European Health for All database (https://gateway.euro.who.int/ru/datasets/european-health-for-all-database/); World Bank Open Data (https://data.worldbank.org/), State Statistics Service of Ukraine (National Health Accounts of Ukraine – http://www.ukrstat.gov .ua /) and working materials on budget expenditures on health care of one of the regional health departments. An analysis was made of total and government health spending as a % of GDP; total and government health spending per capita in US$ and in Purchasing power parity – PPP (current international $); share of health expenditures from different sources of funding; primary health care spending per capita (US$).

The study used bibliosemantic, historical methods and benchmarking.

Statistical processing of results was performed with STATISTICA 6.1 (StatSoft Inc, serial number AGAR909E-415822FA) and Excel-2010, using methods of parametric and non-parametric statistics, time series analysis. To describe the normal distribution of the sample data we used the arithmetic mean (M) with a 95% confidence interval (95% CI); for asymmetric distribution we used median (Me) with interquartile range (25%; 75%). For relative values, 95% CI was calculated using the adjusted Wald method. The relationships between the variables were evaluated using Pearson's correlation coefficient (r). The critical value of statistical significance for all types of analysis was taken at the level of $p < 0.05$.

The study has a positive response on the use of research methods from the commission on bioethics (minutes of the meeting of the commission on biomedical ethics of the Dnipro State Medical University №5 from 07.02.2022).

RESULTS

The level of national health spending, calculated in % of GDP, is considered one of the key indicators of social development. Total health spending (THS) as a % of GDP in Ukraine averaged 6.7% over a 20-year period (6.05; 7.12), growth by 34% (CI 95% 13-55); government health spending (GHS) as a % of GDP – 3.5% (3.23; 3.69), growth by 28% (CI 95% 6-48) (Fig. re 1).

Fig. re 1 shows that the dynamics of total and government spending (% of GDP) for the observation period was not linear, but was characterized by a number of extreme points, when periods of growth were alternated with periods of decline due to features both of internal and external financial and economic situation. For two decades in trends THS (% of GDP) conditionally one can distinguish 5 periods: 1st (2000-2003) – growth (126.9%; from 5.3% to 6, 6% GDP), associated with the strengthening of the national economy; 2nd (2004-2006) – relative stability (97%; 6.2÷6.4% GDP), 3rd (2007-2008) – decline due to

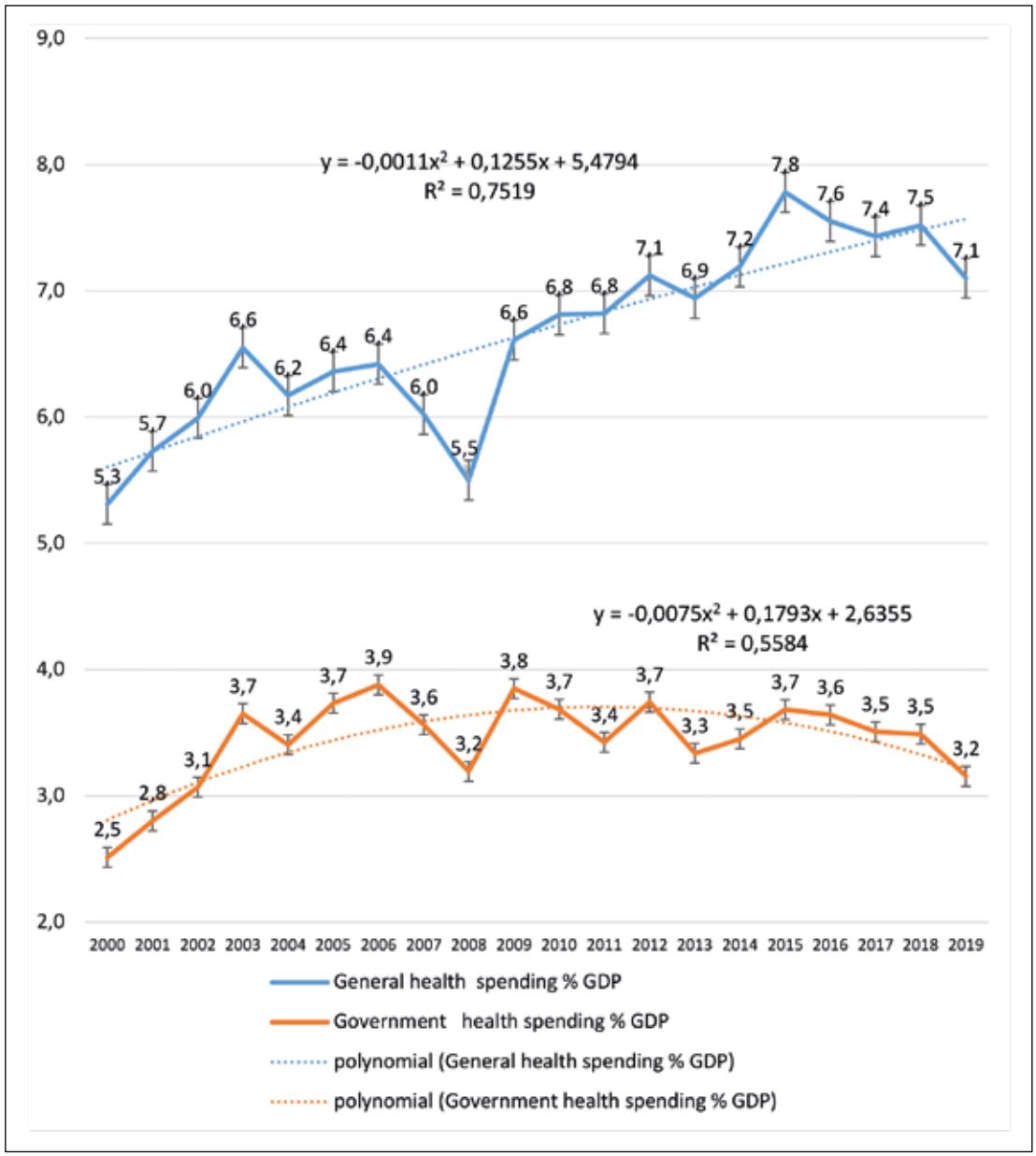

Fig. 1. Dynamics of total and government health spending as a % of GDP in Ukraine for the period 2000-2019
Note. R2 – Reliability Approximation

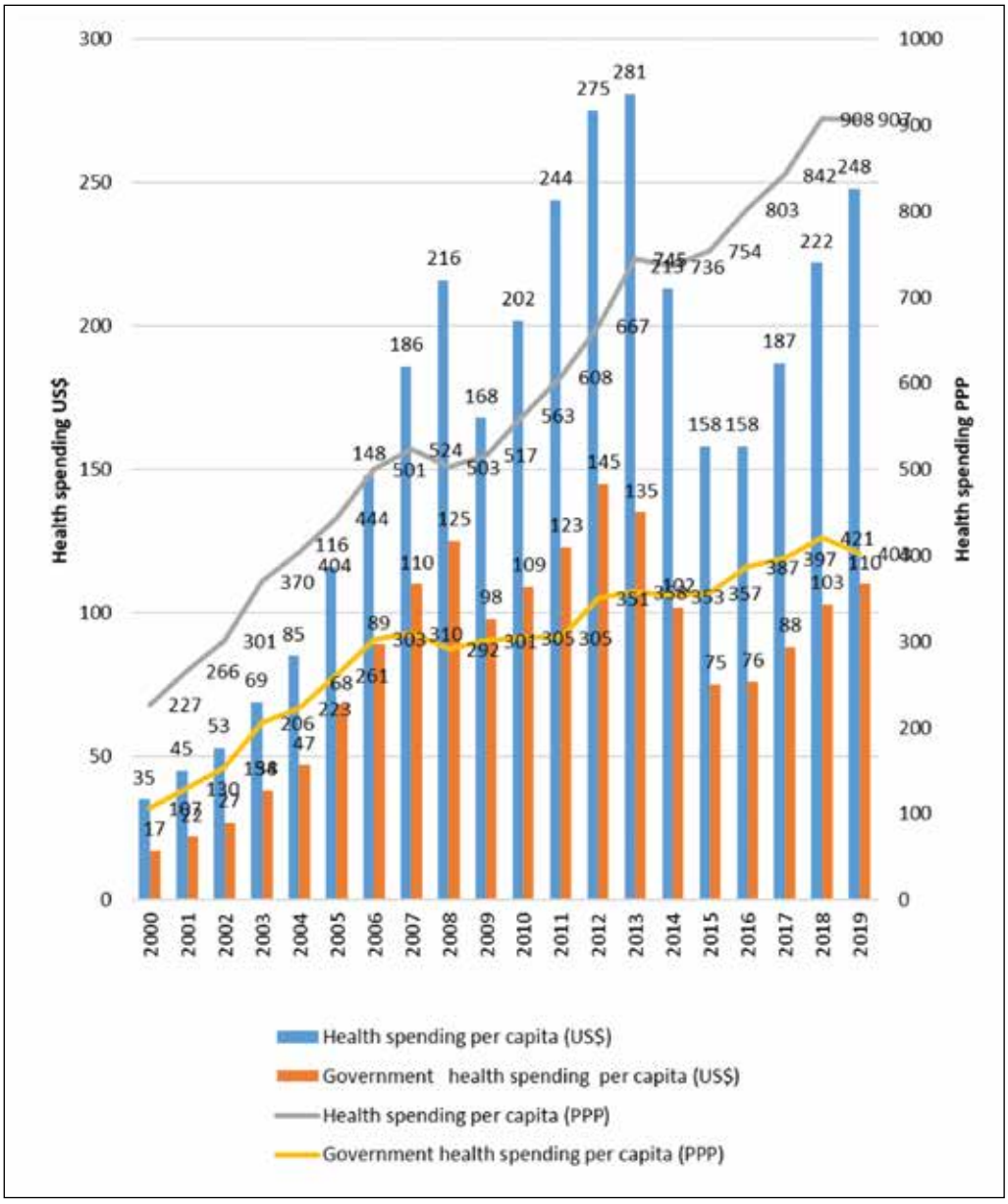

Fig. 2. Dynamics of total and government health spending per capita in Ukraine (in US $ and PPP), 2000-2019

the global financial and economic crisis (85.9%; from 6.4% to 5.5% GDP); 4th (2009-2015) – post-crisis recovery and growth (121.9%; from 5.5% to 7.8% GDP); 5th (2016-2019) – a slow decline, determined by revolutionary events and by the military conflict in the east of the country (91.0%; from 7.8% to 7.1% GDP).

The dynamics of changes GHS (% of GDP) had some differences. The number of periods decreased to 4 due to the extension of the 1st period of growth (2000-2006 – 156.0%; from 5.3% to 6.6%), when the positive trend of the general economic situation was supported by increasing the priority of health care in government spending. Other periods coincided with the dynamics of THS (% of GDP), but the depth of change was greater (Table I). Between the THS and GHS (% GDP) the relationship is average ($r = 0.56$; $p < 0.05$).

THS (% of GDP) in Ukraine, which belongs to the number of countries with incomes below the average, in 2019 amounted to 7.1%. According to this indicator, Ukraine occupied the middle position (28th rank) among 53 countries in the European region. Compared to the CIS countries, which included countries with different income levels (upper-middle, lower-middle, low income) THS (% of GDP) in Ukraine was by 16.3% (95% CI 5-37) higher, almost identical for the European region – 7.11 (6.18; 9.14) and lower by 10% (95% CI 0-20) compared to EU countries, all of which, except Bulgaria, belonged to high income countries.

According to the GHS (% of GDP) Ukraine's ranking was much lower – 43rd (3.15% of GDP). In general, GHS (% of GDP) in Ukraine was by 31.25% (95% CI 5-67) higher compared to CIS countries and by 1.56 and 2.37 times lower compared to European region and the EU countries (Table II).

Over a 20-years' period (2000-2019) in Ukraine THS per capita (US $) increased by 7.1 times (from 35 to 248 US $ per capita); GHS per capita increased significantly, although slightly less – by 6.5 times (from 17 to 110 US $ per capita).

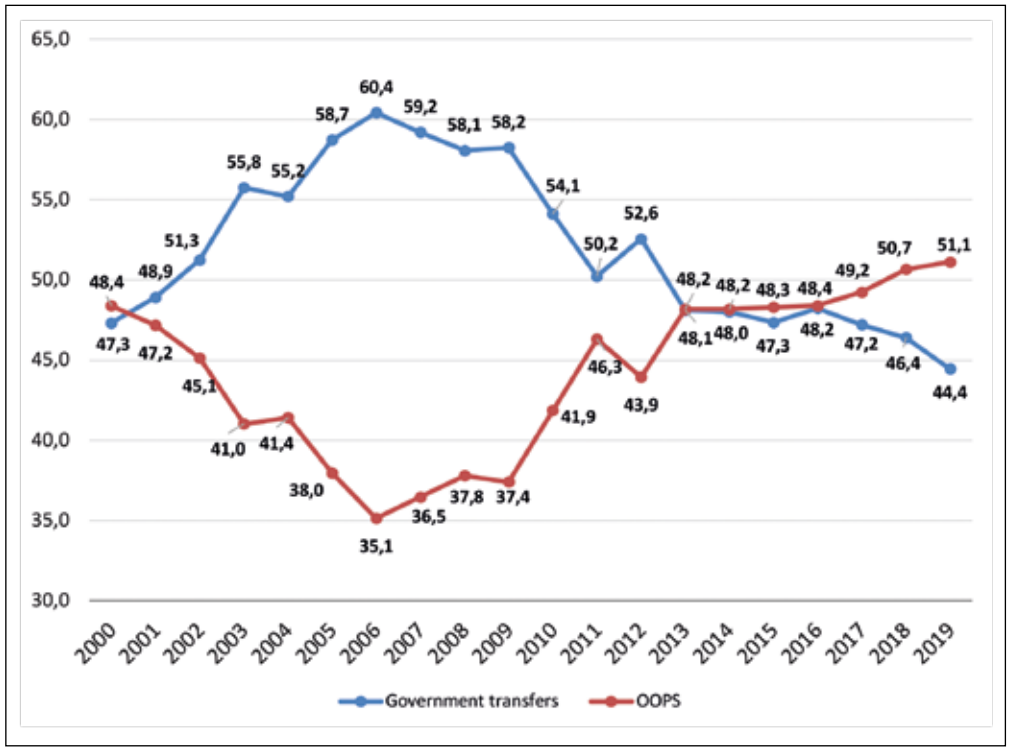

Fig. 3. Relationship between % of government health spending and % of OOPS, Ukraine (2000-2019)

Table I. Analysis of the dynamics of total and government health spending (% of GDP), Ukraine (2000-2019)

Indicators		Characteristic of periods				
		Growth	Stabilization	Decline	Recovery and growth	Slow decline
THS (% of GDP)	Observation period	2000-2003	2004-2006	2007-2008	2009-2015	2016-2019
	Visibility index	126,9	97,0	85,9	121,9	91,0
	Average annual growth rate	7,6	-1,02	-7,3	6,0	-3,1
GHS (% of GDP)	Observation period	2000-2006		2007-2008	2009-2015	2016-2019
	Visibility index	156,0		82,1	115,6	86,5
	Average annual growth rate	7,7		-9,4	2,5	-4,7

Table II. Comparative characteristics of total and government health spending (% of GDP) in Ukraine, CIS countries, European Region WHO and the EU, 2019. (Me (25%; 75%))

Indicators	Ukraine	CIS countries	WHO European Region	EU countries
Total health spending (% of GDP)	7,1	6.12 (4,77;6.99)	7.11 (6,38; 9,14)	7.84 (6,69; 10,045)
Government health spending (% of GDP)	3,2	2.325 (1,47;,38)	4.66 (3,77; 6,39)	5.48 (4,58;7,25)

A more accurate estimate of the dynamics of health spending can be obtained by means of PPP – a purchasing power parity that shows the ratio of prices in national currencies for the same product or service in different countries relative to the currency of the base or reference country (e.g. US $). THS and GHS per capita in PPP have increased almost by 4 times over a 20-years' period (Fig. re 2).

Despite the overall positive dynamics, all health spending indicators are catastrophically different from the Middle European and those of EU countries. In 2019 THS and GHS per capita in US $ were by 9.7 and 15.7 times lower than the average in the European Region WHO (2405 and 1724 US $ respectively) and by 14 and 22.9 times lower than the EU average (3452 and 2520 US $); the levels of THS and GHS per capita in PPP – by 3.5 and 5.2 times lower than in the region as a whole (3167 and 2119 US $) and by 4.7 and 7.4 times less than in the EU (4280 and 3021 US $). In terms of THS and GHS per capita (US $) in 2019, Ukraine ranked 49th and 47th among 53 countries in the European Region WHO; according to THS and GHS per capita in PPP – 46th and 44th place respectively.

Despite the overall positive dynamics, all health spending indicators are catastrophically different from the Middle

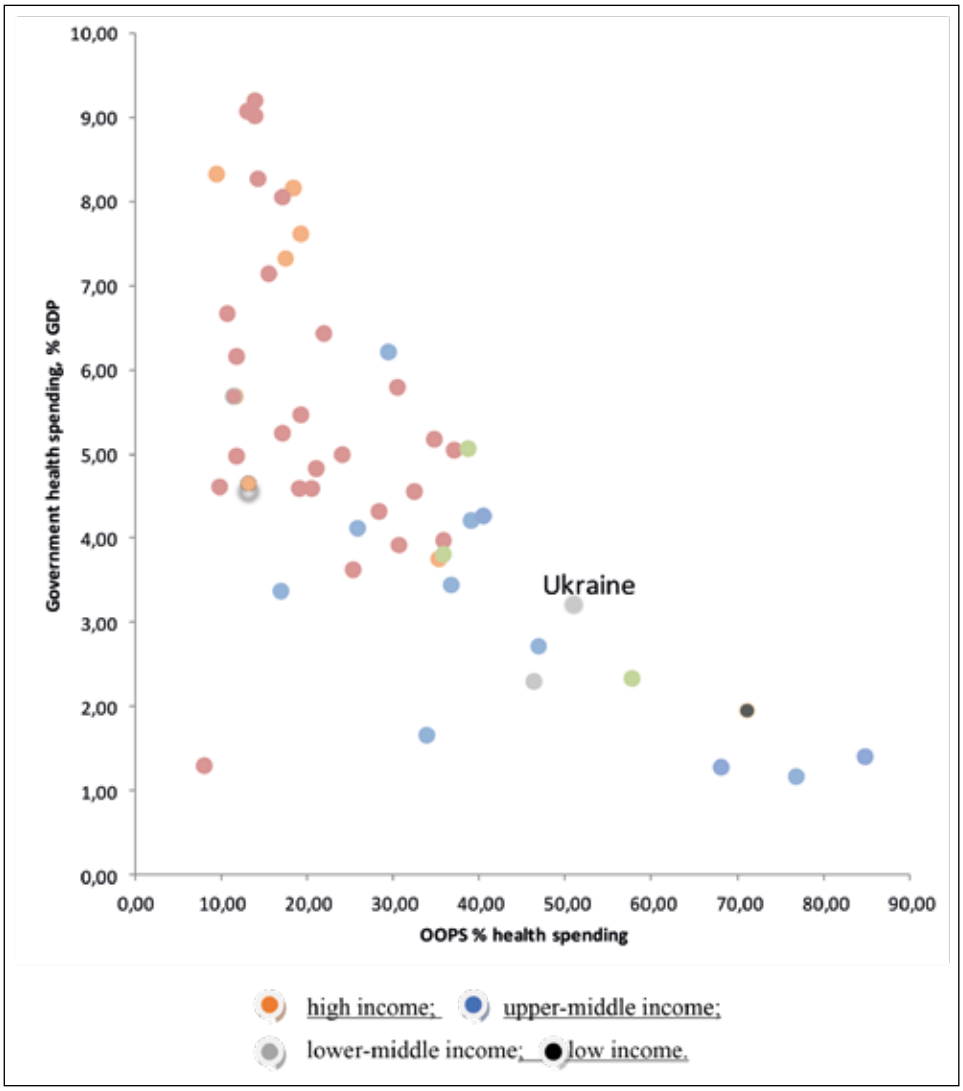

Fig. 4. OOPS share of health spending and government health spending as a share of GDP in the WHO European Region countries, 2019

European and those of EU countries. In 2019 THS and GHS per capita in US $ were by 9.7 and 15.7 times lower than the average in the European Region WHO (2405 and 1724 US $ respectively) and by 14 and 22.9 times lower than the EU average (3452 and 2520 US $); the levels of THS and GHS per capita in PPP – by 3.5 and 5.2 times lower than in the region as a whole (3167 and 2119 US $) and by 4.7 and 7.4 times less than in the EU (4280 and 3021 US $). In terms of THS and GHS per capita (US $) in 2019, Ukraine ranked 49th and 47th among 53 countries in the European Region WHO; according to THS and GHS per capita in PPP – 46th and 44th place respectively.

Funding for health care in Ukraine throughout the observation period came from a variety of sources, but the leading were government transfers – 50.7% (47.8; 56.3) and out-of-pocket (OOPS) – 45.7%. (40.3; 48.3). Contribution from other sources – voluntary health insurance (0.9%, 07; 1.0), other private (2.4%, 1.9; 2.8) and external (0.7%, 0.4; 0.9) expenditure was extremely insignificant. Therewith an increase in % of government health spending was accompanied by a fall % of OOPS (2000-2006, 2011-2012) and vice versa – with a decrease % of government health spending – % of OOPS grows (2007-2019) (Fig. 3). The correlation coefficient between % of government health spending and % of OOPS is negative and very strong (r = – 0.996; p <0.001).

In 2019 in Ukraine the % of OOPS was 51.1%, which is close to the indicator in the CIS countries – 54.4% (36.4; 68.8), but 2.1 times more than the mean values for European region as a whole – 24.0% (15.5; 36.6) and 2.8 times compared to the EU countries – 18.2% (13.1; 25.3). Proportion of households with catastrophic health spending in 2019. was one of the highest in the European region – 16.68% (comparable situation, according to available data recorded only in Bulgaria – 19.23% and Georgia – 17.39%) and increased by 44.8% compared to 2010. (11.52%).

As can be seen from Fig. re 4, which shows the position of the countries of the European Region WHO, based on the ratio of government health spending as a share of GDP and OOPS share of total health spending, Ukraine is one of the 10% of countries with the worst combination of these indicators (low levels of government health spending as % of GDP and high % OOPS in total health spending). It should be noted that this group includes not only countries with low and lower-middle income, but also countries with upper-middle income.

Based on the priority role of primary health care (PHC) in the universal health coverage), the analysis of PHC spending is of particular importance. As there are no national data on PHC expenditures, they were estimated on the basis of regional information (Dnipropetrovsk region) with their subsequent extrapolation to the country level on the basis of international estimates. It is established that Government Primary health care expenditure per capita (US $) in 2021 in the amount of 23.9 US $, of which 73.5% came from the National Health Service of Ukraine, 22.5% – from local budgets, 4 % – the income of health care facilities from paid services. Taking into account that in countries with incomes below the average % of government Primary health care expenditure is 35%, it is estimated that in Ukraine the projected level of total primary health care expenditure per capita (US $) may be 68 US $, which corresponds to the spending of countries in this income group – 61 US $ (38; 66). At the same time, in the structure of total health spending. primary health care expenditure in Ukraine is projected at 27.4%, which is significantly less than the data for lower-middle income countries – 58% (51; 67) [6].

DISCUSSION

For the first time in Ukraine, a health expenditure analysis was conducted in two decades (2000-2019). It was found that during the study period, all indicators of health spending in Ukraine increased, which corresponds to the global dynamics recorded in a number of reports of the WHO and WHO/Europe [4,7]. The annual growth rates of total and government health spending in % of GDP made up 1.5 and 1.2% per year; however, this growth was interrupted during the global economic crisis of 2008, when total and government spending in % of GDP) fell by 7.3% and 9.4%, respectively, compared to the previous period. At the same time, government health spending in % of GDP was negatively affected more than total health spending. The growth rates of nominal total and government spending per capita in US $ and PPP were higher (7.2% and 6.0%). At the same time, there remains a gap in all indicators of health spending, especially government health spending, between Ukraine and the WHO European Region and the EU, which is primarily due to the country's lower middle income [6].

Government health spending largely reflects policy choices regarding the priority of health care and the state's commitment to universal health services [4]. WHO Director-General Tedros Adhan Gebrejesus in 2019 stated: «Increasing public funding for health spending is a prerequisite for achieving overall coverage of health services and health-related goals in the field of sustainable development» [8].

However, in Ukraine, after some recovery from the shock of the 2008 global crisis. government health spending in % of GDP gradually decreased, which is to some extent related to the armed conflict in eastern Ukraine. This trend continued after the adoption in 2017 of the Law of Ukraine on State Medical Guarantees program [9], which stipulates that the amount of state budget funds allocated for the implementation of the Medical Guarantee Program must be at least 5% of GDP of Ukraine. As a result, in 2018 this figure was 3.5%, and in 2019 – only 3.2% of GDP. At the same time, the share of out-of-pocket spending payments increased, which in 2013 – 2016 equaled government health spending, and since 2017. began to exceed them, reaching 51%. The share of households with catastrophic health spending is also growing. The WHO believes that restrictions on public funding for health care are having a negative impact on progress towards universal health coverage [6]. At the same time, Ukraine, like most countries, is able to mobilize more resources to achieve this important task [10].

The low share of Primary health care spending as a share of total health spending (about 30%), which is significantly lower than in countries with different income levels, should be considered as a factor of adverse impact on service coverage [6].

Our study has several limitations, including the following:

1. The Health Expenditure Analysis was conducted prior to the COVID 19 pandemic, as a result of which the world is already experiencing the economic consequences of the global economic downturn, the impact of which on health financing is uncertain.
2. Data on primary health care expenditures are obtained on a regional scale and only on government expenditures and are therefore indicative.

CONCLUSIONS

The study found an unsustainable upward dynamic in health expenditure. In the last decade, there has been a clear trend towards an increase the share of OOPS in total health spending against a background of low with a focus on reducing government health spending (% of GDP). The results of the study can be used in forming a strategy for the development of the health care system to ensure the achievement of the established goals of sustainable development goals of the country.

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Conflict of interest:
The Authors declare no conflict of interest.

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ORIGINAL ARTICLE

NUTRITION OF STUDENTS' YOUTH NOWADAYS AND ITS CORRECTION WAYS

DOI: 10.36740/WLek202205117

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ABSTRACT

The aim: Assessment of students' youth' nutrition by components introduction of nutrition correction methods.

Materials and methods: The following methods have been used in the study: analytical, questionnaire method (the authors composed a questionnaire chart for complex assessment of life style components), statistical (the data received statistical analysis by the licensed in Ukraine software IBM SPSS Statistics Base v.22, with academic lifetime license).

Results: The authors have found that medical students' nutrition style can be characterized as unbalanced and polydeficient. The detected non-observance of the nutritional regimen and real students' youth nutrition justify implementation of preventive measures, aimed at decreasing risks of the alimentary and alimentary-dependent diseases.

Conclusions: The paper contains recommendations on the main ways of the students' youth nutrition regimens correction.

KEY WORDS: nutrition regimen, medical students, alimentary diseases

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INTRODUCTION

Since the 90's of previous century till present time we have observed destructing changes in Ukraine, both in the population structure and size. The last criterion, in any country, is a factor which significantly affects further development of the society, being considered as a basis of economic, social, political, cultural, spiritual and intellectual progress [1, 2].

Especially worrisome is the health condition of working population, among which the largest group is represented with intellectual workers, whose activity is related to high nervous and emotional tension and considerable hypokinesia.

The conducted studies have shown that nutrition of this group is characterized by excessive energy value, is unbalanced by basic nutritional substances and deficient related to certain essential nutrients (poly-unsaturated fatty acids, retinol, ascorbic acid, sulphur-containing amino acids, etc.), with severe violations of the nutrition regimen (excessive supper food consumption, starting working day skipping the breakfast, etc.). Such nutrition leads to considerable occurrence of overweight and obesity (till 36%), as well as high incidence of cardiovascular and gastrointestinal diseases, diabetes mellitus and malignancies [3, 4].

The intellectual workers' group includes young students, for whom rational nutrition is a key factor of their health, necessary for managing the huge intellectual, psycho-emotional and physical loads. Unfortunately, not all students know about problems related to irregular and irrational nutrition, and so they miss the opportunity to prevent the diseases, which doesn't promote healthy nutrition among the population [5, 6]. Even nowadays the physicians still lack in their practice effective assessment measures which would provide for information about students' nutrition, lifestyle, harmful habits and nutrition status. So, the problem is still relevant nowadays.

It is worth mentioning that numerous studies of students' morbidity related to irrational nutrition have been held in Ukraine recently. The general level of the gastrointestinal morbidity among the students equals 1614.4 cases per 100,000 people, which greatly exceeds the pathology values in general population over 18 years old (1149.7 cases per 100,000 people.) [7]. Most often, the students are diagnosed with gastritis and duodenitis. The morbidity of these diseases is 477.0 cases per 100,000 students, and the occurrence is 2954.6 cases per 100,000 people, with 148.3 and 2453.3 cases detected among the adults, respectively [8, 9].

The study of the cardiovascular diseases morbidity of the students-future technicians and economists [7] showed that in 2010-2015 the pathology morbidity increased in students of both specialties by 22.9%, in future economists – by 67.5%, and the endocrine diseases, respectively, – by 46.1% and 89.8%. The results confirm that these characteristics depend on the university profile as well as the students' awareness about healthy lifestyle and main risk factors of chronic non-infectious diseases [7, 9].

Of great significance are the long-term students' cross-specialty group studies of their awareness about healthy lifestyle and main non-infectious diseases risks, firstly nutritional

ones, conducted by specialists of the Institute of Public Health after O.M. Marzeev affiliated to National Academy of Medical Sciences of Ukraine, under supervision of academician A.M. Serdiuk. The study analyzed the data of the Kyiv National Trade-Economical university (KNTEU) and Sumy State Pedagogical university (SSPU) students [9].

The scientists state that the curricula of higher educational institutions contain significant differences in teaching the health-maintaining courses. Most higher educational institutions, the educational profile of which is unrelated to human health, don't approve such courses in the curriculum. This results in low level of awareness by most students about the non-infectious diseases risks, particularly about the irrational nutrition [9].

The study, conducted with the Vinnytsa National Medical university students, showed continuous increase in gastrointestinal diseases: gastritis, gastroduodenitis, pancreatitis, stomach ulcer, complaints of heartburn and flatulence [10-12].

So, the obtained data evidence about considerable problems of the students' nutrition, which makes potential risks for polynutrient deficiencies, and, consequently, alimentary-dependent diseases. Though, complex studies of justification of the youth nutrition correction related only to some aspects of the problem. Regarding all this, the study was aimed at:

Hygienic assessment of real students' nutrition and justification of correction of the basic essential nutrients' deficiency for prevention of the alimentary and alimentary-dependent diseases among the students.

THE AIM

Assessment of students' youth' nutrition by components introduction of nutrition correction methods.

MATERIALS AND METHODS

The following methods have been used in the study: analytical, questionnaire method (the authors composed a questionnaire chart for complex assessment of life style components), statistical (the data received statistical analysis by the licensed in Ukraine software IBM SPSS Statistics Base v.22, with academic lifetime license).

The questionnaire chart was published in professional edition: http://medpers.dsma.dp.ua/issues/2017/N3/104-112.pdf. E-chart: https://docs.google.com/forms/d/e/1FAIpQLSevB1JT-sK-PdpD8vHk2zBbVz-wPP3Ub-Je1pynL3pDCpu5oHQ/viewform

The study design is: cross-section blinded study. The survey was carried out from January till March 2017. The manifestations of nutritional deficiency in student's body are most expressed during this period (winter-spring). The survey was conducted by pre-trained interviewers (education period was 2 weeks).

The study includes medical students of the 2nd, 4th and 6th study years of Bogomolets National Medical University affiliated to the Ministry of Health of Ukraine.

A total sample is 5000 students, with 858 respondents questioned. Random sample choice principle was applied. All students had equal chances of being chosen. The representative sample included male and female medical students, aged 18-25 years old.

The questioning was anonymous, which didn't affect psychological, procedural and financial characteristics of the respondents, thus preventing the questioning bias. The questioning was held upon the previous informed consent of all respondents.

RESULTS

The students' morbidity has increased by 25% for the last 10 years (State Committee of statistics, 2018). The causes of this include insufficient adaptation of the first university study years, hypodynamics, psycho-emotional exertion, harmful habits and irrational nutrition.

The nutrition of medical students has recently been emphasized, as these students make a separate category of students related to the human welfare. They should consider the matter deeper, preventing its manifestations and promoting healthy nutrition among working people [6].

The study estimated real nutrition of medical students and introduced correction of the essential nutrients content in the dietary regimen of students. The study was held under the supervision of professor S.T. Omelchuk in Bogomolets National Medical University [3-5, 13-18].

The authors composed a questionnaire chart for assessment of various population group nutrition, including the students' youth [13]. It was used and evaluated by the specialists of leading institutions of nutritional hygiene, gastroenterology and dietology. The expert evaluation of the questionnaire chart made by appropriate specialists confirmed its universal character as for the primary information collection.

Overall, 858 Bogomolets National Medical University students (570 females and 288 males) of the 2nd, 4th and 6th study years were questioned about their nutritional regimen and nutritional ratio, frequency of consumption of basic food product groups (11 groups), daily and weekly consumption of basic food product groups (20 groups), in order to justify the recommendations on preventing the alimentary-dependent diseases [3, 4, 13-18].

The study results reflect gaps in the nutritional regimen: food courses number, neglecting basic meal courses, inappropriate intervals between meals, speed of food consumption and distribution of the consumed food volume according to the meals. The authors established that only 14.6% of men and 15.1% of women consume four meals daily. About 43.7% of men and 45.8% of women neglect breakfast, and, generally, 85.5% don't keep to the optimum interval periods between the main meals. For only 31.0% of men and 28.6% of women dinner is the basic meal, while for 32.0% of men and 25.0% of women supper is the main meal of the day. Most men and women consume food in public restaurants and cafes. According to the obtained results of the disturbed food regimens, the authors composed the ways and methods of their correction [4, 5].

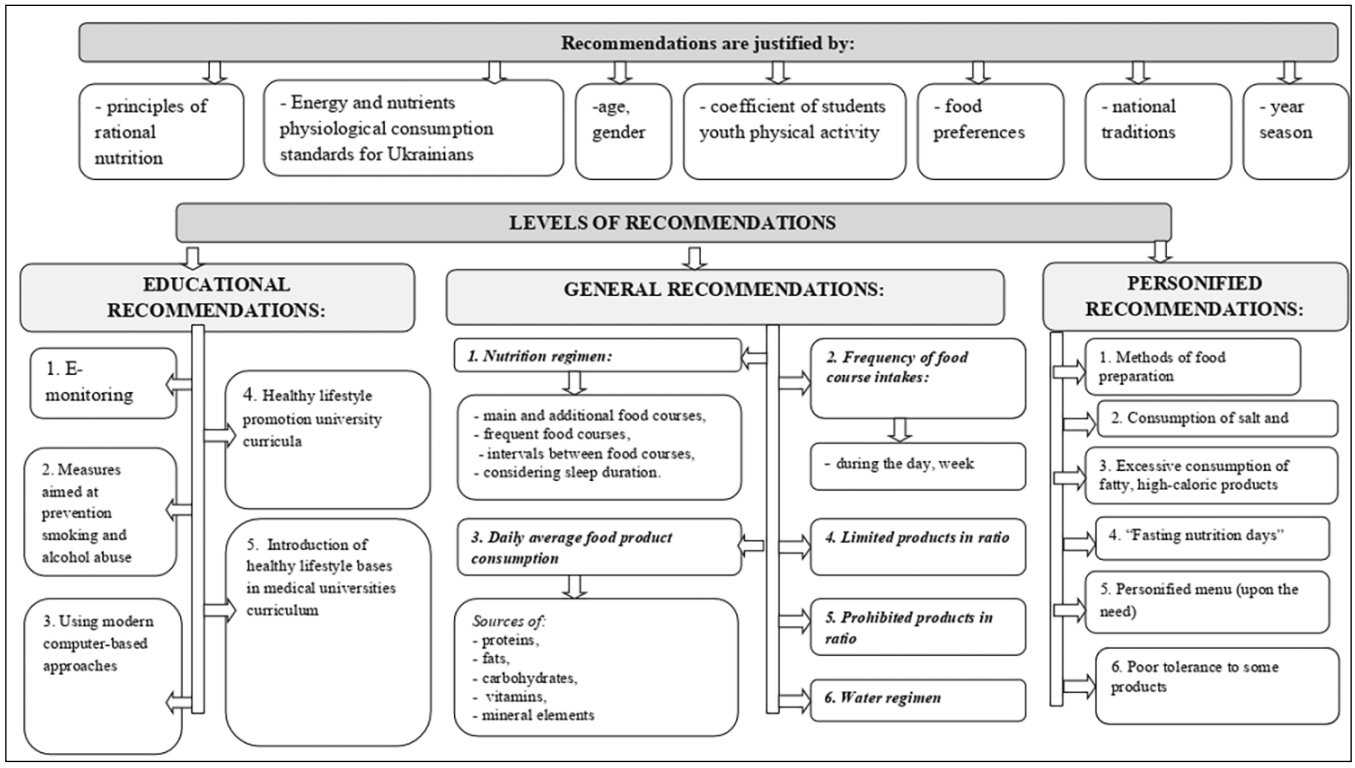

Fig. 1. Recommendations on main ways of correcting the students youth nutritional regimens

In general, more than 2/3 of the medical students' ratios by their consumption of animal origin food go contrary with the national recommendations on people nutrition. Less than 30% of respondents, regardless of their gender and study year, include in their ratio meat and meat products, milk and milk products once a day or almost every day. Less than 20% respondents include in the ratio fish and seafood, eggs and fat-containing products. A third of the respondents don't consume milk, 1/5 of the respondents consume 250-400ml of milk. A half of the junior students, regardless of gender, don't include in their ratio sour milk products. One fifth of junior and middle-course students consume daily 250-400ml of sour milk products, regardless of gender, and 1/3 of the 6th year female students and 1/5 male students of the same age [14-16].

About 1/3 of junior males and half of junior female students don't consume pork; 1/3 of all respondents consume 100-250grams of it. A half of the respondents don't consume the beef. About 1/5 of males and 1/3 of females, regardless of the study year, consume daily 100-250 grams of beef [14, 16].

A half of all respondents consume poultry (chicken), 100-250gr daily. One-fourth of junior male students, one-sixth of senior male students and one-tenth of female students don't consume poultry. More than one third of all respondents consume sausage and smoked sausage, about 100 g a day. One third of men and half of women, regardless of the study year, do not consume sausage [14, 16].

A half of respondents do not consume sea-fish and river-fish. Only one-fifth of males and one fourth of females, regardless of the study years consume 100-200g of sea-fish daily. About 70% of all respondents refused seafood, regardless of gender and study year. The analysis of interview data showed that more than one third of the respondents include one or two eggs in their daily ratio. Only one tenth of respondents don't consume eggs at all [14, 15, 16].

According to the study, 70% of student ratios by their plant origin product content are inappropriate to the national recommendations. Only one third of female respondents and 15% – 25% of male respondents consume vegetables daily. From 17% of female students (the 2nd study year) till 25% (6th study year), and a third of male students, regardless of the study year, consume potatoes daily. Up to 40% of male respondents and 31% of female respondents consume fruit daily [3, 5, 17].

The study reveals that 50% of the student ratios, by food assortment and daily average fruit and vegetable consumption, don't correspond to the national recommendations on nutrition. Ten percent of all respondents refuse vegetables and fruit [3, 5, 17].

Up to 40% of male and 30% of female respondents consume bread and bread products daily. Every day up to 30% of male and 15-19% of female respondents consume cereals and pasta products. A third of male and 10-2% of female respondents consume sweets (sugar, jams, honey) daily [5, 18].

A half of all respondents add daily to their ratio up to 100g of confectioneries, and one-third consumes 100-200g of the product. A half of senior students and 1/3 of senior students add sugar into the ratio, up to 25g daily. Mostly middle year students and senior students consume more than 100g of sugar daily [5, 18].

DISCUSSION

The study revealed that the real nutrition of students is ill-balanced, characterized by nutrients polydeficiency, it needs correction and introduction of preventive measures to decrease the risk of alimentary and alimentary-dependent diseases. Similar results have been obtained in other European universities [19, 20].

The described diet with deficient animal products may lead to protein deficiency and thus increase the risks of protein-deficiency diseases.

The ratios of the questioned students are rich in carbohydrates, which may lead to overweight, insulin-resistance, and further – diabetes mellitus.

Nowadays, some high school curricula include the course "Nutrition science" promoting healthy lifestyle.

CONCLUSIONS

The conducted studies helped to justify basic methods of the students' nutritional regimen correction as for the essential nutrients content [5]. General recommendations on correcting the lifestyle, nutritional regimen, frequency of certain food groups' consumption during the day and week, daily average consumption of food products with essential nutrients as well as correction of certain food products consumption and strict water regimen should be emphasized [5]. The advice on personified menu composition should be based on rational nutrition principles, considering the Ukrainian population physiological needs in basic food substances and energy [21], according to the gender, age, body mass, physical activity coefficient, food preferences, national, family and individual traditions as well as the seasonal food consumption (fig. 1).

The key aspects of recommendations on the lifestyle and nutrition of the students' youth should be not only general, but personified. Introduction of such recommendations into the students' life, firstly, life of medical students, will help to shape their health-maintaining skills, behavior and competences, which are an essential part of their professional knowledge and will be used in the further medical practice.

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ORIGINAL ARTICLE

NATIONAL TRENDS IN MORBIDITY AND MORTALITY FROM CIRCULATORY SYSTEM AND CEREBROVASCULAR DISEASES AND STROKES

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ABSTRACT

The aim: To determine national trends in morbidity and mortality from diseases of the circulatory system, cerebrovascular diseases and strokes.

Materials and methods: Data from official sources of statistical information of Ukraine were used and systematic analysis and generalization of the obtained data was performed and trends in morbidity and mortality from diseases of the circulatory system, cerebrovascular diseases and strokes in Ukraine were calculated.

Results: Were found tendencies to decrease of national levels of prevalence and primary morbidity in Ukraine for DCS (-16.3 % and -28.0 %), CVD (-22.8 % and 24.1 %) and strokes (-12.2 %) with significant trends (+83.9 %) of increase in primary incidence of strokes in 2010-2017 with fairly high and threatening levels for 2017 (respectively 22199563, 2521601 and 96978 – prevalence and 1725137, 290557 and 96978 – primary incidence). National levels of reduction of deaths from DCS in Ukraine from 440369 (2013) to 389348 (2019) with a trend of -11.6 % and a decrease in mortality due to CVD from 94267 (2013) to 76232 (2019) with a trend -19.1 % were found.

Conclusions: The trends to reduce of national prevalence, primary morbidity and mortality rates in Ukraine for DCS, CVD and stroke are fully consistent with other global trends of reduction of these levels among world countries.

KEY WORDS: diseases of the circulatory system, cerebrovascular diseases, strokes, prevalence, primary morbidity, mortality, trend

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INTRODUCTION

The WHO points to the high importance of cardiovascular diseases for humanity due to the significant levels of prevalence and mortality due to these diseases. Thus, it is estimated that about 18 million patients worldwide die prematurely from cardiovascular disease each year [1], most due to coronary heart disease and stroke (15.2 million premature deaths in 2016) [2]. According to other data, the global annual mortality due to strokes is more than 6.7 million patients (about 11.9 % of total global mortality) [3, 4].

According to world researchs, the problem of strokes is very relevant due to the high medical and social importance of these diseases, which is provoked by their high prevalence; constant growth; high levels of morbidity and mortality and the need for such patients to carry out many medical, rehabilitation and social measures [5-9]. According to WHO definitions and global research and meta-analysis, stroke is the second most common after coronary artery disease cause of disability and mortality in the world and in Ukraine [10]. According to the WHO [11] and Norrving B. et al. [12] the global incidence of stroke is differs in different countries: in Europe, annual prevalence rates are more than 1.2 million cases with a 2-3-fold increase in Eastern Europe compared to Western Europe. According to Kissela B. M. et al. [13], up to 30 million new cases of stroke occur worldwide each year: in economically developed countries (European Union, Iceland, Switzerland, Norway) about 1.1 million, in the United States more than 550 thousand. It is stated that of all new cases of stroke, about 40 % end with death in the first month, 50 % — in the first year; and 20–40 % of patients become completely dependent on outside help and only 10 % have complete recovery of their functions.

According to WHO experts, the global incidence of stroke will continue to increase due to global aging and increasing risk factors for their development (heart disease, hypertension, diabetes, dyslipidemia, hypercholesterolemia [14], hypodynamia, malnutrition, alcohol abuse, chronic stress, smoking and others) and by 2035 will increase by 34.0 % among European countries [4].

In Ukraine, according to the WHO, the prevalence of stroke also has a negative trend [15]. According to official statistics, up to 150,000 new cases of stroke and about 40,000 to 45,000 deaths are registered in Ukraine each year. It is known from official sources that the prevalence of strokes in Ukraine is 30.0 % higher than the European average and has 280-290 new cases per 100 thousand population (100-120 thousand diseases). Mortality in Ukraine due to stroke is at 30.00-40.00 % in the first 30 days and up to 50.00 % in the first year after stroke.

Table I. Prevalence and primary incidence of DCS, CVD and stroke among adults (18 years and older) in Ukraine in 2010-2017 (excluding the temporarily occupied territory of the Autonomous Republic of Crimea and Donetsk and Luhansk regions) (n)

Year	Number of cases					
	DCS		CVD		Stroke	
	Total	Primary	Total	Primary	Total	Primary
2010	26523102	2397059	3268100	382916	110421	52739
2011	109329	28191	3192923	361974	110753	110753
2012	26231358	2234607	3170428	351436	111615	111615
2013	26200923	2176805	3122985	348881	111953	111953
2014	22354901	1813572	2557591	308256	94104	94104
2015	22381985	1779828	2551645	298854	96319	96319
2016	22303564	1766188	2528013	299734	97805	97805
2017	22199563	1725137	2521601	290557	96978	96978
Trend	-16,3	-28,0	-22,8	-24,1	-12,2	+83,9

Table II. Mortality from DCS and CVD among the adult (18 years and older) population of Ukraine in 2013-2019, excluding the temporarily occupied territory of the Autonomous Republic of Crimea and Donetsk and Luhansk regions (abs., Per 100 thousand)

Year	Number of deaths											
	DCS						CVD					
	Total		Urban		Rural i		Total		Urban		Rural	
	n	Per 100 thousand	n	Per 100 thousand	n	Per 100 thousand	n	Per 100 thousand	n	Per 100 thousand	n	Per 100 thousand
2013	440369	970,6	266287	855,6	174082	1221,655	94267	207,8	66121	212,5	28146	197,5
2014	425607	992,0	256541	869,6	169066	1261,6	87890	204,9	61530	208,6	26360	196,7
2015	404551	1038,8	237849	921,7	166702	1268,8	79775	204,8	53839	208,6	25936	197,4
2016	392298	1010,7	230751	896,1	161547	1236,5	76733	197,7	51363	199,5	25370	194,2
2017	384810	995,8	226964	884,8	157846	1215,0	75733	196,0	50835	198,2	24898	191,6
2018	392060	1000,8	234397	882,6	157663	1225,0	76906	182,0	52117	181,2	24789	183,4
2019	389348	993,4	235466	882,2	153882	1205,6	76232	179,5	51774	178,3	24458	181,8
Тренд	-11,6	+2,3	-11,6	+3,1	-11,6	-1,3	-19,1	-13,6	-21,7	-16,1	-13,1	-7,9

Thus, conducting a study to determine national trends in morbidity and mortality from diseases of the circulatory system, cerebrovascular diseases and strokes in Ukraine is an actual task.

THE AIM

To determine national trends in morbidity and mortality from diseases of the circulatory system, cerebrovascular diseases and strokes.

MATERIALS AND METHODS

Data from official sources of statistical information of Ukraine (State Institution "Center for Medical Statistics of the Ministry of Health of Ukraine") were used to determine national trends in morbidity and mortality of diseases of the circulatory system, cerebrovascular diseases and strokes in Ukraine. A systematic analysis and generalization of the obtained data was performed and trends in morbidity and mortality from diseases of the circulatory system, cerebrovascular diseases and strokes in Ukraine were calculated.

RESULTS

According to the official data of the Center for Medical Statistics of the Ministry of Health of Ukraine, significant levels of prevalence and primary incidence of circulatory diseases (DCS) with high levels of cerebrovascular disease (CVD) and stroke were found [16] – Table I.

During 2010–2017, there was a tendency to reduction of prevalence and primary incidence of DCS, CVD and stroke, but they are still quite significant and threatening. Thus, the prevalence of DCS had trends (-16.3 %) to reduce the overall incidence from 26523102 cases (2010) to 22199563 people (2017) and downward trends (-28.0 %) for the first time in the life of detected CVD diseases from 239705 to 1725137 patients (Table I).

There was also a decrease in CVD levels from 3268100 (2010) to 2521601 cases (2017) with a trend of -22.8 %

(prevalence of CVD) and a decrease in first-time CVD levels from 382916 (2010) to 290557 2017) patients with a trend of -24.1 % (Table I).

There was also some (trend -12.2 %) decrease in the incidence of stroke from 110,421 (2010) to 96,978 (2017) patients with a significant increase in first-time stroke from 52,739 (2010) up to 96,978 (2017) persons with a trend of +83.9 % (Table I).

Significant national levels of prevalence and primary incidence of DCS, CVD and stroke in Ukraine according to official sources [17 20] provoke negative consequences as high mortality and disability rates due to DCS, CVD and stroke (Table II).

It is determined that the mortality from DCS according to the State Institution "Center for Medical Statistics of the Ministry of Health of Ukraine" [17 20] for 2013-2019 in Ukraine tends to decrease from 440369 (2013) to 389348 (2019).) cases with a trend of -11.6 %. It is established that mortality from CVD according to the State Institution "Medical Statistics Center of the Ministry of Health of Ukraine" [17 20] also tends to decrease in Ukraine from 94,267 cases (2013) to 76,232 people (2019) with a trend -19.1 %. It was stated that the levels of mortality reduction from DCS did not differ between urban and rural residents and had trends of -11.6 %. In terms of CVD mortality rates, urban residents had higher downward trends (-21.7 %) than rural residents (-13.1 %). Per 100,000 population, the death rate from DCS in 2013–2019 tended to increase with a trend of + 2.3 % due to urban residents with a trend of +3.1 % (Table II).

DISCUSSION

Our data are in complete agreement with other studies that indicate a reduction in morbidity and mortality from DCS and CVD in recent years. Thus, according to the results of the study Wu H. et al. [21] for 2007–2016, there was a decrease in mortality from stroke with age-adjusted rate by 21.6 %. Age-adjusted stroke mortality decreased by an average of 2.67 % annually. According to Soto Á. et al. [22] in the countries of the European Union there was a decrease in standardized age-related mortality rates from stroke per 100,000 population in 1996-2015 by an average of 4.2 %. All countries had declining trends (the largest in Estonia, Portugal and Austria). There was a statistically significant reduction in mortality among sick men and women by 4.2 % and 4.3 %. According to Baek J. et al. [23], it has been found that the overall mortality rate from DCS has increased in recent years due to global aging. It was determined that in 1983–2018 DCS tended to increase but CVD tended to decrease. From 1983 to 2018, there was a significant reduction in age-standardized mortality from all DCS, hypertension and CVD. Age-standardized mortality from coronary heart disease and myocardial infarction peaked in the 2000s, after which they tended to decline. Study of Cortesi P. A. [24] also confirmed significant reduction in the severity of DCS (especially age-standardized prevalence (-12.7 %), mortality (-53.8 %) and disability-adjusted life expectancy (-55.5 %) for 1990 2017 in most European countries.

CONCLUSIONS

1. The tendencies to decrease of the national levels of prevalence and primary incidence in Ukraine of DCS (-16.3% and -28.0%), CVD (-22.8% and 24.1%) and strokes (-12, 2%) with significant trends (+83.9%) of increase in primary incidence of stroke in 2010-2017 with fairly high and threatening levels for 2017 (respectively 22199563, 2521601 and 96978 – prevalence and 1725137, 290557 and 96978 – primary morbidity) were found.
2. National levels of reduction of mortality due to DCS in Ukraine from 440369 (2013) to 389348 (2019) with a trend of -11.6% and a decrease in mortality due to CVD from 94267 (2013) to 76232 (2019) with a trend of -19.1% were established.

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ORIGINAL ARTICLE

APPROVAL OF THE USE OF THE SHORT FORM 19 OF THE CHILD'S ORAL HEALTH IMPACT PROFILE (COHIP-SF 19) FOR DENTAL PUBLIC HEALTH NEEDS

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ABSTRACT

The aim: Is an adaptation, determination of psychometric properties, and approbation of the use of COHIP-SF 19 for the needs of dental public health in the Ukrainian sample of children and teenagers.

Materials and methods: A cross-sectional validation study was conducted on a sample of 236 Ukrainian children aged 6 to 18. The psychometric indicators of the questionnaire were evaluated; analysis of the reliability and internal structure of the methodology based on correlation and factor analysis, calculation of Chronbach's alpha; reliability of re-testing (Intraclass Correlation Coefficient); assessment of convergent and discriminant validity (Mann-Whitney U test, ROC analysis, and correlation analysis). STATISTICA 6.1 (StatSoftInc., № AGAR909E415822FA) was used to analyze the results. The ethics of the study was confirmed by the conclusion of the relevant commission.

Results: After cultural direct and reverse translation of the original version, the Ukrainian version of COHIP-SF 19 UK was obtained. The internal consistency of the subscales and COHIP-SF 19 UK was generally sufficient (Cronbach's alpha is greater than 0.7).

Sufficient reliability of retesting, convergent and discriminant validity of the methodology was proved. The presence of a correlation between COHIP-SF 19 UK indicators and self-assessment of children's health and quality of life was determined.

Conclusions: The study proved that COHIP-SF 19 UK is a reliable valid method for assessing the quality of life-related to oral health among Ukrainian children and adolescents, and its good psychometric properties are sufficient for research in the field of dental public health.

KEY WORDS: child oral health impact profile-short form 19 (COHIP-SF 19), oral health-related quality of life (OHRQoL), children, questionnaire validation, dental public health

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INTRODUCTION

Dental Public Health (DPH), which defines both the science and the art of oral disease prevention at both the individual and population levels through the organized efforts of society, is not integrated into the public health system in a quarter of the world, but in 62% of countries are only partially integrated [1].

Recognizing the fact that oral and non-communicable diseases have common modifiable risk factors, the World Federation of Public Health Associations (WFPHA) in collaboration with the World Health Organization (WHO) has developed a Global Charter for Public Health integrating oral health with public health systems through effective advocacy, partnerships and collaboration [2].

It is noted that DPH should be developed based on a systematic approach using feedback mechanisms [3], which can be carried out based on population surveys, determining their quality of life and quality of life related to oral health-related quality of life (OHRQoL).

OHRQoL, one of the main goals of dental public health, is an integral part of the general state of human health and well-being and provides a theoretical basis for the development of oral hygiene measures [4]. Preventive dental measures are most effective among school-age children, as oral diseases among children and adolescents are a serious public health problem. It is during childhood and adolescence that sustainable patterns of health behavior are formed, and beliefs and guidelines related to dental health are effective [5].

The study of OHRQoL in children is becoming increasingly popular in population-based research. Researchers have used a variety of measurements to assess oral health-related quality of life, some for children under 6 and others for older age groups. These measurements are usually assessed through interviews with children who can speak and write, or by completing questionnaires by children or their parents. [6].

There are currently about 18 COHQoL indicators for children aged 2 to 18 [7], among which the most common are the Child Perceptions Questionnaire (CPQ), the Child Oral Impacts on Daily Performances (C-OIDP), and the Child Oral Health Impact Profile (COHIP), which cover a wide age range and different conditions and, therefore, can be used in studies of different profiles [8].

The Child Oral Health Impact Profile Short Form (COHIP-SF) 19 is an abbreviated version of the 34-item COHIP scale that has been found to be a reliable tool for measuring oral health-related quality of life in the school population age. [8].

COHIP-SF was developed in 2012 to meet the challenge of reducing the number of questions. The questionnaire contains 19 items, grouped by three subscales: oral health, functional well-being, and socio-emotional well-being.

The short form, with less time spent on research, retains the good psychometric properties of the original version, is designed for children aged 7-18, is suitable for longitudinal research, and is a good tool for international comparisons of OHRQoL in children and adolescents. [9, 10].

The COHIP-SF method was validated and showed good psychometric properties in Chinese, French, German, Arabic, and Japanese child populations [10 – 14]. Its good discriminant and convergent properties have also been confirmed in the English, Dutch, Korean and Persian versions of [12].

The relevance of the study was that COHIP-SF was not validated in the Ukrainian sample of children, and the method itself was used mainly for clinical purposes, while there is a growing need to obtain reliable and reliable data on OHRQoL for dental public health.

THE AIM

Adaptation, determination of psychometric properties, and approbation of the use of COHIP-SF 19 for the needs of dental public health in the Ukrainian sample of children and adolescents.

MATERIALS AND METHODS

The original English COHIP-SF 19 [15] was translated into Ukrainian (COHIP-SF 19 UK) using a cross-cultural direct and reverse translation procedure involving a professional linguist and 2 public health professionals.

COHIP-SF 19 UK, like the original version, consists of 19 questions that form 3 conceptual subscales: oral health (5 questions), functional well-being (4 questions), and socio-emotional well-being (10 questions) and an additional question regarding self-assessment of oral health.

Answers to the questions, as in other international studies, were assessed on a five-point Likert scale from «never» (4 points) to «almost constant» (0 points) and on the reverse scale for two questions with positive wording. The total score was calculated by summing the scores on all responses, the maximum possible score was 76 points and corresponded to the highest quality of life OHRQoL [9 – 11].

To adapt the questionnaire, a cross-sectional validation study was conducted on a sample of 236 Ukrainian schoolchildren and college students aged 6 to 18. The inclusion of children from the age of 6 was due to the fact that in Ukraine it is at this age that children go to school.

The approbation of the questionnaire included several stages: data collection to assess the psychometric indicators of the questionnaire; analysis of reliability and internal structure of the methodology based on correlation and factor analyses; reliability of re-testing; assessment of convergent and discriminant validity of the methodology.

To assess the reliability of the method, 94 children (39.8%) were examined by dentists, among 70 respondents (29.7%) after 1 month was re-interviewed. The recommendations of Chinese experts on surveying children according to this questionnaire [11] were used.

Convergent validity was assessed by assessing the correlation between COHIP-SF scores and self-assessment of oral health and overall quality of life assessment using the EUROHIS-QOL 8-item index (WHOQOL-8) [16].

Discriminant validity of the method was assessed by evaluating the results among different categories of subjects (with and without oral diseases), comparing the results of COHIP-SF 19, and assessing the condition of the oral cavity of children according to dentists.

Before the start of the study, the informed consent of each child and one of their parents (guardians) was obtained. Compliance of the study with the requirements of the Declaration of Helsinki and the principles of biological ethics and medical deontology was confirmed by the conclusion of the Committee on Biological Ethics of the Dnipro State Medical University (Protocols №6 dated 30.09.2020).

Methods of descriptive and analytical statistics were used during the analysis and evaluation of the results. Estimation of the distribution of quantitative traits was determined by the Shapiro-Wilk and Kolmogorov-Smirnov criteria, as amended by Lilliefors.

Correlation analysis was performed using Spearman's rank correlation coefficient (r_s). The internal consistency of COHIP-SF 19 was measured using Chronbach's alpha α for the overall scale and separately for the subscales, with a coefficient of $\alpha \geq 0.7$ considered to be an indicator of satisfactory internal consistency [10]. The reliability of retesting was studied using the Intraclass Correlation Coefficient (ICC). Confirmatory factor analyzes (CFA) were performed to verify the factor structure of the scale. The Mann-Whitney U test was performed to determine differences between groups.

To determine the discriminatory possibilities of the method, ROC analysis was performed to determine the sensitivity, specificity, and area under the ROC curve (AUC). Relationship between the area under the ROC curve and diagnostic accuracy: 0.7-0.8 – good; 0.8-0.9 – very good; 0.9 – 1.0 – excellent [17].

The significance level was set at $p<0.05$ for all types of analysis.

Statistical processing was performed using Microsoft Excel (Microsoft Office 2016 Professional Plus, Open License 67528927) and software product STATISTICA 6.1 (StatSoftInc., Serial № AGAR909E415822FA).

RESULTS

The average age of the surveyed students and adolescents was 11.3 years with a 95% confidence interval of 95% CI 10.9 – 11.6 years. Of the total number of respondents, 58.9% were girls and 41.1% were boys; 61.0% lived in cities and 39.0% in rural areas.

Table I. Descriptive statistics for COHIP-SF 19 UK and subscale scores (n= 236)

Scale (possible range, scores)	Mean (SD)	95% CI for Mean	Median (95% CI for Median)	25th quartile	75th quartile
Oral health (0 - 20)	14.0 (3.6)	13,6 - 14,5	14 (13 - 15)	12	17
Functional well-being (0 - 16)	13.5 (2.9)	13,2 - 13,9	14 (14 - 15)	12	16
Socio-emotional well-being (0 - 40)	30.5 (6.1)	29,8 - 31,3	32 (31 - 32)	27	35
Overall COHIP-SF 19 UK (0 - 76)	58.1 (10.9)	56,7 - 59,5	60 (58 - 61)	52	67

Table II. Internal reliability analysis of COHIP-SF 19 UK and each subscale

Scale (number of items)	Chronbach's alpha	95% lower confidence limit	Effect of dropping variables
Oral health (5)	0.71	0.66	0.62 - 0.66
Functional well-being (4)	0.78	0.74	0.70 - 0.75
Socio-emotional well-being (10)	0.82	0.79	0.77 - 0.81
Overall COHIP-SF 19 (19)	0.89	0.87	0.79 - 0.88

Table III. Spearman correlations of self-perceived assessment of oral health and overall quality of life (WHOQOL-8) with the overall COHIP-SF 19 UK and each subscale scores (n = 236)

Scale	Perceived general health		Perceived oral health		Perceived WHOQOL-8	
	rs	p value	rs	p value	rs	p value
Oral health	0.26	p=0.014	0.53	p<0.001	0.28	p<0.001
Functional well-being	0.28	p=0.006	0.48	p<0.001	0.21	p=0.001
Socio-emotional well-being	0.32	p=0.001	0.31	p<0.001	0.26	p<0.001
Overall COHIP-SF 19 UK	0.33	p<0.001	0.31	p<0.001	0.30	p<0.001

In general, the respondents rated the health of their oral cavity as poor – 6 participants (2.5%), satisfactory – 43 (18.2%), mediocre – 57 (24.2%), good – 103 (43.6%) and very good 27 (11.4%) . Among the 94 examined among dentists, 31 (33.0%) were diagnosed with diseases of the oral cavity.

The general state of their health was assessed as very bad and bad – 17 people (7.2%), satisfactory – 75 (31.8%), good – 103 (45.8%), and very good 36 (15.3%).

A direct, statistically significant correlation was found between self-assessments of general health and oral health – r_s=0.30 (p<0.001).

According to WHOQOL-8, the overall quality of life was assessed as bad and very bad – 5 people (2.1%), neither bad nor good – 56 (23.7%), good – 125 (53.0%), very good 50 (21.2%).

Estimation of the distribution showed that the distribution of total COHIP-SF 19 UK scores and scores on all subscales differed significantly from normal (p<0.001). Descriptions of the central values of the overall COHIP-SF 19 UK score and subscale scores are given in Table I. The median Overall values of the Overall COHIP-SF 19 UK score were 60.0 (95% CI 58.0 – 61.0) points with a maximum of 76 points, Oral health 14.0 (95% CI 13.0 – 15.0) points with a maximum of 20 points, for Functional well-being 14.0 (95% CI 14.0 – 15.0) points with a maximum of 16 points, for Socio-emotional well-being 32.0 (95% CI 31.0 – 32.0) points with a maximum of 40 points.

There were no gender differences in the overall assessment of overall COHIP-SF 19 UK (p=0.179), oral health (p=0.262), functional well-being (p=0.413), and socio-emotional well-being (p=0.351). There were also no discrepancies in estimates in the age groups up to 12 years and older than 12 years (respectively, according to the general estimate and subscales p=0.273; p=0.273; p=0.565; p=0.267).

There were statistically significant differences in the overall COHIP-SF 19 UK score among urban residents compared to rural residents – Me (25%; 75%): 63 (54; 67) vs. 57 (50; 65); p = 0.011. A similar situation is determined for all subscales (Fig. 1).

According to the theoretical model, when conducting factor analysis, we chose a 3-factor solution, which ultimately explained 65.5% of the data variance. The factor load factor matrix after Varimax raw is fully in line with the theoretical model: all points belong to their scales with loads: 0.23 – 0.88. Three questions, Q6, Q16, and Q19 had the lowest factor load (<0.3); Q1, Q5 Q8 Q11 Q12 Q14 Q15 had the highest factor load (>0.7).

The internal consistency for the overall COHIP-SF 19 UK score in general and by individual subscales is given in Table II. Internal consistency for the overall COHIP-SF 19 UK score for Chronbach's alpha was α=0.71, for Functional well-being – α=0.78, for Socio-emotional well-being – α=0.82, for Overall COHIP-SF 19 – α=0.89, which is considered a sufficient level (α>0.7). Chronbach's alpha value did not increase if any of the items were removed.

All correlations between the elements were positive and ranged from 0.22 to 0.79 for COHIP-SF 19 and its sub-

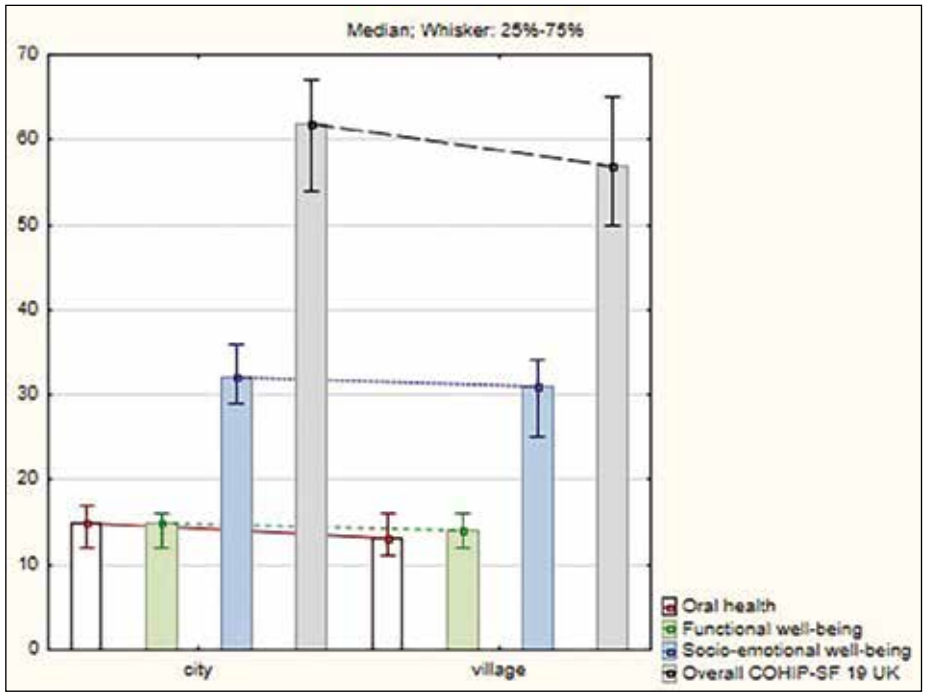

Fig. 1. The average OHRQoL score of the surveyed urban and rural residents according to COHIP-SF 19 UK

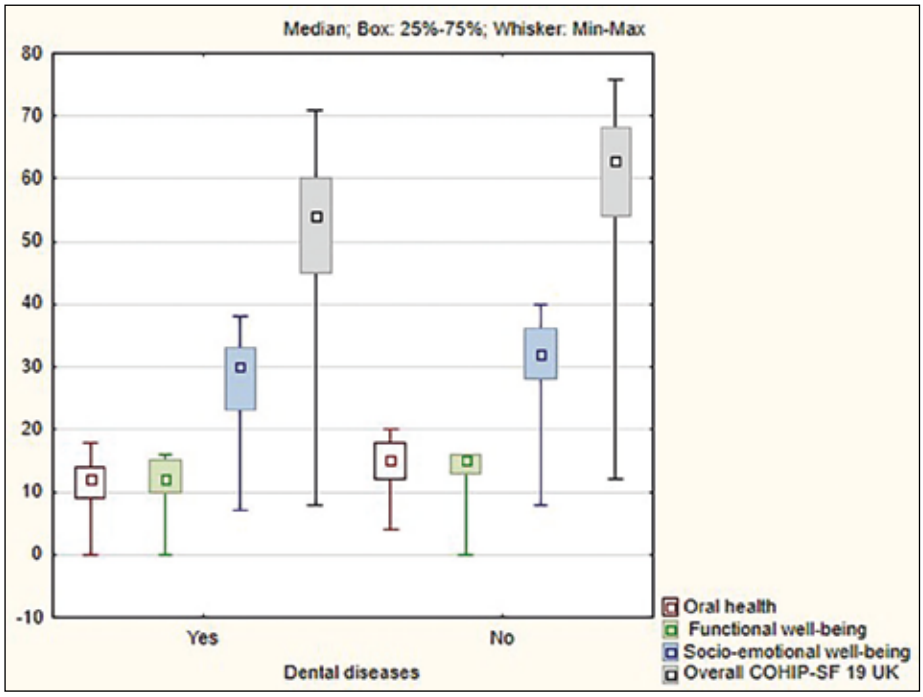

Fig. 2. The average score of COHIP-SF 19 UK and each subscale in the subjects depending on the presence of oral diseases

scales. Reliability in repeated tests by Intraclass Correlation Coefficient was for the overall test COHIP-SF 19 UK ICC = 0.81 (p<0.001); for subscales oral health – ICC = 0.87 (p<0.001), functional well-being – ICC=0.80 (p<0.001), socio-emotional well-being – ICC = 0.64 (p<0.001), which indicates good reliability of repeated tests.

Discriminant validity was assessed by comparing the results obtained with COHIP-SF 19 UK and its subscales with the results of an examination by a dentist who determined the presence or absence of oral health problems (Fig. 2). Children without dental problems had a significantly higher overall score on the COHIP-SF 19 UK scale – 54.0 (45.0; 60.0) versus 63.0 (54.0; 68.0); p <0.001 and all three subscales: Oral health – 15.0 (12.0; 18.0) vs. 12.0 (9.0; 14.0); p <0.001; Functional well-being – 15.0 (13.0; 16.0) vs. 12.0 (10.0; 15.0); p <0.001; Socio-emotional well-being – 32.0 (28.0; 36.0) vs. 30.0 (23.0; 33.0); p <0.001.

Discriminant validity was assessed using ROC analysis, which showed its good diagnostic characteristics: Sensitivity 80.1%; Specificity 71.1%; AUC=0.722 (p <0.001), 95% CI 0.661 – 0.779.

The Convergence Validity Assessment (Table III) showed that all correlation coefficients between COHIP-SF 19 UK, its subscales, and self-assessment of oral health were statis-

tically significant (p <0.05), positive and ranged from 0.21 to 0.53 (p <0.05). The highest correlation coefficients were between the overall COHIP-SF 19 UK score and its oral health self-assessment subscales. The highest correlation was found between perceived oral health and oral health – r_s=0.53 (p<0.001).

Statistically significant correlations were found between all COHIP-SF 19 UK subscales and WHOQOL-8 quality of life assessments, the largest of Overall COHIP-SF 19 UK being r_s=0.30 (p<0.001).

DISCUSSION

Improving the quality of life associated with oral health is a leading public health goal [1], so it is essential to have a short, valid methodology for assessing OHRQoL [9].

Unlike other studies [9 – 14], ours focused on the wider application of the methodology for the needs of the public health sector, at the level of which all measures to support dental health should be developed and coordinated from childhood.

Overall score Overall COHIP-SF 19 UK (maximum possible value 76) in the sample of Ukrainian children was 60.0 points (95% CI 58.0 – 61.0) with statistically significant differences in place of residence (p=0.011) and no age differences and article (p>0.05). The Functional well-being subscale score was the closest to the highest possible value, indicating that Ukrainian children have little or no problems with their mouths due to sleep, pronunciation, eating, and maintaining clean teeth.

The majority of surveyed children rate oral health (55.0%) and general health (61.1%) as good and very good. Self-esteem on these indicators is directly correlated with each other (r_s=0.30; p<0.001), so the worse the health of the oral cavity, the worse the assessment of the general condition and vice versa. This is confirmed in many other studies [8].

We obtained good psychometric properties of the technique, similar to the Chinese, Japanese, and most other versions [10 – 12].

Internal consistency for the overall score of COHIP-SF 19 UK as a whole and for individual subscales was sufficient (more than 0.7), for Overall COHIP-SF 19 was the highest – 0.89, the lowest for Oral health – 0.71.

The three-factor model COHIP-SF 19 UK was confirmed by factor analysis.

The validity of repeated studies was proven using the Intraclass Correlation Coefficient and ranged from 0.64 to 0.87 (p<0.001) for COHIP-SF 19 UK and its subscales.

Discriminant validity of the method was proved by comparing the results of COHIP-SF 19 UK among children in whom the dentist found abnormalities in the health of the oral cavity and without them – significantly lower values (p <0.001) in general and on all subscales were determined in the surveyed, who had dental health problems. ROC analysis showed a good discriminant ability of COHIP-SF 19 UK to detect oral health problems – AUC=0.722 (p<0.001).

The convergent validity of the method was proved by correlation analysis, which determined the presence of direct statistically significant correlations (p<0.05) COHIP-SF 19 UK and its subscale with self-assessment of health in general, oral health, and quality of life assessments for WHOQOL-8. The latter proves that the deterioration of OHRQoL has a lower health-related quality of life, so a positive impact on OHRQoL can lead to improved public health.

At present, the definition of OHRQoL among children and adolescents is used more for clinical practice [6] than for dental public health. COHIP-SF 19 was developed for use in clinical situations, OHRQoL assessment of children with different clinical conditions and different disease severity. This has some basis, as a subjective assessment of oral health provides unique data that correlates with clinical outcomes [9].

However, oral health is currently one of the determinants of quality of life. In recent years, many studies have been conducted on the impact of oral hygiene on quality of life, both general and specific – OHRQoL [8]. This was confirmed in our study. Therefore, the definition of OHRQoL is important for strengthening the public health system and building the dental public health sector.

Methodological limitations of the study include the inclusion of children from the age of 6 in the sample, which may lead to a certain shift in the sample. Also, the use of WHOQOL-8 quality of life assessment methods is more suitable for high school children and adolescents. Prospects for further research include a survey of a larger sample of children according to the methods of COHIP-SF 19 UK, oral health self-assessment (WHO), quality of life according to WHOQOL-8 to assess the impact of dental health on children's quality of life.

CONCLUSIONS

The study proved that COHIP-SF 19 UK is a reliable valid method for assessing the quality of life-related to oral health among Ukrainian children and adolescents, and its good psychometric properties correspond to those of other countries and are sufficient for research in the field of dental public health.

Recognizing that oral hygiene is an important component of overall health and well-being, it is important that national public health systems intensify the inclusion of oral hygiene and preventive measures in the field of DPH.

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ORIGINAL ARTICLE

THE TRENDS OF THE DENSITY OF SURGEONS IN SOME EUROPEAN COUNTRIES AND 16 OECD COUNTRIES DURING 2005-2018

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ABSTRACT

The aim: To establish that there are differences in the density trends of surgeons in some European countries and 16 OECD countries and to compare the trends of the density of surgeons in some European countries and 16 OECD member countries, 2005 – 2018.

Materials and methods: The study is based on data of the Centre for Medical Statistics of the Ministry of Health of Ukraine obtained during 2005-2020 and OECD data obtained during 2005-2018. The Difference-in-Differences method has been used to determine the density trends differences, the regression analysis method – to predict the number of surgeons in 2020.

Results: In 2020, there were 28,559 surgeons (0.687 per 1,000) in Ukraine, which is by 17.7% less than in 2005. From 2005 to 2018, the density of surgeons per 1000 in Ukraine and the United States decreased (-7.45% and -2.5%). In Korea (+ 78.38%), Greece (+ 65.52%), Lithuania (+ 58.57%), Slovenia (+ 45.65%) and other 11 countries the surgeon's density increased. In 2030, Ukraine is predicted to significantly reduce the number of surgeons, general surgeons, ophthalmologists and urologists; as well as to increase the number of cardiovascular surgeons. The number of proctologists, oncologists-surgeons, neurosurgeons, thoracic surgeons, orthopaedists-traumatologists and anaesthesiologists will not change significantly.

Conclusions: It is possible to state the availability of **s**urgical care according to the density of surgeons in Ukraine, similar to the level of OECD countries. In 2030, the number of surgeons is projected to decrease, with the exception of cardiovascular surgeons.

KEY WORDS: surgeons, density, trends

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INTRODUCTION

In 2015 the World Health Assembly adopted Resolution WHA68.15, in which surgical and anaesthesia care are recognized as the most important components of overall health coverage [1]. The goal of sustainable development of the United Nations are high-priority public investments in surgery, aiming to create sustainable health care systems with public access to comprehensive surgical care [2].

Safe and affordable surgical care, including anaesthesia, obstetrics and trauma care, is an important component of the health care system. However, in many countries globally, especially in those with below-average and low incomes, surgical care remains inaccessible to the population [3].

Lack of affordable surgical care leads to premature death and disabilities, which places a burden on country's economies. This global crisis is worsened by a lack of data on limited surgical infrastructure and manpower in many low- and middle-income countries [4].

Ukraine is a country with a per capita income below the World Bank's average ($ 3,540 per capita in 2020). Ukraine spent 3.2% of gross national product on health care in 2019 [5, 6]. Despite insufficient state funding of the health care system, Ukraine has a significant number of hospitals, beds and doctors. According to the data of Centre for Medical Statistics of the Ministry of Health of Ukraine in 2020, the health care system included 1186 hospitals (institutions), 232393 beds (5.58 beds per 1000), 123645 practitioners (2.96 per 1000) [7]. Physicians' density in Ukraine in 2020 was higher than that of some countries with high per capita incomes. According to the Organization for Economic Co-operation and Development (OECD), the physicians' density in Ukraine was higher than that of Japan (2.49 per 1,000) and Korea (2.39 per 1,000) in 2018.

In 2015, the Lancet Commission on Global Surgery (LCoGS) identified 6 indicators for assessment of the availability, safety, timeliness of surgical and anaesthesia care and the goal of developing surgical care by 2030 [2]. The indicators identified access to timely necessary surgical care, medical density of doctors per 100,000, the volume (extent) of surgery, 30-day mortality, protection against impoverishment and catastrophic costs of surgical treatment. By 2030, it is planned to provide 20 doctors (surgeons, obstetricians, anaesthesiologists) per 100,000 population worldwide.

So, the issue relevance of studying the achievement of the United Nations Sustainable Development Goals in Ukraine, as a representative of the countries with GNI per capita below average, and the availability of surgical care by the indicator of medical density of doctors in the surgical group is evident.

THE AIM

The aim of the study was to establish that there are differences in the density trends of surgeons in some European countries and 16 OECD countries, to compare the trends in density of surgeons in some European countries and 16 OECD member countries during 2005-2018.

MATERIALS AND METHODS

The study used data from the reporting form № 17 «Medical Staff Report» (http://medstat.gov.ua/ukr/statdan.html) of the Centre for Medical Statistics of the Ministry of Health of Ukraine for 2005-2020 and data from the Organization for Economic Co-operation and Development (OECD) for 2005-2018 [8].

The density of surgeons per 1,000 population for Ukraine and 16 OECD member countries (Canada, Estonia, France, Germany, Greece, Israel, Italy, Korea, Latvia, Lithuania, Norway, Poland, Portugal, Slovenia, USA) was calculated. These countries had complete data for the period of 2005-2018, except for Poland (data only for period of 2008-2017 was available) and were included in the group of high-income countries according to GNI per capita. Ukraine is in the group of countries with income below the GNI per capita average.

According to the OECD website, the specialists termed as surgeons include general surgeons, proctologists, oncologists, neurosurgeons, thoracic surgeons, cardiovascular surgeons, orthopaedists, traumatologists, anaesthesiologists, ophthalmologists, urologists, and emergency physicians.

The density of surgeons in Ukraine and 16 OECD countries was analyzed. Differences in the density trends of this group in Ukraine and 16 OECD countries in the period of 2005-2018 were determined using the statistical method Difference-in-Differences (DID). This study design is used to estimate the magnitude of the effect of an event in a study group compared to a control group (not subject to that effect) when observing groups over a period of time [9, 10].

The study group is subject to interference at some (but not initial) point of observation, while the control group is not subject to intervention at any point of time. The magnitude of the effect of the event is estimated by subtracting changes in the control group from the effects in the study group. Thus, DID design will eliminate the impact of trends and persistent differences between the two groups and correctly assess the effect of the intervention.

ATT (Average Time Treatment Effect) is the difference between the change, which took place under the influence of the event (2014 year), in Y (density of doctors in surgical group) since 2014 by the timepoint we are interested in, in the study group (Ukraine) and the control group (OECD countries):

ATT = () – ()

This method was used to assess the differences between trends in the period from 2005 to 2013 and in the period from 2014 to 2018 for Ukraine and OECD countries. In 2014, an extraordinary event took place in Ukraine, which affected population and doctors. This year, a part of Ukraine, along with the population and doctors, was occupied by Russia.

For each specialty of surgical profile in Ukraine, the growth rate was calculated using the method of regression analysis; and the estimated density for 2030 was determined.

Data analysis was performed using the license analysis package MedCalc v.19.4.1 (MedCalc Software Inc, Broekstraat, Belgium, 1993–2020) and statistical software EZR v. 1.54 (graphical user interface for R statistical software version 4.0.3, R Foundation for Statistical Computing, Vienna, Austria) [11].

RESULTS

In 2020, 28,559 surgeons worked in health care institutions of Ukraine (0.687 per 1,000 population or 68.7 per 100,000), which is by 17.7% less than in 2005 (34691 surgeons (0.736 per 1000 population or 73.6 per 100,000) (Figure 1).

In terms of the surgeon's density (0.74 per 1000), Ukraine ranked the 4th among 15 OECD countries in 2005 after Germany, Greece, Italy, and in 2018 ranked the 8th (0.68 per 1000) after Greece, Germany, Lithuania, Italy, Estonia, United Kingdom, Portugal, Latvia (Figure 2).

In the period from 2005 to 2018, the dynamics of surgeon's density in Ukraine, as in the United States, had a downward trend (-7.45% and -2.5% growth rate, respectively). In the other 15 OECD countries, the density of surgical group doctors during this period had a positive trend (Figure 3).

During this period, the largest rate of increase in surgeon's density was in Korea (+ 78.38%), Greece (+ 65.52%), Lithuania (+ 58.57%), Slovenia (+ 45.65%), Portugal (40.74%) (Figure 4).

In Ukraine, the density of surgeons in the period from 2005 to 2020 was described by 2 trends: positive trend from 2005 to 2013 (from 0.74 to 0.77 per 1000) and negative trend from 2014 to 2020 (from 0.69 to 0.68 per 1000) (Chart 1). In 2014, a part of Ukraine, together with the population and doctors, was occupied by Russia. This extraordinary event affected the population and the density of surgeons.

Using the DID method, we compared density of surgeon's trends in Ukraine and 16 OECD countries from 2005 to 2013 and from 2014 to 2018. For the DID method, surgeon's density indicators in Ukraine were included in the study group indicators, and the density indicators of 16 OECD countries were included in the control group indicators. Initially, differences in surgeon's density trends up to 2014 between the study group (Ukraine) and the control group (OECD countries) were clarified. No significant differences in trends during this period between Ukraine and 16 OECD countries were found (p-value for pre-test of parallel trends assumption: 0.9864).

The results of determining the differences in the change of the indicator (Δ = ATT) in the period from 2005 to 2018, i.e., the differences in the change in the density of surgeons

Fig. 1. Dynamics of the quantity and density of surgeons per 1000 population in Ukraine, 2005- 2020

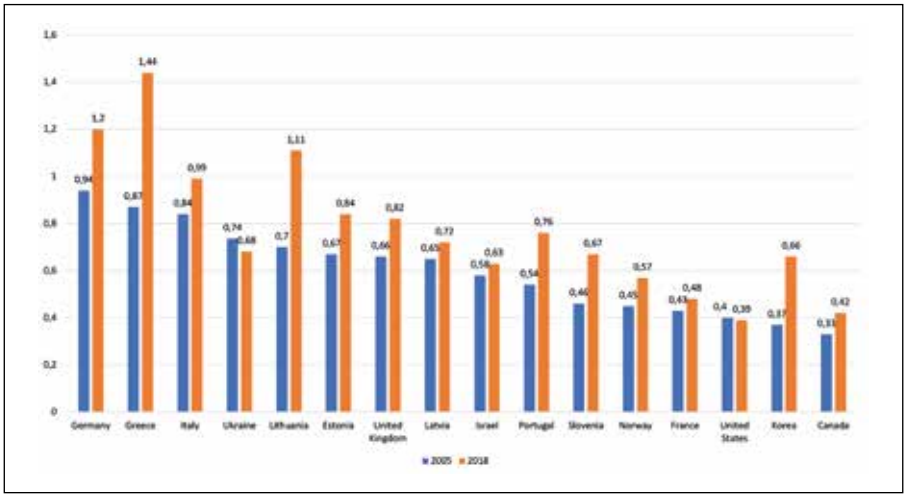

Fig 2. Surgeons in Ukraine and OECD countries. Density per 1000 population, 2005; 2018

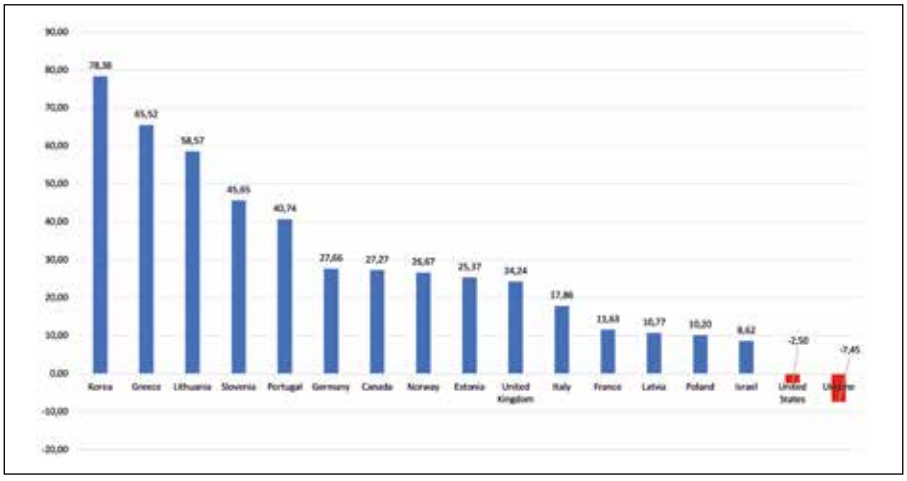

Fig 3. Density growth rate of surgeons in Ukraine and OECD countries, 2005-2018

in Ukraine and OECD countries are presented in Figure 5.

And if prior to 2014 there were practically no differences between the two groups – in 2013 Δ = – 0.020 (95% CI – 0.036 – – 0.004) Units, there was indeed a difference in 2014 between the change in the density of doctors of surgical group in Ukraine and OECD countries, Δ = –0.107 (95% VI – 0.176 – – 0.038 Units. The difference has been growing since 2014, by an average of 0.015 Units per year and in 2018 reached Δ = – 0.165 (95% CI – 0.239 – – 0.090) Units. DID-method confirms the significant impact of the events of 2014 on the dynamics of the density of surgeons in Ukraine. Therefore, the forecast of surgeon's density can be calculated only in the period from 2014 to 2020. The surgeons include 11 specialties (general surgeons, proctologists, oncologists-surgeons, neurosurgeons, thoracic surgeons, cardiovascular surgeons, orthopaedists-traumatologists, anaesthesiologists, ophthalmologists, urologists, emergency physicians).

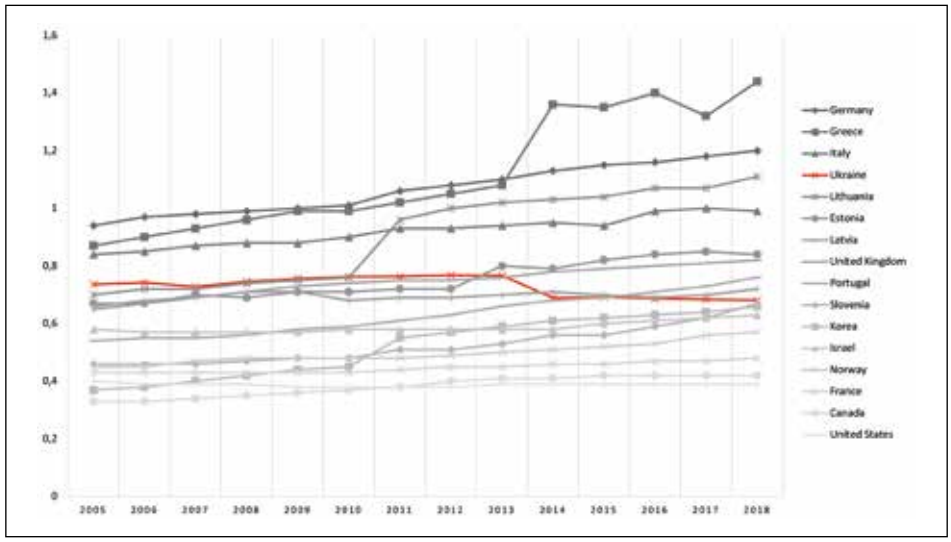

Fig 4. Density dynamics of surgeons in Ukraine and OECD countries, 2005-2018

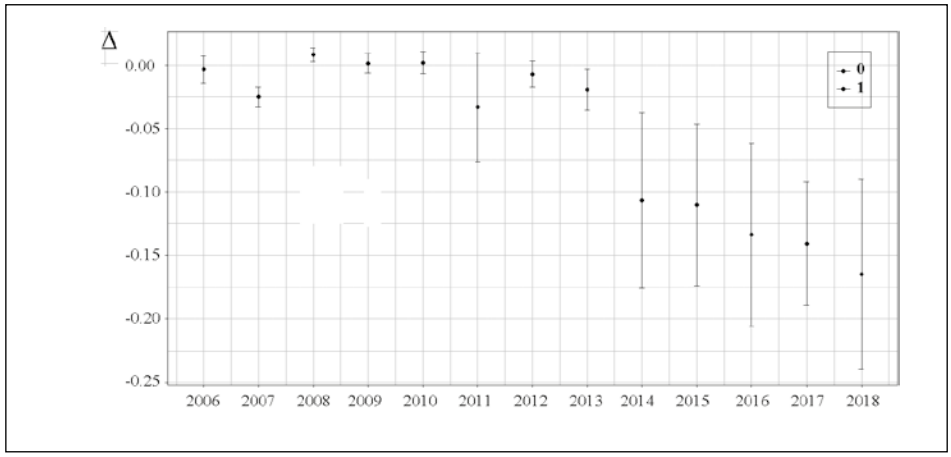

Fig 5. The results of determining the differences in the change of the indicator (Δ=ATT(g,t)), 0 – there are no differences, 1 – differences are identified.

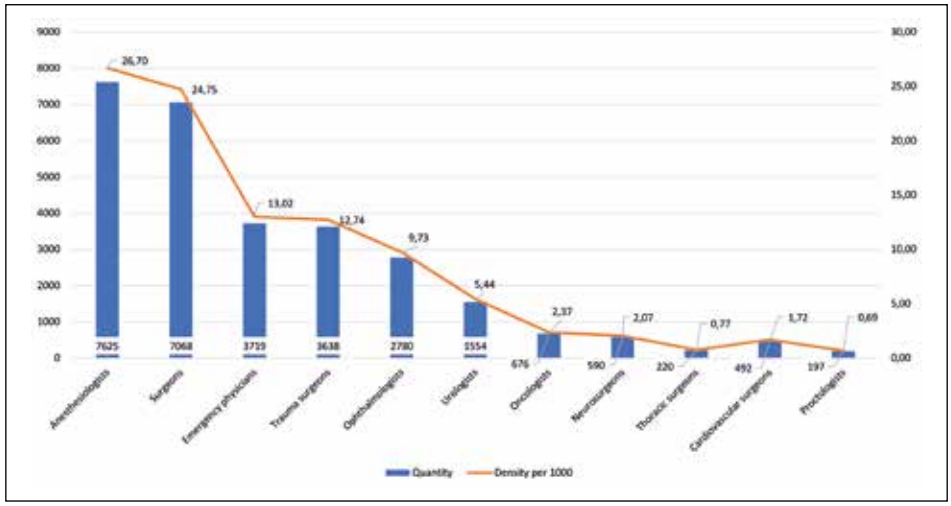

Fig 6. The quantity and density of surgeons by specialties in 2020 in Ukraine

The number and density of surgeons per 1000 population by specialties in Ukraine in 2020 is presented in Figure 6.

Using the method of regression analysis, we identified trends in the number of surgeons by specialty based on the indicators of 2014-2020. This period was chosen due to the change in the trend of surgeon's density in 2014. We found no significant dynamics of changes in the number of proctologists (R2 = 0.47, p = 0.0874), oncology surgeons (R2 = 0.53, p = 0.0653), neurosurgeons (R2 = 0, 52, p = 0.0676), thoracic surgeons (R2 = 0.30, p = 0.20), orthopaedist and traumatologists (R2 = 0.38, p = 0.1432), anaesthesiologists (R2 = 0.52, p = 0.0690) during the period. For these specialties, the correlation of the change in the number of surgeons and the year in Ukraine is not defined (p> 0.05). The number of surgeons and the number of general surgeons, cardiovascular surgeons, ophthalmologists,

Table I. The quantity of the surgeons by specialties is projected in 2030

Name of specialty	Coefficient of determination R2	p	The actual quantity of surgeons in 2020	Estimated number of surgeons in 2030	Growth rate from 2020 to 2030,%
Surgeons (all specialties)	0,9598	0,0001	28559	26520	-7,69
General surgeons	0,9427	0,0003	7068	5817	-21,51
Cardiovascular surgeons	0,9447	0,0002	492	630	+21,90
Ophthalmologists	0,9953	<0,0001	2780	2111	-31,69
Urologists	0,8741	0,002	1554	1451	-7,09
Emergency physicians	0,7812	0,0083	3719	3154	-17,91

urologists, doctors of the Ministry of Emergencies in the period from 2014 to 2020 shows a significant correlation with the year (p <0,05). For this group, using the method of regression analysis, we calculated their probable number in 2030. (Table I).

Therefore, in 2030 in Ukraine the number of cardiovascular surgeons is projected to increase, the number of doctors of surgical group, general surgeons, ophthalmologists, urologists, MOE doctors will decrease and the number of proctologists, oncologists-surgeons, neurosurgeons orthopaedists-traumatologists, anaesthesiologists will remain unchanged.

DISCUSSION

Based on the results of the study, Ukraine has reached the Lancet Commission on Global Surgery (LCoGS) recommended by 2030 target for the development of surgical care in countries with low and below average GNI per capita: by the surgeon's density per 100,000 population indicator in 2020, even without obstetricians and gynaecologists [2]. This figure in Ukraine is 68 per 100,000, which is three times more than the recommended indicator. The density of surgeons in Ukraine in 2017-2018 was higher than in high-income countries (Korea, Israel, France, Canada, Slovenia, USA, Norway, Poland). Thus, per surgeon's density indicator, Ukraine has already made partial progress in universal coverage of available surgical care. However, it is known that the key factor for achieving total universal coverage of health services is public funding, and, in particular, funding from national revenues. World experience has shown that the countries closest to the goals of universal coverage of health services, spend more than 80% of resources on health care from public sources [12]. Countries with GNI per capita with below average income, in particular Ukraine, spend on average only 40% of public funds [13]. The share of out-of-pocket expenditures on medical care in Ukraine in 2016 was 52.3%. [12]. This indicator leads to limited access to surgical care and impoverishment of the households, when it is necessary to receive surgical care.

It is known that in countries with below-average and low-income incomes, increasing health care costs will increase investment in facilities and human resources [14]. In Ukraine, it is not enough to increase funding for health care, it is necessary to optimize assets and human resources. As per the joint report made by the WHO European Bureau and the World Bank, only 24% of cases in Ukrainian hospitals are accompanied by surgery, compared to 70% in other countries [12].

In the period from 2005 to 2020 in Ukraine there has been an increase in per capita income from $ 1829.2 (2005) to 3725.6% (2020) [15]. At the same time, in contrast to OECD countries, there is a decrease in the density of surgeons (-7.45%), due to the surplus of these doctors in Ukraine.

In 2030, Ukraine is expected to reduce the number of surgeons, with the exception of cardiovascular surgeons. It is known that in high-income countries the density of cardiac surgeons is 7.15 surgeons per million population, and in low-income countries only 0.04 per million [16]. In Ukraine in 2020, the rate of cardiovascular surgeons was 12 per million population. However, this group of doctors includes vascular surgeons and cardiac surgeons. In Ukraine, the group of cardiac surgeons was not reported separately [17]. Therefore, we can only talk about a certain trend of growth within number of cardiac surgeons as well. The growth of this group is relevant against the background of the need to develop reperfusion centres in Ukraine for surgical care of patients with acute myocardial infarction [12].

CONCLUSIONS

In Ukraine, the availability of surgical care is ensured as an indicator of the density of surgeons at the level of OECD countries. In 2030, the number of surgeons is projected to decrease, with the exception of cardiovascular surgeons. At the same time, regarding Ukraine, it is necessary to ensure the availability, timeliness, safety of surgical care as indicators of prevention of catastrophic household payments.

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ORIGINAL ARTICLE

SOCIO-PSYCHOLOGICAL READINESS FOR MANAGEMENT OF FUTURE HEALTH CARE MANAGERS

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ABSTRACT

The aim: To determine the content, components and levels of formation of social and psychological readiness of future managers of the health care system for management activities.

Materials and methods: The research was conducted among students of master's programs that prepare future managers for the health care system of Ukraine. The basic motivators of their social and psychological activity as a person, the formation of metacognitive strategies, the diagnosis of communicative and characterological features of personality and signs of leadership are determined.

Results: These studies indicate the readiness of students for future activities. 80% of respondents were diagnosed with a high level of such potential, 20% – medium. The results indicate that the respondents have a significant potential of communicative and characterological abilities that can affect their further professional activity: intellectual (4,11±0,66) and volitional (4,17±0,33) traits, attitude to themselves (4,02 ± 0,36), focus on achieving goals (4,22 ± 0,42). The evaluation of the above characteristics was made on a 5-point scale. Future managers have formed a metacognitive "profile", identified high levels of metacognitive abilities (47,6 ± 4,182 points).

Conclusions: It is established that the respondents have a high and appropriate moderate level of formation of the main components of readiness for managerial activity and have the appropriate managerial potential.

KEY WORDS: Leadership, socio-psychological characteristics, competencies, personnel

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INTRODUCTION

A modern health care manager must master a powerful arsenal of approaches and methods of effective management. In addition, in the context of the outbreak of the COVID-19 pandemic, the problem of readiness of health care managers for management activities is becoming increasingly important and encourages its urgent solution. A significant role in solving this issue is played by the formation of socio-psychological readiness of managers to lead health care facilities.

Socio-psychological readiness from the standpoint of personal approach is seen as a result of preparedness of the future manager for a particular activity, which involves a combination of many components that meet the requirements, content and conditions of a particular activity and together determine its productive implementation [1].

Socio-psychological readiness for management is influenced by a number of factors. These are the following: (1) the presence of general and special abilities, motivation for management, special knowledge and skills; (2) readiness to manage risks, as well as solving complex issues, overcoming stressful situations in order to achieve goals; (3) the ability to operate under high stress; (4) willingness to act in a rapidly changing environment; (5) value attitude to professionalism; (6) the formation of the "I-concept", which includes ideas about professional activities and their own careers; (7) the development of cognitive and metacognitive processes [2-5].

Socio-psychological readiness characterizes the actual and potential resources of a person, which determine his ability to achieve mastery in the profession, includes specific actions and deeds of the individual that contribute to the productive functioning and development of the organization he manages [6].

In preparing and conducting this research, the approaches and competencies catalogue of management positions in the medical field, recommended by the Healthcare Leadership Alliance (HLA), were used. This catalogue of competencies of health care managers includes 802 competencies of health care managers in five main groups:
- communication and relation management;
- leadership;
- professionalism;
- knowledge of health care;
- business knowledge and skills [7].

Analysis of the content of HLA competencies indicates a significant role for the acquisition of socio-psychological resources of the health manager: professional and personal motivation, the formation of intellectual processes (cognitions and metacognitions), communication skills, development of certain personal characteristics.

THE AIM

The aim of the study was to determine the content, components, and levels of formation of socio-psychological

readiness of future managers of the health care system for management activities.

MATERIALS AND METHODS

The research was conducted among students of master's programs who studied at the School of Public Health of the National University of Kyiv-Mohyla Academy, NaUKMA, specialization "Health Care Management", and the Institute of Business Education of Kyiv National Economic University named after Vadym Hetman, KNEU, specialization "Business Administration in the field of health care": a total of 30 respondents (15 of whom studied at NaUKMA, the other 15 – KNEU). The study was conducted in March – June 2021.

The following methods were used in the research:

1. Determining among respondents the levels of such basic motivators of activity as (1) success in general, (2) desire for power, (3) tendencies to affiliation (group recognition and respect) was carried out according to the method of diagnosing motivators of socio-psychological activity of person.
2. To diagnose the level of formation of metacognitive strategies in respondents, a scale of self-assessment of metacognitive behavior was used (maximum score of 60 points).
3. Diagnosis of communicative-characterological features of personality was used to determine the basic features of personality in the process of interpersonal relationships [8], which allowed to form a profile of communicative-characterological features of respondents on 7 indicators: personality orientation, intellectual, volitional, emotional traits and attitudes to others and to oneself.
4. The Multifactor Leadership Questionnaire was used to assess leadership competencies, including those related to transformational leadership by indicators such as influence, inspiration, intellectual stimulation, individual approach, motivation, management, independence and overall factor of transformational leadership (total for all these factors) [9].
5. To differentiate managerial capacity by levels (low, medium, high), rapid assessment of managerial potential was used. Evaluation of results according to this method: the range of values from 1 to 6 points – a low level of management capacity, the average from 7 to 13 – average, from 14 to 20 points – high.
6. A special questionnaire was developed to study the socio-psychological characteristics of respondents (age, gender, general and managerial experience, availability of medical education).
7. Methods of mathematical statistics were used to process the obtained results: descriptive analysis to determine the formation of the main components of socio-psychological readiness for management of future managers of the health care system; statistical criteria of Mann-Whitney U test and Kruskal–Wallis H test to determine the differences between the structural components of the socio-psychological readiness of future managers of the health care system to manage at different levels of its formation [10].

We considered various ethical concerns while carrying out this research. The research methodology was considered at the meeting of the NaUKMA Academic Council Committee on Research Ethics (protocol № 6 from May 27th, 2021).

The informed consent was obtained from each respondent. Information about the aim, objectives and scope of this study was provided at the beginning of the investigation. The complete confidentiality of the respondents was therefore guaranteed. All data collected for the purpose of this study was used only for the study.

The Statistical Package for the Social Sciences (SPSS for Windows, version 25, 2017, SPSS, Chicago, IL, USA) was used for data analysis.

RESULTS

The main characteristics of the respondents are presented in the Table I. The study involved 6 men and 24 women, mean age – 37.97 ± 1.3 years (median – 33), work experience as a manager in the field of health care – 4.83 ± 0.73 years (median – 4). 50% of respondents had medical heigh education (NaUKMA – 8; KNEU – 7).

The results of the study on the motivational component indicate that the need for success in all students without exception is at a high level (100% of respondents); for 73.3% of respondents such a motivator as "Desire for power" is fixed at a high level, 26.7% – average. The motive-tendency to affiliation as a group recognition and respect or desire for social prestige does not occupy such high levels as the above-mentioned motivators. 40% of master's students have a high level of its formation, 60% of master's students – medium level.

Table I. General characteristics of respondents

		NaUKMA	KNEU	General sample
Number		15	15	30
Age, years		23-44	21-45	21-45
Sex	Male	3	3	6
	Female	12	12	24
General work experience		from 3 to 22 years	from 5,5 to 35 years	from 3 to 35 years
Management experience		from 1 to 15 years	from 1 to 15 years	from 1 to 15 years
Number of people with medical education		8	7	15

Table II. Frequency characteristics of self-assessment levels of metacognitive behavior

		Frequency	Interest	Accumulated interest
Admissible	33,00	1	3,3	3,3
	43,00	1	3,3	6,7
	44,00	3	10,0	16,7
	45,00	3	10,0	26,7
	46,00	3	10,0	36,7
	47,00	4	13,3	50,0
	48,00	3	10,0	60,0
	49,00	3	10,0	70,0
	50,00	3	10,0	80,0
	52,00	2	6,7	86,7
	53,00	3	10,0	96,7
	55,00	1	3,3	100,0
	Total	30	100,0	

Table III. Distribution of respondents' data by levels of leadership abilities

Components of leadership	Level					
	Low abilities		Moderate abilities		High abilities	
	Number of people	%	Number of people	%	Number of people	%
Influence	0	0	7	23,3	23	76,7
Inspiration	0	0	4	13,3	26	86,7
Intellectual stimulation	0	0	17	56,7	13	43,3
Individual approach	0	0	15	50,0	15	50,0
Motivation	0	0	9	30,0	21	70,0
Management	1	3,3	13	43,3	16	53,3
Granting independence	1	3,3	16	53,3	13	43,3

Peculiarities of the intellectual component among the respondents were studied according to the method "Scale of self-assessment of metacognitive behavior" (maximum score of 60 points). The individual results of the respondents according to this method were located in the zone of mostly high and medium values (average value 47.6 ± 4.182 points). Frequency characteristics of self-assessment levels of metacognitive behavior of respondents are presented in the Table II.

The study of the profile of communicative-characterological features of personality included such basic features of personality as orientation, intellectual, volitional and emotional traits of character, attitude to activity, to others and to oneself. Among the respondents, orientation as one of the communicative and characterological features of personality, which determines all the behaviour of the individual, attitude to oneself, others and work, has the highest level (4.22 ± 0.42). Among the communicative and characterological features of the respondents, the most important character traits are those that describe the intellectual (4.11 ± 0.66) and volitional traits (4.17 ± 0.33) of the character, as well as the attitude to oneself (4.02 ± 0.36). Emotional traits (3.77 ± 0.46) have a lower weight, which characterizes future managers mainly as more restrained in emotional manifestations. The lowest rate is the attitude towards others or service to others (3.65 ± 0.56).

Leadership abilities of future managers were investigated using a standardized questionnaire "Multifactor Leadership Questionnaire" [9] to identify three levels of 7 factor-scale associated with transformational leadership indicators: influence, inspiration, intellectual stimulation, individual approach, motivation, management and representation of independence. The results for the levels of individual components related to leadership are presented in Table III.

In general, such socio-personal competence as leadership among respondents is formed at the appropriate level. The highest results were obtained on the scales "Inspiration" (diagnosed in 86.7% of respondents), "Influence" (76.7%) and "Motivation" (70%). The results between the average and high levels were almost equally distributed according to other factor-scales: "Intellectual stimulation" and "Granting independence" (high levels in 43.3% of respondents, medium – 56.7% and 53.3%, respectively), "Individual approach" – distribution of 50: 50% between moderate and high levels of ability.

Table IV. Data of statistical analysis of managerial potential of respondents

Socio-psychological characteristics		N	Middle rank	The sum of the ranks	Manna-Whitney U test	Wilcoxon signed-rank test	Standard score, z-score	Asymptotic 2-sided significance
Age	Medium level	6	18,25	109,50	55,500	355,500	-,857	,391
	High level	24	14,81	355,50				
	Total	30						
General work experience	Medium level	6	16,08	96,50	68,500	368,500	-,182	,855
	High level	24	15,35	368,50				
	Total	30						
Work experience in a managerial position	Medium level	6	15,67	94,00	71,000	-,052	,958	,980b
	High level	24	15,46	371,00	371,000			
	Total	30						
Motivator of activity: achieving success	Medium level	6	12,50	75,00	54,000	-,961	,336	,374b
	High level	24	16,25	390,00	75,000			
	Total	30						
Motivator of activity: the desire for power	Medium level	6	16,92	101,50	63,500	-,446	,655	,667b
	High level	24	15,15	363,50	363,500			
	Total	30						
Motivator of activity: the desire for affiliation	Medium level	6	13,75	82,50	61,500	-,550	,582	,595b
	High level	24	15,94	382,50	82,500			
	Total	30						
Leadership: influence	Medium level	6	14,17	85,00	64,000	-,435	,664	,705b
	High level	24	15,83	380,00	85,000			
	Total	30						
Leadership: the ability to inspire	Medium level	6	13,50	81,00	60,000	-,640	522	,561b
	High level	24	16,00	384,00	81,000			
	Total	30						
Leadership: intellectual stimulation	Medium level	6	14,67	88,00	67,000	-,266	,790	,820b
	High level	24	15,71	377,00	88,000			
	Total	30						
Leadership: individual approach	Medium level	6	14,00	84,00	63,000	-,483	,629	,667b
	High level	24	15,88	381,00	84,000			
	Total	30						
Leadership: motivation	Medium level	6	20,17	121,00	44,000	-1,486	,137	,158b
	High level	24	14,33	344,00	344,000			
	Total	30						
Leadership: management	Medium level	6	13,85	132,50	32,500	-2,083	,037	,038b
	High level	24	22,08	332,50	332,500			
	Total	30						
Leadership: giving independence	Medium level	6	19,17	115,00	50,000	-1,155	,248	,273b
	High level	24	14,58	350,00	350,000			
	Total	30						
Leadership: transformation	Medium level	6	14,90	107,50	57,500	-,754	,451	,462b
	High level	24	17,92	357,50	357,500			
	Total	30						

Self-assessment of metacognitive behavior	Medium level	6	13,00	78,00	57,000	-,781	,435	,462b
	High level	24	16,13	387,00	78,000			
	Total	30						
Communicative and characterological features: orientation	Medium level	6	15,00	90,00	69,000	-,156	,876	,900b
	High level	24	15,63	375,00	90,000			
	Total	30						
Communicative and characterological features: intellectual	Medium level	6	12,58	75,50	54,500	-,937	,349	,374b
	High level	24	16,23	389,50	75,500			
	Total	30						
Communicative and characterological features: volitional	Medium level	6	10,75	64,50	43,500	-1,491	,136	,143b
	High level	24	16,69	400,50	64,500			
	Total	30						
Communicative and characterological features: emotional	Medium level	6	14,67	88,00	67,000	-,263	,792	,820b
	High level	24	15,71	377,00	88,000			
	Total	30						
Communicative and characterological features: attitude to activity	Medium level	6	11,42	68,50	47,500	-1,286	,198	,210b
	High level	24	16,52	396,50	68,500			
	Total	30						
Communicative and characterological features: attitude to others	Medium level	6	18,08	108,50	56,500	-,817	,414	,432b
	High level	24	14,85	356,50	356,500			
	Total	30						
Communicative and characterological features: attitude to oneself	Medium level	6	9,75	58,50	37,500	-1,836	,066	,073b
	High level	24	16,94	406,50	58,500			
	Total	30						

b. Not adjusted for connections.

Thus, in general, it can be stated that these studies indicate the formation of the respondents of 7 studied factors of leadership as the main characteristic of personal competence, readiness for management activities in the field of health care.

The results of comparing the levels of managerial potential between respondents studying at NaUKMA and KNEU indicate the presence of only one difference on the scale "Management" of the methodology "Multifactor Leadership Questionnaire" ($p = 0.037$) (Table IV). This scale indicates the peculiarities of the formation of personal competence to the implementation of the management process, the organization of effective work of employees or subordinates.

In terms of managerial capacity, 80% of respondents were diagnosed with a high level of such capacity, 20% – average, which indicates a significant willingness of future managers to work in the health care sector.

Thus, the results of the study indicate the appropriate level of formation of all the main components of social and psychological readiness of future managers studying in the master's programs of NaUKMA and KNEU, for management activities in the field of health care.

DISCUSSION

The results of the study on the formation of the main components of readiness for management showed its proper level among all respondents. This is due to the diversification of educational training of future managers in the field of health care, their involvement in independent activities, solving professional issues, as pointed out by other researchers [11,12]. Some researchers also note that "manager" competency in the health care system was redefined as "leader" competency [13].

The need to study the main components of socio-psychological readiness of future managers in terms of leadership

qualities is confirmed by other studies [14]. According to Maddalena V., the concept of leadership belongs to teamwork with a common model of decision-making, so it should be applied and strengthened among all health care professions [15].

The presence of a high level of managerial capacity among 80% of respondents indicates their readiness for future activities, as this may affect the productivity of work processes and the activities of the health care institution [16].

These studies indicate that intellectual competence, as one of the main components of readiness for management activities of future managers, is formed at the appropriate level. According to some researchers, the developed intellectual competence expands the cognitive support of human life, the formation of his overall life experience [17], which is important for further professional activity.

Data from the study of the general profile of communicative and characterological features of students-future managers indicate that the respondents are most characterized by orientation, intellectual and volitional traits. This is an important "finding" of this study, as the role of the manager in setting the goals of the institution or its structural unit, responding to challenges and obstacles, making decisions to ensure productive activities, etc. are the key in its activities [18]. Emotional character traits have a lower weight, which characterizes future managers mainly as more restrained in emotional manifestations.

CONCLUSIONS

1. A model for determining the socio-psychological readiness of future health care managers for leading activities, which included motivational, intellectual, communicative and personal components, was used during the study.
2. It is established that the respondents have a high and appropriate moderate levels of formation of the main components of readiness for management activities and have the appropriate management potential, in particular:
   - the motivational component in terms of the need-motivator to achieve success in general is formed in all respondents at a high level, because the desire to succeed, rather than the desire to avoid failure, is an important characteristic of managerial efficiency;
   - the level of the intellectual component of the respondents is high, which is acceptable for identifying readiness for management activities;
   - communicative component, which is closely related to characterological features, is also formed, which indicates the commitment of respondents to collective forms of interaction, the appropriate level of communication, focus on the result of interaction with others, building friendly relationships with colleagues, promoting constructive interaction between people and groups in any situation;
   - personal competencies, which were considered mainly through the socio-personal competence of leadership in terms of: influence, inspiration, intellectual stimulation, individual approach, motivation, management, representation of independence, have mostly high and moderate levels of ability, indicating that respondents are able to overcome obstacles on the way to achieving goals, build self-confidence, motivate others to achieve goals, create an environment that allows employees to show their abilities and self-realization.

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ORIGINAL ARTICLE

NATIONAL ASSESSMENT OF PNEUMONIA MORBIDITY IN CHILDREN IN THE PERIOD 1993-2017 AND PROGNOSIS FOR 2025

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ABSTRACT

The aim: To assess national trends in the morbidity of pneumonia in children aged 0-6 years, 7-14 years and 15-17 years in the period from 1993 to 2017 and mathematically predict the dynamics of the morbidity in 2025.

Materials and methods: Data from the Center for Medical Statistics of the Ministry of Health of Ukraine for the period 1993-2017 were used to calculate the morbidity rate of pneumonia in children aged 0-6 years, 7-14 and 15-17 years.

Result: The period from 1993 to 2017 is characterized by high incidence of pneumonia in children in Ukraine (from 6.74 to 8.21 per 1000). In children aged 0-6 years, the morbidity 1000 ranged from 11.45 to 11.17, in children aged 7-14 years – from 4.65 to 6.46, in adolescents aged 15-17 years – from 1.99 to 10.47 . In Ukraine, the morbidity rate has significantly exceeded the that in European countries. In 2025, the morbidity of children under 6 years old in Ukraine may make up 3.84 per 1,000.

Conclusions: In Ukraine, a significant increase in the morbidity rate of pneumonia in adolescents is predicted by 2025. It is necessary to develop a national strategy to improve the health of children and adolescents to implement policy and management measures in the health care system, aimed at effective prevention and quality treatment of pneumonia in children and adolescents.

KEY WORDS: pneumonia, children, morbidity rate, national trends

Wiad Lek. 2022;75(5 p1):1175-1179

INTRODUCTION

Respiratory diseases are the leading cause of death and morbidity among infants and children under 5 years of age worldwide [1]. The range of diseases varies from acute infections to chronic non-communicable diseases. Pneumonia is the leading cause of infant mortality, causing nearly 1.3 million deaths each year, most of which could have been prevented [1]. Hospitalization of pediatric patients for pneumonia is a heavy burden on patients, families, and the health care system. 75.9% of hospitalizations for pneumonia are registered among children under 1 year of age and 2% of children under 19 years of age [2]. In addition, after having pneumonia, 5.5% of outpatients and 13.6% of hospitalized children have a high risk of at least one serious complication [3].

In the Integrated Global Plan of Action to Prevent Childhood Mortality from Pneumonia and Diarrhea by 2025 (GAPPD), the World Health Organization aims to reduce pneumonia mortality among children under 5 years of age (up to 3 cases per 1,000) and reduce the morbidity rate of severe pneumonia by 75% in children under 5 years of age compared to 2010 [4]. GAPPD proposes to achieve such indicators by ensuring the availability of treatment for pediatric pneumonia and by monitoring the morbidity rate.

It should be noted that the ratio of mortality to the morbidity rate of pneumonia in children under 5 years is one of 23 indicators used for assessing the effectiveness of medical services in the health care system [5].

In addition, pneumonia continues to be the leading cause of illness in children under 5 years, especially in low- and middle-income countries [2]. Ukraine belongs to the group of countries with below-average income according to the World Bank classification ($ 3,540 per capita in 2020) [6].

Therefore, the issue of assessing the dynamics of pneumonia morbidity rate among children in Ukraine to improve the availability and quality of health care is relevant. Especially since during the last 3 years in Ukraine there has been an ongoing reformation of the health care system, which involves a change in funding, the acquisition of priorities of the primary level of medical care and introduction of medical guarantees [7]. In these conditions, predicting pneumonia morbidity rate trends among children is of particular importance for the organization of a high-quality medical care.

THE AIM

Assess national trends in the morbidity of pneumonia in children aged 0-6 years, 7-14 years and 15-17 years in the period from 1993 to 2017 and mathematically predict the dynamics of the morbidity in 2025.

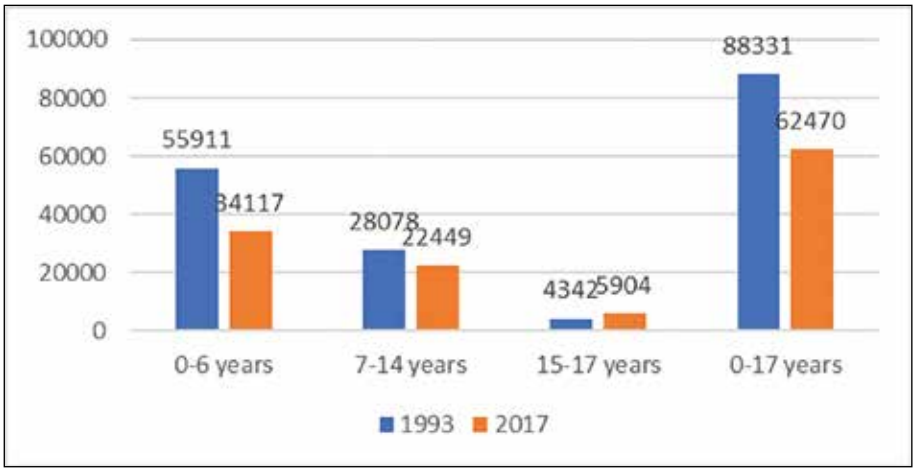

Fig. 1. The number of cases of pneumonia in children in the age groups 0-6 years, 7-14 years and 15-17 years in 1993 and 2017

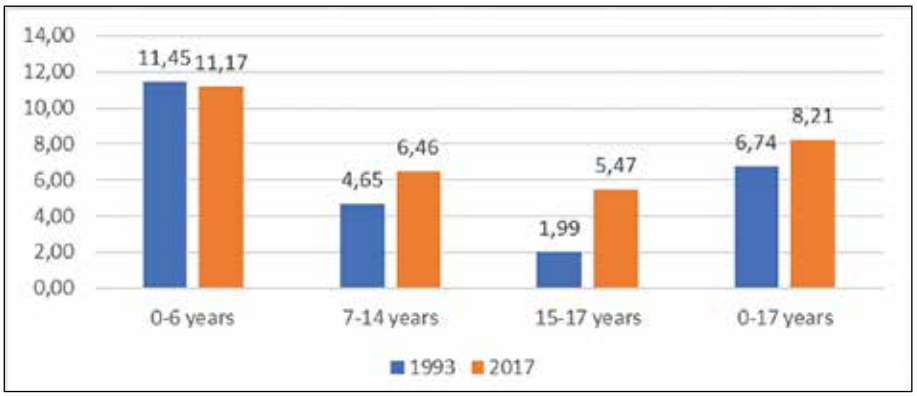

Fig. 2. The morbidity of pneumonia per 1000 in different age groups of children in 1993 and 2017 in Ukraine

MATERIALS AND METHODS

The data of reporting form nº 12 "On number of diseases registered in patients living in the service area of the medical institution" offered by the Center for Medical Statistics Ministry of Health of Ukraine, covering the period 1993-2017, were used in order to calculate the morbidity rate of pneumonia in children aged 0-6 years, 7-14 and 15-17 years [8]. Since 2018, cases in Ukraine have not been officially registered and monitored. Therefore, it is impossible to determine the morbidity rate in the period after 2017 in Ukraine.

The data obtained from the State Statistics Center of Ukraine were used to calculate the morbidity per 1,000 population [9]. For each age group, the morbidity for 1,000 children of the corresponding age, in the period from 1993 to 2017, has been calculated .

To compare the morbidity rate in 3 groups, mean and standard deviation were calculated. Analysis of variance (ANOVA) was used to compare age groups. Scheffé test was used for *a posteriori* comparison.

Prediction is based on the method of regression analysis. Data analysis was performed using the license analysis package MedCalc v.19.4.1 (MedCalc Software Inc, Broekstraat, Belgium, 1993–2020).

RESULTS

In 1993, 88,331 cases of pneumonia were registered in Ukraine, of which 63.3% (55,911 cases) in children aged 0-6 years, 31.8% (2,878 cases) in children aged 7-14 years and 4.9% (4,342 cases) in adolescents aged 15-17 years. In 2017, the number of cases of pneumonia among children decreased by 29.3% compared to 1993. In 2017, 62,470 cases of pneumonia were registered, of which 54.6% (34,117 cases) in children aged 0-6 years, 35.9% (22,449 cases) in children aged 7-14 years and 9.45% (5,904 cases) in adolescents 15-17 years (Fig. 1).

The morbidity of pneumonia in 1993 was 6.74 per 1,000 children, and in 2017 – 8.21 per 1,000 children (Fig. 2). Hence, in 2017 there was an increase in the morbidity rate by 21.8% compared to 1993.

In 2017, there was a slight decrease in the morbidity rate of pneumonia in children aged 0-6 years (-2.5%), an increase in the groups 7-14 years (+ 38.8%) and a significant increase in the group 15-17 years (+175 .5%).

For further analysis, we determined the mean values and standard deviations of pneumonia morbidity per 1,000 by age groups in the period 1993-2017 (Table I).

Significant differences in the age groups in terms of morbidity per 1,000 children in the period 1993-2017 were determined using analysis of variance ($p < 0.001$). The highest morbidity rate was determined in the group of 0-6 years (12.97 + 1.78 per 1,000), the lowest – in the group of 15-17 years (4.19 + 1.40 per 1,000).

The morbidity of pneumonia per 1,000 population in the period 1993-2017 was characterized by a certain dynamic pattern, which is shown in Fig. 3.

The dynamic pattern of morbidity at the age of 0-6 years and 7-14 years in the period from 1993 to 2017 was described

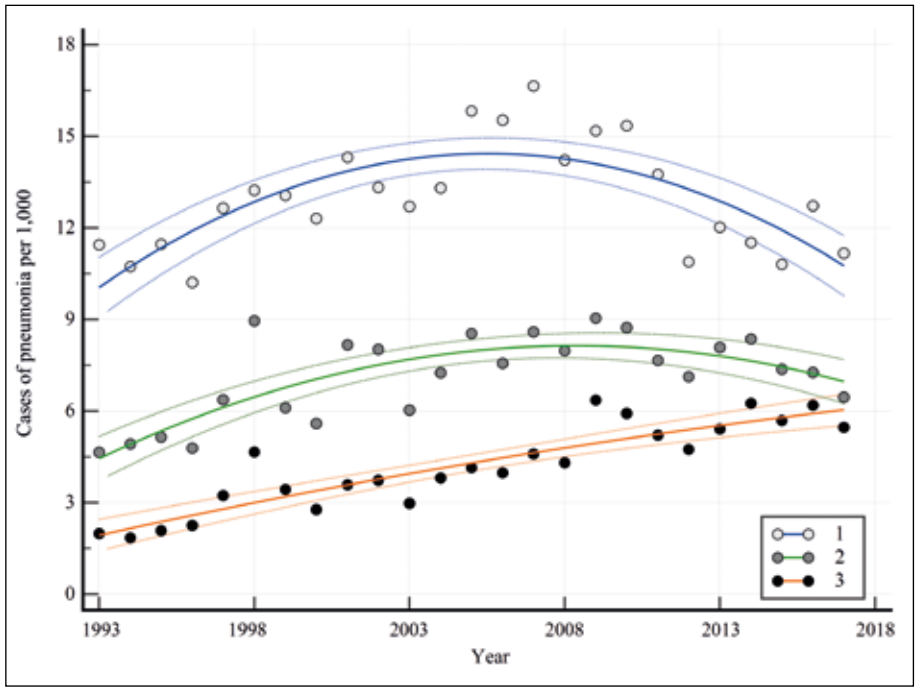

Fig. 3. Dynamics of pneumonia per 1,000 at the age of 0-6 years (1), at the age of 7-14 years (2), at the age of 15-17 years (3) in the period 1993-2017.

Table I. The mean values and standard deviation of the pneumonia morbidity in children of different age groups in the period 1993-2017

№ groups	Age of children in the group	Number of years for analysis 1993-2017	The mean morbidity in the group	Standard deviation
1	0-6 years	25	12.97	1.78
2	7-14 years	25	7.15	1.37
3	15-17 years	25	4.19	1.40

Table II. The formulas for regression analysis of morbidity for each age group.

Age group	Formula	R^2	P
0-6 years	$y = 10.0577 + 0.6992 x + -0.02792 x^2$	0.5648	P = 0.0001
7-14 years	$y = 4.4485 + 0.4818 x + -0.01570 x^2$	0.6094	P <0.0001
15-17 years	$y = 1.9375 + 0.2232 x + -0.002178 x^2$	0.8079	P <0.0001

Table III. Actual morbidity of pneumonia per 1,000 in 2010, 2017 and the forecast for 2025 in Ukraine

Group	The morbidity of pneumonia			Growth rate from 2010 to 2025,%
	2010 actual	2017 actual	2025 predicted	
0-6 years	15.35	11.17	3.8420	-74.9%
7-14 years	8.73	6.46	3.7993	-56.6%
15-17 years	5.93	5.47	6.8496	+ 15.5%

with a parabolic curve. The morbidity curve in the group 0-6 years had the maximum value in 2007 (16.55 per 1,000), in the group 7-14 years – in 2009 (9.04 per 1,000). After reaching the maximum values in the two age groups, there is a gradual decrease in the morbidity rate. The dynamics of morbidity in the age group of 15-17 years is linear with a pronounced tendency to increase. However, to unify this approach, we used the parabolic trend and the linear trend, which are presented for the group of 15-17 years in Fig. 3.

We identified formulas for regression analysis of morbidity for each age group (Table II)

These formulas were used to determine the estimated pneumonia morbidity rates in 2025, which are presented in Table III. The growth rates in 2025 compared to 2010, which was determined by the WHO as the year of comparison in the Integrated Global Plan of Action to Prevent Childhood Pneumonia and Diarrhea Mortality by 2025 (GAPPD) were also determined [4].

Hence, mathematical modeling shows a projected reduction of pneumonia morbidity rate in children aged 0-6 years and 7-14 years in 2025 compared to 2010 in Ukraine (respectively -74.9% and -56.5%). However, in the group of adolescents aged 15-17 years there is a probability of increasing the morbidity rate of pneumonia by 15.5%.

DISCUSSION

The presented results of the study show that in Ukraine the largest number of cases of pneumonia is registered in the group of children aged 0-6 years (54.5%), the least – in the group of adolescents aged 15-17 years (9.45%). The group of children aged 7-14 years accounted for 35.9% of all cases among children from 0 to 17 years. In the world, the vast majority of all cases of pneumonia are registered at the age of 6 years [5, 4]. For example, in South Korea, the children with pneumonia aged 0-6 years accounted for 89.2% of all cases in children aged 0-17 years, children aged 7-12 years – for 7.4% of cases, children aged 13-17 years – for 3.4% [10].

In the period from 1993 to 2017 in Ukraine there was observed high pneumonia morbidity rate in children (from 6.74 to 8.21 per 1,000). The highest morbidity rates in this period were found in children aged 0-6 years (from 11.45 to 11.17 per 1,000), the lowest rates – in adolescents aged 15-17 years (from 1.99 to 5.47 per 1,000) . During this period, the morbidity rate in children aged 7-14 years ranged from 4.65 to 6.46 per 1,000.

The obtained morbidity rates are much higher than the morbidity rates of pneumonia in children in European countries. During this period in European countries, the morbidity rate of pneumonia in children under 5 years of age was 3.38 per 1,000, in children over 5 years – 1.44 per 1,000 [11]. In Ukraine, the morbidity rate of pneumonia exceeds similar values almost three times.

According to the WHO, more than 14 cases of pneumonia per 1,000 children were registered in the world in 2019, or 1 case per 71 children per year, with the highest morbidity in South Asia (25 cases per 1,000 children), as well as in West and Central Africa (6.20 cases per 1000 children) [12]. According to the WHO in Ukraine, the morbidity rate of pneumonia among children in 2019 was 5.4 per 1000 [12]. In the United States, the morbidity rate of pneumonia was 1.57 cases per 1,000 children [13].

In 2010, the WHO by the Integrated Global Plan of Action to Prevent Pneumonia and Diarrhea Mortality by 2025 (GAPPD) recommended that governments around the world should take steps to reduce morbidity in children under the age of 5 years to 3 per 1,000 population [4]. The conducted mathematical modeling on the basis of regression analysis in our study shows that the morbidity trends in 1993-2017 in Ukraine in children 0-6 years are decreasing. In 2025, the morbidity rate in Ukraine for children under 6 years of age may be 3.84 per 1,000. Hence, there is a probability that the recommended morbidity rate in Ukraine will be reached in 2025.

However, in the group of adolescents aged 15-17 years, the pneumonia morbidity trend is growing. In this group, in 2025 the morbidity is expected to increase by 15.5%. It is likely that in 2025 the morbidity rate in this group will be 5.47 per 1,000. This is a disappointing prognosis for the state, which necessitates focusing on research of the pneumonia cases growth in adolescents.

It is known that one of the causes of pneumonia in adolescents is tobacco smoking [14,15]. In Ukraine, according to the European School Survey Project on Alcohol and Other Drugs (ESPAD), a trend since 2003 to reduce the experience of smoking among adolescents has been observed [16]. It is likely that the reason for the increase in pneumonia in adolescents in Ukraine is due to other reasons. Among the other reasons there may be poorly managed obligatory vaccination of adolescents against common respiratory infections, lack of standards for the treatment of pneumonia and shortcomings in the organization of medical care for adolescents [17].

CONCLUSIONS

In Ukraine, a significant increase in the morbidity rate of pneumonia in adolescents is predicted by 2025. It is necessary to develop a national strategy to improve the health of children and adolescents to implement policy and management measures in the health care system, aimed at effective prevention and quality treatment of pneumonia in children and adolescents.

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ORIGINAL ARTICLE

COMPARISON OF PREVALENCE OF TOBACCO USE AMONG YOUNG PEOPLE IN DIFFERENT COUNTRIES

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ABSTRACT

The aim: The prevalence analysis of three ways of tobacco use among young adults: traditional (smoking of cigarillos or cigars) and alternative (hookah smoking and use of E-cigarettes) as well as the development of ways of tobacco smoking prevention.

Materials and methods: Cross-section anonymous survey among young adults 18-44 years of age (n=410) has been conducted. The obtained results were compared with the data of the similar studies from different countries. The statistical methods (analysis of the mean and relative values), structural and logical analysis and systemic approach.

Results: Among those who were interviewed, aged 18-44 years, there are 24.15±2.11 % of respondents – hookah smokers, 9.02±1.42 % persons prefer the traditional method of tobacco use (smoking of cigarillos or cigars), while 6.34±1.20 % ones use E-cigarettes. Such forms of smoking are more common among males. The smokers of cigarillos, cigars and hookahs have appreciated their high availability when buying – 9 (7;10) points out of 10 possible. The study has found that 11.54±1.58 % of smokers of E-cigarettes and 8.08±1.35 % of hookah smokers consider them safe types of smoking and harmless to their health.

Conclusions: The prevention methods of smoking prevalence among young people must be based on the tougher rules of tobacco market and latest devices for smoking at the legislative level.

KEY WORDS: young adults, young people, hookah, E-cigarettes, cigars and cigarettes

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INTRODUCTION

Tobacco smoking remains a global problem of humanity. There are 1.3 billions of tobacco smokers in the world. Every year, 7 millions of active smokers and 1.2 millions of passive smokers who are influenced by the passive smoking, died [1].

The problem of prevalence of tobacco use among youth has acquired the global significance. In comparison with the adults, the young people need smaller number of cigarettes and less time to become nicotine dependent [2].

In the WHO report on the global tobacco epidemic of 2021 [3], the information is given concerning the prevalence of new forms of tobacco use, in particular such as electronic nicotine delivery systems (ENDS).

Simultaneously, in view of propaganda conducted by the tobacco manufacturers as to security of such forms of smoking, the number of users of this type of tobacco consumption continues to grow, and particularly with involvement of youth.

Within limits of the WHO Framework Convention on Tobacco Control, the cooperation between the participating countries as to strengthening the evidence base continues as well as the development of relevant legislation in the field of another form of tobacco use – hookah smoking [4].

The relevance of this research is stipulated by the analysis of prevalence of the latest forms of tobacco use, and particularly among young people, as well as the development of educational and political activities in the field of public health for prophylaxis [5, 6].

THE AIM

The prevalence analysis of three ways of tobacco use among young adults: traditional (smoking of cigarillos or cigars) and alternative (hookah smoking and use of E-cigarettes) as well as the development of ways of smoking prevention.

MATERIALS AND METHODS

One-time anonymous survey among young adults aged 18-44 years in Lviv region (n=410) has been conducted; out of them 200 males (48,78±2,47 %) and 210 females (51,22±2,47 %). Time of the survey: 15 of January – 14 of February 2020.

The obtained results were compared with the data of the similar studies from different countries. The statistical methods (analysis of the average and relative values), conceptual modeling, structural and logical analysis and systemic approach were used.

During the analysis of the average values in order determine the normality of distribution, the Shapiro-Wilk criterion/test was used. In case of Gauso skirstinys, the

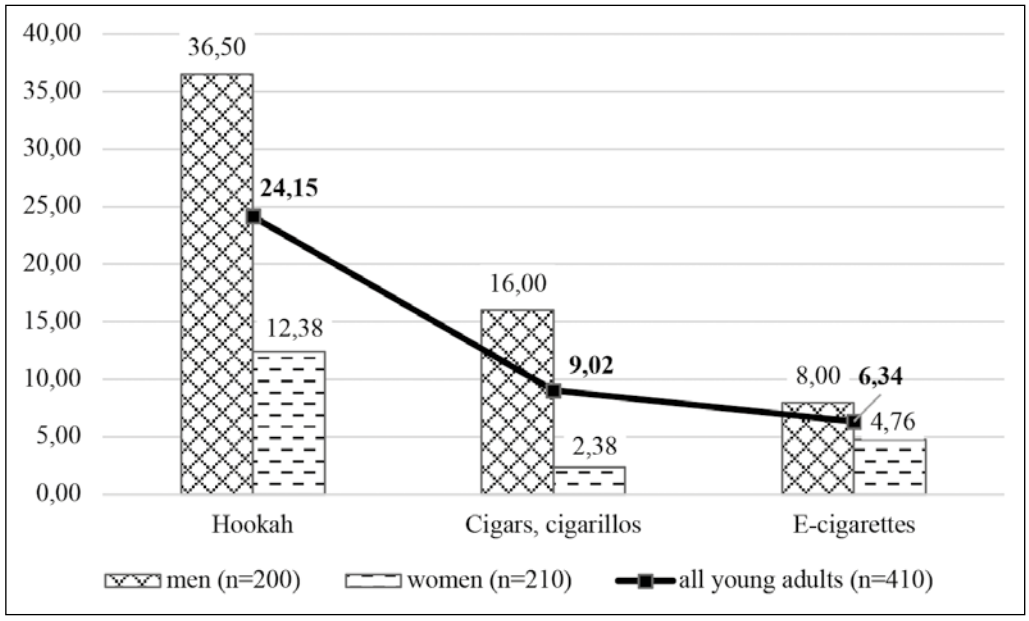

Fig.1. Prevalence of separate forms of tobacco use among young people (%)

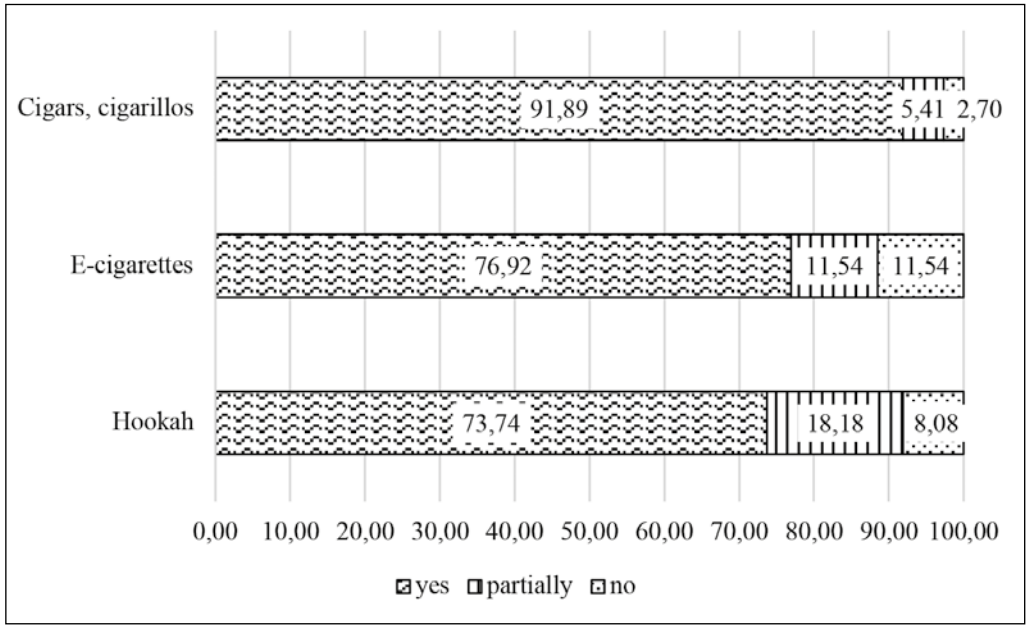

Fig.2. Awareness of smokers as to the harmful effect of tobacco use on their health status (%)

results were given as M±SD (arithmetic mean and its standard deviation); in case of non-Gauso skirstinys, the results were given as Me (25%; 75%), where Me – median, 25% – the first quartile, 75% – the third quartile.

The results of analysis of the relative values were given as intensive indicators and their mistakes, which were calculated by Wild method (P±p). The reliability of difference between the relative values was established with the help of xi-square.

The difference of samples was considered reliable in $p<0,05$. All statistical calculations were performed using software RStudio v. 1.2.5042.

RESULTS

The research has found that a quarter of young respondents (24.15±2.11 %) are smokers or were hookah smokers, 9.02±1.42 % prefer to smoke cigarillos or cigars, while 6.34±1.20 % use E-cigarettes.

The distribution by sex allows us to state that such forms of smoking are more common among males: so, the number of young males who smoke hookah is 2.8 times higher in comparison with females, the E-cigarettes are preferred by males, 1.6 times higher than by females, as to the traditional method of tobacco use, i.e., smoking of cigarillos or cigars is in 6.4 times more common among males (Fig.1).

The median (middle) value of age for the start of active cigarillos or cigars' use – 18 (16; 20) years (the minimum value of age for the start of active cigarillos or cigars' use among young people – 14 years, the maximum value of age – 37 years). The middle age for the start of active hookah smoking – 18 (17; 20) years, (the minimum value of age – 15 years, the maximum 35 years). Young people start to use E-cigarettes actively in the middle in 25 (19; 37) years (the minimum age –16 years, the maximum age – 41 years).

The age distribution of smokers considering their gender, no significant gender differences as to smoking of cigarillos or cigars and hookah were established. But the start of E-cigarettes use actively by young males is 29 (19.75; 37.25) years, while for the young females – 22.5 (18.25; 27) years.

The frequency analysis of the analyzed methods of tobacco use has testified that among the smokers of cigarillos or cigars 43.24±2.45 % smoke them every day, 37.84±2.40 % – at leisure, parties, celebrations, 13.51±1.69 % – several times a week and 5.41±1.12 % – several times a month.

The majority of the interviewed young people, namely 69.70±2.27 %, smoke hookah at leisure, parties, celebrations, 25.25±2.15 % use it several times a month and only 5.05±1.08 % – several times a week.

One third of smokers of E-cigarettes (34.62±2.35 %) use them several times a month, 30.77±2.28 % – at leisure, parties, celebrations, a quarter of respondents use them every day and 7.69±1.32 % – several times a week.

The mean number of smoked cigarillos, cigars is equal to 4 (1; 8) cigars for a week. The minimum quantity of smoked cigars – 1 cigar for 3 weeks, while the maximum – 20 cigars for a week.

There is a significant difference in the mean number of the smoked cigarillos, cigars among males and females, namely, 4 (1; 8,25) cigars in males and 2 (1; 5) cigars in females. The minimum quantity of smoked cigars by females is 1 cigar once every 2 weeks, while the maximum – 10 cigars a week.

The median value of smoked hookahs is 0,5 (0,5; 1) of hookah a week, i.e., 1 hookah once every 2 weeks. The minimum quantity of hookahs – 1 hookah once every 2,5 months, while the maximum – 4 hookahs a week.

57.69±2.44 % of smokers of E-cigarettes use them instead of common tobacco smoking.

The analysis of the respondents' answers as to their awareness of the harmful effects and health risks from those forms of tobacco which they use, has testified that 91.89±1.35 % of cigarillos smokers, cigars, 76.92±2.08 % of electronic cigarette users and 73.74±2.17 % of hookah smokers know about the danger of smoking.

Instead of this, 18.18±1.90 % of hookah smokers partially aware the negative influence of hookah on their health, and 8.08±1.35 % consider it harmless for their health.

In its turn, among the users of E-cigarettes, 11.54±1.58 % of respondents partially aware the negative influence of these products on their health and the same number (11.54±1.58 %) of smokers consider them a safe type of smoking (Fig.2).

The reported results allow us to make a conclusion that perception by youth the E-cigarettes and hookah as a safe and harmless methods of smoking to their health, is erroneous. Consequently, it is necessary to strengthen the informational, educational and elucidatory policy among young adults concerning harm to their health of the methods of tobacco use that have been considered as well as negative consequences in remote perspective.

Further, it was suggested to respondents to assess availability of the selected methods of smoking, using a ten-point scale (1-unavailable, 10 – available), when buying tobacco products. Smokers of cigarillos, cigars and hookahs assessed their availability in 9 (7;10) points, while the users of E-cigarettes – in 7,50 (5; 9,75) points.

High availability of cigarillos, cigars and hookahs can be seen as an extra stimulus of young people to start smoking. Therefore, at the state level, it is necessary to strengthen the restrictive measures as to selling these products, to strengthen the educational work at higher educational institutions, that, in its turn, will contribute to the reduction of their attractiveness and accessibility for young people.

Tobacco smoking is not only harmful to smokers' health, but it causes significant financial damage. So, during the research, we've calculated the median value of smokers' weekly expenses as to these specified methods of tobacco use.

In particular, the smokers of cigarillos and cigars, on average, spend on these tobacco products 200 (100; 400) hrn a week, hookah smokers – 120 (85; 200) UAH / a week and those young people who use E-cigarettes 60 (50; 100) hrn a week.

The purchase costs of those young people who prefer the traditional form tobacco use, i.e., cigarillos or cigars smoking are from 50 to 1000 hrn a week. Those young people who use alternative methods of smoking spend 20 – 750 hrn a week on a hookah smoking and 30 – 350 hrn – for E-cigarettes.

We've calculated during the research that in case of recalculation, taking into account the current US dollar exchange rate, the median annual costs of cigarillos or cigar smoking wasted by youth in Lviv region were equal to 428.87 US dollars per year, for hookah smoking – 257.32 US dollars, for the E-cigarettes – 128.66 US dollars.

The majority of respondents (76.92±8.26 % of electronic cigarette smokers, 68.69±4.66 % of hookah smokers and 40.54±8.07 % cigarillos or cigars smokers) failed to give a clear answer what was the reason for their smoking start. However, among the answers given by respondents, we have identified the main ones.

In particular, 16.22±6.06 % of young smokers of cigarillos or cigars claim to have smoked for the first time in order to relax in stress situations; 13.51±5.62 % of young people recognize that were influenced by propaganda and start to smoke because it was fashionable and cool; 10.81±5.10 % smoked for the first time for the company.

However, 12.12±3.28 % of hookah smokers decided to try it for first time for a pleasant pastime in the company of friends, i.e., as a means of socialization.

It is noteworthy that interest and curiosity were the dominant factors for smoking start in 10.81±5.10 % of cigarillos or cigars smokers and 9.09±2.89 % – hookah smokers.

Wherein, 23.08 % of electronic cigarettes users, 10.10 % of hookah smokers and 8.11 % of respondents who smoke cigarillos or cigars have indicated other reasons that were much less common.

DISCUSSION

The study of the latest methods of tobacco use by youth is the circle of interests of the international scientific community.

A significant number of scientific research is dedicated to finding out the reasons of using the alternative methods of smoking by young people such as E-cigarettes and hookah. In particular, Okawa S., Tabuchi T., Miyashiro I. (2020) according to the results of the cross study which was carried out among the individuals, 15-29 years of age, have found that the main reasons of the E- cigarettes' use are interest in fruit flavors, a stylish design and as well as the influence of friends who are already in use of E-cigarettes [7].

Kinouani S at al. [8] based on the systematic review of literature have summed up that regardless of smoking status, interest is the most frequent reason of smoking start of E-cigarettes among young people.

In turn, for young people, 18-23 years of age, who are hookah smokers, this procedure is associated with relax and social experience (Barnett T.E., Lorenzo F.E., Soule E.K., 2017) [9].

The similar data of hookah use as a means of socialization were received by Nicksic N.E. at al. [10] based on the personal interviewing the hookah smokers, from 18 to 29 years, who live in the city of Austin (State of Texas); according to it, only one third of the study participants smoked hookah alone and not in the company.

This study confirms the fact of influence of the hookah flavoring peculiarities when it is consumed: all study participants used the flavored tobacco on the first try of hookah smoking. Wherein, the fruit aromas were the most popular both at the beginning of smoking and for further current use [10].

The age research of smokers of E-cigarettes is given in the publication of the Polish scientists Jankowski M., at al. (2020) [11], who has carried out a cross poll among the Polish university students; it has shown that the middle age of those who firstly use the traditional cigarettes was much lower if compared with the consumers of E-cigarettes.

Much attention of scientists is focused on the study of subjective evaluation of consumers of alternative methods of smoking and harm to their health.

Despite the fact that the hookah smokers consider it harmful and addictive, however, most of them are not sure whether hookah is just as harmful for health as smoking of traditional cigarettes [10].

The results of the study of hookah smoking among young people in Mumbai (India) are interesting. The survey was conducted among 500 college students. The obtained results of the survey were classified into 2 groups: hookah smokers and those who do not use it. Dani K.K., at al. [12] state that perception of hookah use among its users and non-users, as well as between males and females showed significant differences as to the harmful effect on their health and the possibility of causing cancer and addiction. Whereas the differences in perception of hookah as a means of communication and its security compared with the traditional cigarettes in a group of hookah smokers and non-smokers, were not observed.

The disappointing trend as to the level growth of constant use of hookah tobacco among young Americans is reflected in the work of the American scientists Soulakova J.N., at al (2018). Based on data analysis from the Addition/Annex as to the tobacco use for за 2010–2011 and 2014 – 2015 years, a team of scientists was able to find out that the level growth of constant hookah tobacco use was the highest among the people 26–30 years of age and was due to many socio-demographic factors [13, 14].

The information provided below shows the importance of further research in this direction, in particular it will be relevant as to efficient use of the alternative (latest) methods of tobacco consumption by young people with the aim to stop smoking the traditional cigarettes.

CONCLUSIONS

For the purpose of prevention the prevalence use of tobacco products, including the latest forms of tobacco consumption among the young people, it is necessary to strengthen measures of primary prophylaxis aimed to impede the desire to start smoking as well as creating tougher conditions of anti-tobacco legislation. It is also important to strengthen the educational work among education applicants on pre- and postgraduate levels in all educational institutions (primarily medical) concerning the questions on prevention all types and forms of tobacco use.

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ORIGINAL ARTICLE

THE INFLUENCE OF DYNAMIC SOCIETY ON STUDENTS' HEALTH

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ABSTRACT

The aim: The article examines the impact of a dynamic society on the health of students of pedagogical specialties, identifies approaches to the formation of self-preserving and health-preserving behavior in student youth.

Materials and methods: A set of methods was used in one-step (cross-sectional) research: general scientific (analysis, synthesis, comparison, systematization, generalization), empirical (observations, interviews, questionnaires) to determine the impact of negative factors of a dynamic society on student health. The object of research is the process of the impact of a dynamic society on student health. Subject – factors influencing the dynamic environment on the health of students of the first (bachelor's) educational level of pedagogical specialties.

Results: In our opinion, the dynamism of modern society is an important factor in changing the personality of a young person to understand the value of their own health, awareness of the relationship of physical, social, spiritual, and intellectual development in health. The results of the study are based on a survey of students. The questions were formulated in such a way as to investigate the influence of the factors of a dynamic society on the well-being and health of the respondents. The study was conducted remotely during the COVID-19 pandemic using a Google questionnaire.

Conclusions: The results of the survey of students provided an opportunity to study the impact of dynamic society factors on the well-being and health of respondents and find out the importance of responsible self-preservation and health-preserving behavior and professional career.

KEY WORDS: life strategy, healthy behavior, factors, student youth

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INTRODUCTION

Modern society is characterized by a high level of dynamic development of all its spheres: manufacturability of production processes, material, spiritual, communication and other spheres of life, leading to changes in personality, especially perceptions of health and factors that affect it. On the one hand, these changes are positive because they stimulate the competitiveness of the individual, his/her creativity, flexibility in acquiring and applying knowledge and skills. On the other hand – the dynamic development of modern society has a negative impact on human well-being, health, not only causing stressful situations, but also forcing neglect of health in favor of other needs: the desire to be realized professionally and personally, "catch up", to combine education with earning money, etc. Thus, there are contradictions between society's requirements for the level of human health and its real state: society needs the health of its citizens, but in the conditions of its dynamic development it is difficult to achieve. The constant changes and transformations of the living space of modern man are so serious that society is forced to comprehend its consequences, developing appropriate strategies to prevent minimizing the negative impact of various factors on various spheres of life and taking care of health. Research shows that today's human health is not only deteriorating, but also the "fashion" for health is disappearing, and states that educational institutions mostly do not pay due attention to the formation of a positive attitude to health and do not consider factors that destroy health [1].

Young people are a progressive part of any society. During the student years, a person actively masters various areas of life: studying in a higher education institution, work, communication of interests, personal relationships, building one's own life strategy etc. Adolescents develop ideas about the value of health, responsible health-preserving behavior.

The state of health of young people is an important indicator of social well-being of the society. "Analysis of modern domestic and foreign literature on issues of health of students' youth indicates the presence of negative trends to deterioration of health students" [2]. At the same time, the state of youth health is one of the acute medical and socio-economic problems of our country [3]. In addition, in recent years there is a tendency of negative impact of

the intensification of the educational process of higher education institutions on the motor activity of students [4].

Note that the modern approach to the concept of "health", based on the definition of the World Health Organization, is systemic, integrated, holistic, considering not only physical well-being but also other parameters of human condition, namely: emotional, level of its sociality and spirituality, intellectual development, way of life. All components of health are the result of the interrelated impact of the ecology, social environment, lifestyle, including its guidelines for health. In modern market conditions, the success of self-realization in professional activities is determined not only by professional knowledge, but also mental and physical well-being and attitude to their health [5]. The educational policy of our state is aimed at the formation of the growing generations of health in all its components: physical, mental, social, spiritual, which is reflected in the regulations [6-10] and others.

THE AIM

To determine the influence of the factors of a dynamic society on the health of students and approaches to the formation of self-preserving and health-preserving behavior in student youth; to analyze the results of the survey of students of the first (bachelor's) level of specialties 012 Preschool education and 013 Primary education.

MATERIALS AND METHODS

Conducted a one-step (cross) study using a set of methods: general science (analysis, synthesis, comparison, systematization, generalization), empirical (interviews, questionnaires) to identify levels of understanding of the factors influencing a dynamic society on the health of student youth. The object of research is the process of the impact of a dynamic society on student health. Subject – factors influencing the dynamic environment on the health of students of the first (bachelor's) educational level of pedagogical specialties.

RESULTS

During the research, a survey of students was conducted. The questions were formulated in such a way as to reveal an understanding of the influence of the factors of a dynamic society on the well-being and health of students. Factors in the context of research are understood as a condition, driving force, the cause of the process of impact of a dynamic society on student health. Students got acquainted with them in the disciplines of the psychological and pedagogical cycle, which students study within the educational and professional program, and in the Center for Self-Knowledge and Self-Development, which operates at the Pedagogical Institute of Borys Grinchenko Kyiv University. Students also take an active part in organizing a safe, healthy, inclusive educational environment of higher education institutions and preschool and general secondary education institutions in the process of pedagogical practice, in the formation of spirituality, healthy lifestyle.

After analyzing the answers to the question: "Identify, in your opinion, the main factor on which human health depends", we positively note the high level of students' understanding of the value of their own health by defining lifestyle (79.2%) as a major factor in health impact. At the same time, 6.2% and 6.3% of respondents prefer social factors and the quality of modern medicine, 7.3% – the importance of environmental factors in the impact on human health. Moreover, the progressive views of modern youth on their own responsibility for health should be noted in contrast to many of our citizens who tend to shift the responsibility for deteriorating health to adverse environmental conditions and inadequate, in their opinion, quality of health care, not considering negative factors of their lifestyle: smoking, alcohol, unhealthy diet, sedentary lifestyle, etc. Confirmation of the previous result can be found in the answers of the respondents to the question "How do you think health affects a person's lifestyle, spirituality, worldview, attitude to one's own health and to other people and nature." Again, we note as a positive fact the answers of 69.8% of respondents – "very strong influence" and the fact that no student noted the position – "does not affect at all." It should be said that 69.8% of respondents showed an understanding of the importance of health for building and implementing a life strategy and professional career, and 30.2% – said that it affects in some way.

Unfortunately, a large part of our society does not tend to pay attention to the spiritual component of health, noting the importance, first of all, of the physical and mental components of health. Instead, the spiritual component of health is extremely important for the person of the XXI century, which is evidence of his/her acceptance of universal values, cultural heritage of mankind, desire for self-improvement, including health, understanding of the environment and one's place in it. This is confirmed by the students' answers to the question: "Determine how a person's health is affected by his/her spiritual development, which determines the purpose of his/her existence, ideals and values". Thus, 27.1% of respondents said "very strong influence"; 71.9% – "affects in a certain way"; 1% – "does not affect". Young people need to realize that it is impossible to achieve spiritual health without maintaining physical health, and vice versa. Violation of human harmony between the physical and spiritual negatively affects both areas of one's life [11]. It is important for future teachers to understand the focus of modern education on the formation of children's spirituality, a healthy lifestyle that will ensure the harmonious development of a growing personality.

The answers to the questions: "How do you think health is affected by the ability to properly assess and perceive their feelings and sensations, consciously manage their emotional state" were distributed as follows: 55.2% – "very strongly affects"; 44.8% – "affects in a certain way"; 0% – "does not affect at all". In further communication, students noted that negative emotions from the mismatch of expec-

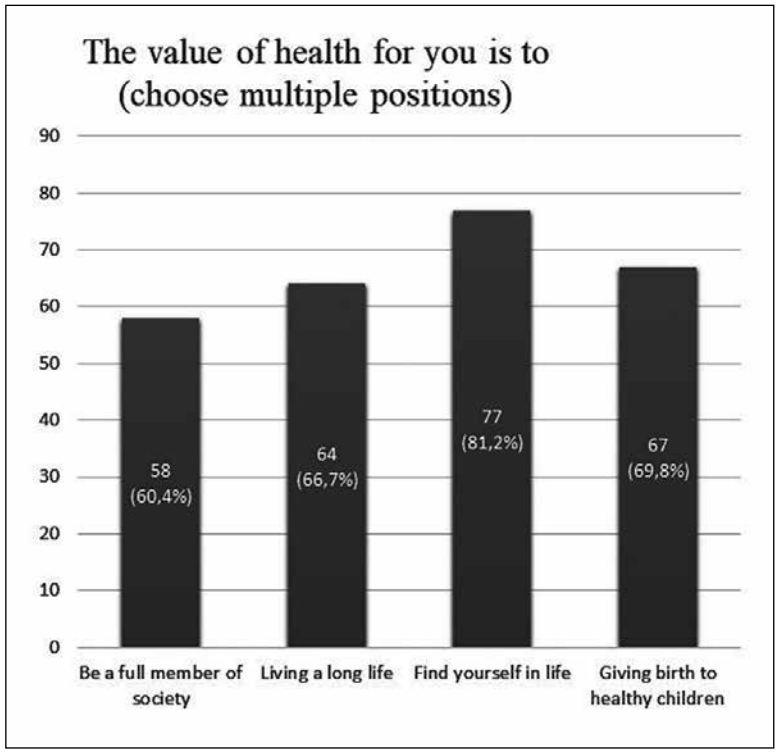

Fig. 1. Factors determining the value of health for students

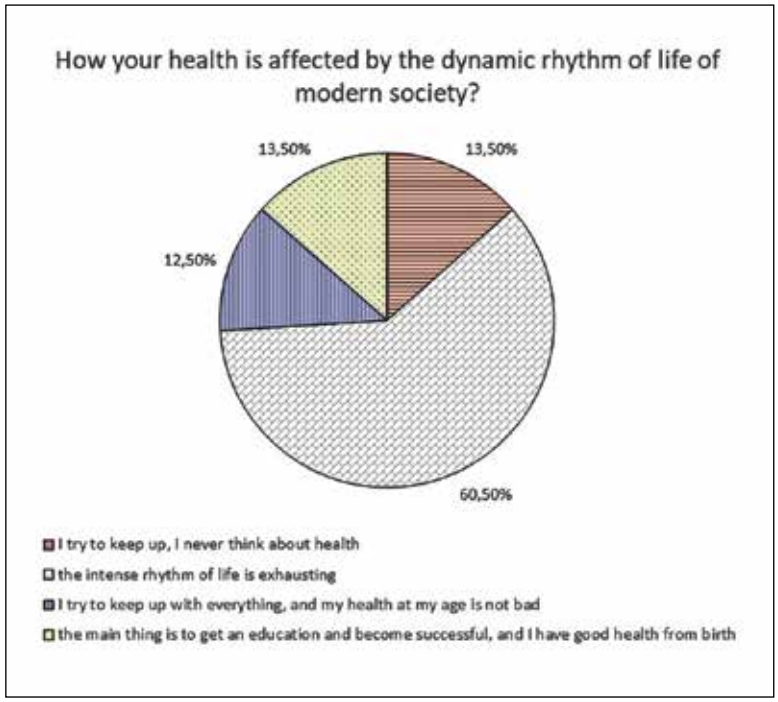

Fig. 2. Indicators of the impact on students' health of the dynamic rhythm of life in modern society

tations of real life, tension in communication with family and friends lead not only to bad moods and depression, but also cause headaches, tachycardia, fatigue. At the same time, 47% of students said that human health depends not so much on the events that take place in our lives, but on the reaction to them. If one mobilizes, assess the situation realistically, can manage one's emotional state, it will not affect one's well-being. Thus, 53% of students agreed with this statement, but noted that it takes a long time to develop psychological mechanisms of protection against the negative factors of the environment. Indeed, man becomes alienated from nature, instead absorbed by the problems of society and lives by them, immersing himself in various sources of information, often from the inability to dissociate from secondary stimuli. This not only causes internal disharmony, but also destroys physical health. Students are right that good health depends on the ability to work on oneself. It should be borne in mind that the guidelines of human existence are the values that organize one's life, significantly affect the direction and content of one's social activity, behavior and actions, the attitude to the world, to oneself, including one's own health. Young

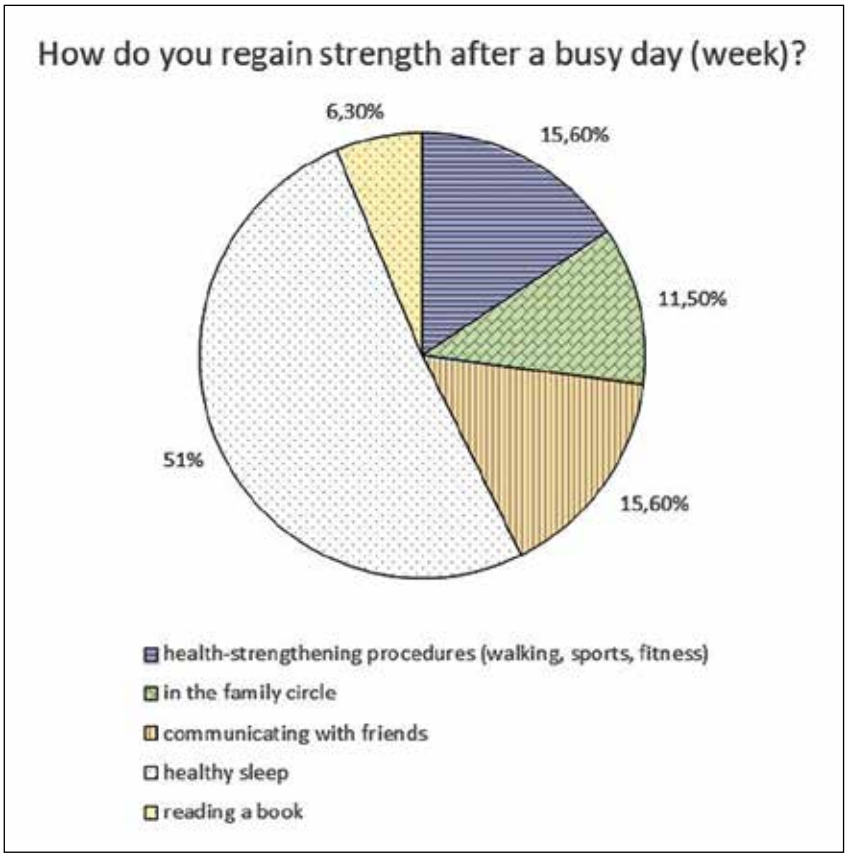

Fig. 3. Methods and indicators of recovery of students after a busy day (week)

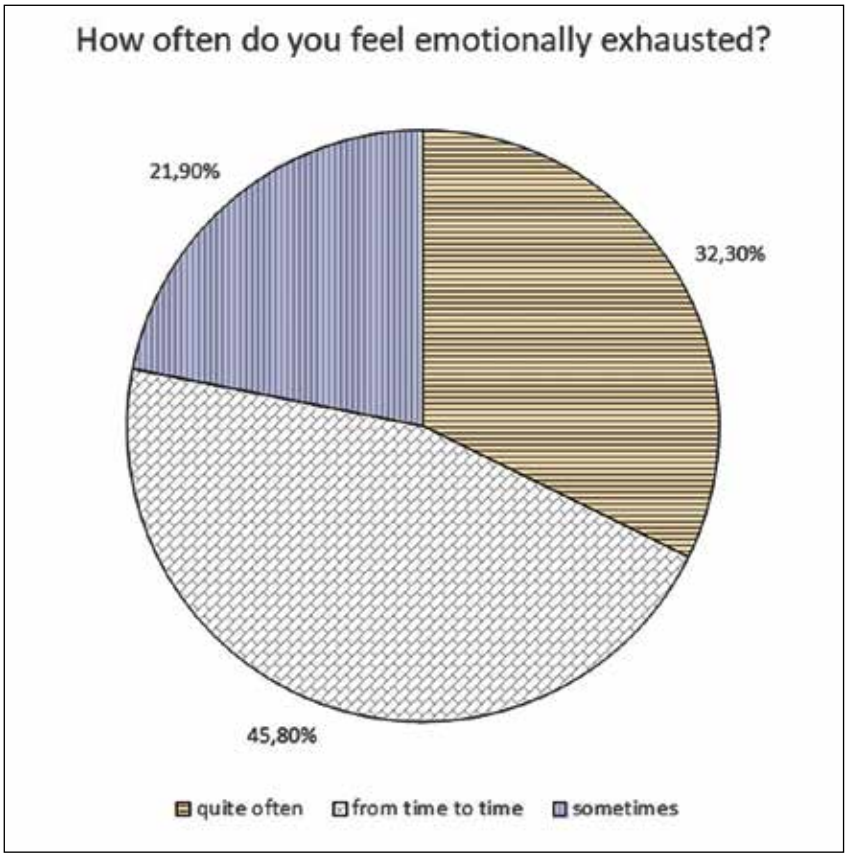

Fig. 4. Indicators of the frequency of emotional exhaustion of students of the institute

people experience psychological comfort and satisfaction when the environment is in tune with their value system. Otherwise – they feel stress, inner anxiety. For example, students who came to study at a higher education institution from small towns and villages, accustomed to closer, direct, warm relationships with family members, friends,

neighbors. In a big city, this seems impossible: people are quite treacherous from each other. Young people also attach great importance to the concept of "personal space", in which students include not only the area within which a person feels comfortable, cozy, and free, but also its essential feature – "personal development" [12].

Students' answers to the question "The value of health for you is to…" (with the possibility to choose several positions) were as follows: 60.4% of respondents said that it is important for them to be a full member of society; 66.7% – live a long life; 80, 2% – to find yourself in life; 69.8% – to give birth to healthy children (Fig. 1).

In response to the question "Do you agree with the opinion of scientists that health is one of the conditions for achieving maximum success in education, training, productivity, optimistic and life-affirming attitude to everything that is happening" 52.1 % of respondents completely agreed; 44.8% – partially agreed: success in education and training depends more on other factors; 3.1% disagreed: these achievements are not related to health at all, but depend on other personality traits. Thus, most students are aware that health determines a person's ability to self-actualize.

When asked "How does the dynamic rhythm of life in modern society affect your health", 13.5% of students answered: "I try to keep up, I never think about health"; 60.5% – "Tense rhythm of life is exhausting"; 12.5% – "I'm trying to keep up, and health at my age is so good"; 13.5% – "The main thing for me is to get an education and become successful, and my health is strong from birth" (Fig. 2). In this aspect, it is important to note that most young people are not aware of the detrimental effects of chronic fatigue on the body. Modern living conditions cause a growing remoteness of man from nature, immersed in the problems of society. Clarifying students' perceptions of the impact of a dynamic environment on their health, they approved the ability to achieve their personal and professional aspirations through certain long-term constraints (1-3 years), including: rest, study and work, study at two higher education institutions at the same time and work. Some of the young people were even proud of their endurance and good functioning, but most admitted that it is difficult to combine work and study, it is impossible to "catch up", and therefore there is a risk of "falling behind" the pace of modern society.

Regarding the answer to the question "How do you regain strength after a busy day (week)", 15.6% of respondents said that they are engaged in procedures that promote health (walking, sports, fitness); 11.5% – regain strength in the family, 15.6% – regain strength in pleasant communication with friends; 51% – trying to sleep; 6.3% relax by reading books (Fig. 3).

The answers to the question "Do you follow a healthy lifestyle" were distributed as follows: 17.7% of students said that they must follow a healthy lifestyle; 66.7% – try, but do not have time; 15.6% – do not follow. Importantly, among the reasons that most often cause students stressful situations (it was suggested to choose several positions): 54.2% said that stress causes them fear of the future; 18.8% – pandemic; 39.6% – disappointment in the future profession; 80.2% – heavy training load; 30.2% – fear of not being interesting to others; 63.5% – feelings for the health of loved ones; 43.8% – unsatisfactory financial condition. To the question "How often do you feel emotional exhaustion?" 32.3% of respondents said "quite often"; 45.8% – "from time to time"; 21.9% – "sometimes"; 0% – "never" (Fig. 4). Students detailed what they associated with emotional exhaustion (it was suggested to choose several positions). Thus, 16.7% of respondents said that emotional exhaustion is associated with the fact that they do not like the future profession, and learning takes a lot of effort and time. Note that this is a worrying factor for teachers, as the teaching profession is difficult in organizational and psychological terms, associated with great responsibility. The formation of a growing personality depends on the educator, the teacher, so there should be no random people in this profession. The study found that such students experience anxiety and stress from thinking about the profession, and entered the pedagogical specialties on the advice of parents. 56.2% of students noted the reason for the feeling of emotional exhaustion, the mismatch of real life expectations; 8.3% – dissatisfaction with personal relationships; 16.7% – conflict in the immediate environment; 2.1% – excessive control by relatives.

To the question "How often do you feel tired?", the answers of students were distributed as follows: 45.8% – "quite often"; 43.7% – "from time to time"; 10.5% – "sometimes", no student answered – "never". Among the factors associated with the occurrence of fatigue, students noted (it was suggested to choose several positions): 70.8% – heavy workload; 60.4% – some subjects are difficult and require more effort, at the same time there is a desire to study well and get high scores; 56.3% – a combination of study and work; 33.3% – performance of economic duties; 13.5% – exhausting personal relationships. When asked about the amount of time needed to recover, only 1% of respondents said 1-2 hours; 8.3% – 3-4 years; 16.8% – 1 day; 20.8% – 2 days; 12.5% – a week. The majority of students (40.6%) noted the importance of a good night's sleep. The living conditions and well-being of the young man were undoubtedly affected by the pandemic: distance learning has reduced the number of direct contacts with friends, classmates, and relatives.

DISCUSSION

Modern means of communication save time by providing distance learning and work, communication, entertainment, etc., and at the same time create an additional burden on mental health, including risks of immersion in virtual life instead of overcoming the challenges of reality. This is also the reason that affects the lack of recovery, fatigue, stress of modern youth. Of concern is the high percentage of responses to the emergence of stressful situations in students due to the heavy workload, the complexity of educational programs. At the same time, a significant number of students consider education and the development of professional competencies important.

On the positive side, students from other cities have gone through a difficult phase of adaptation to living conditions in a big city, found friends, advisers among their teachers, and some even the workplace. As a result, anxiety and worry disappear, which negatively affects well-being. Clarifying students' perceptions of the impact of a dynamic environment on their health, they found the advantage of achieving dreams and aspirations in professional and personal life. Some students continue to be proud of their endurance and stable functioning of the body. However, most agree that even young people find it difficult and often impossible to have time to work and study well, successfully build personal relationships and act in the rhythm of modern society, which hinders their well-being.

"Components of learning: social comparison and evaluation, dissatisfaction with the process and the result of learning, feelings of injustice in the assessment of knowledge, unjustified hopes, difficulties in communication are factors of emotional burnout" [13]. For comparison, according to foreign researchers: "The academic, social and emotional adjustment is influenced by a number of factors. As freshmen arrive at university with different personal, social, cultural and linguistic backgrounds, and characteristics, the factors that affect the adjustment process necessarily vary from one student to another. However, gender, self-esteem, and student expectation of university life have been identified as important factors influencing successful adaptation" [14]. Many studies explored the challenges and hurdles experienced by students attending institutions of higher education in the US. In particular: "These difficulties include, but are not limited to, difficulties adjusting to the academic culture, misunderstanding, and complications in communication with faculty and peers; stress, anxiety, feeling of isolation, social experiences, culture shock, financial hardships, lack of appropriate accommodation, isolation and loneliness, and any adaption in their daily life" [15].

CONCLUSIONS

Theoretical understanding and the results suggest that the health of young people in general and its components such as emotional state, physical well-being are influenced by social factors: dynamism and saturation of modern life, economic condition of society, industrial, family, and personal relationships. Obviously, the socio-economic situation in the country directly affects the opportunities and needs of young people, including in the field of health: the opportunity to attend sports, fitness clubs, etc., but above all it affects the emotional state of young people, causing uncertainty in the future.

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ORIGINAL ARTICLE

THE INFLUENCE OF THE REGULATORY SYSTEM ON THE STUDY DESIGN AND DATA MANAGEMENT PRACTICES IN CLINICAL TRIALS

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ABSTRACT

The aim: To review real-life regulatory-dependent study design and data management practices of post marketing multicenter studies of medical devices conducted in 2021 in Ukraine and Poland.

Materials and methods: This article presents the case study of 4 post marketing multicenter studies of medical devices conducted in 2021 in Ukraine and European Union.

Results: The case study presented effective cross-border cooperation between Ukrainian and European actors. Despite the gaps in Ukrainian legislative framework on medical devices, complex solutions on employment of the most stringent regulatory provisions led to appropriate study design. Usage of the highly compliant electronic data capture led to fast-track study start-up and solid clinical data collection.

Conclusions: Publications on real-life regulatory-dependent clinical trials conduct might be essential to innovate the regulatory system in Ukraine. The cross-border cooperation might assist the advancement of clinical trials industry in Ukraine. Gaps in medical devices regulations in Ukraine impede the context-specific clinical trials solutions for biotech industry in Ukraine. The regulatory framework and practice in Ukraine may be perceived as externally driven due to gaps in medical devices regulations, lack of capacities of domestic notified bodies and business interests of Sponsors.

KEY WORDS: Clinical trials design, medical devices, clinical trials regulation, clinical data management

Wiad Lek. 2022;75(5 p1):1192-1196

INTRODUCTION

The literature on the clinical trials' management in Ukraine is scarce. Hence, most scientific, and legal sources on clinical trials in Ukraine from 2012 to 2020 are part of the scientific discussion on the legal aspects of clinical trials regulation. Therefore, a review of these sources might be incomplete without mentioning the primary sources – regulatory documents.

Kornatsky V. at al. discussed in 2012 that since independence Ukraine has made significant progress in the industry of clinical trials of drugs since the first study in 1996. The period of the industry from 1996 to 2012, according to the article, can be characterized by the introduction of new regulations and harmonization of existing regulatory acts with the Declaration of Helsinki, Good Clinical Practice, Directive 2001/20/EC of the European Parliament and of the Council of 4 April 2001 (international regulatory acts) [1].

In several reviewed articles the global regulations, such as the World Medical Association's Declaration of Helsinki – Ethical Principles for Medical Research Involving Human Subjects [2], the International Covenant on Civil and Political Rights, and Article 7. [3], Article 4 of the Convention for the Protection of Human Rights and Dignity of the Human Being regarding the Application of Biology and Medicine were highlighted [4].

Particular attention is also paid to Article 28 of the Constitution of Ukraine, which pinpoints the right to respect for one's dignity and the prohibition of medical, scientific, and other research on humans without their voluntary consent, and Article 32, which explicitly prohibits the collection, storage, use and dissemination of confidential information. a person without their consent [5].

These legal principles are elaborated in the regulation, that establishes the rules and basic requirements for clinical trials of medicines in Ukraine is the Order of the Ministry of Health of Ukraine dated 23.09.2009 № 690 and designates the main notified body with an expert function – the State Expert Centre of the Ministry of Health of Ukraine. It is a state enterprise designated by the Ministry of Health. Almost all sources focusing on clinical trials in Ukraine are devoted to the analysis of this order and the activities of the state enterprise State Expert Centre of the Ministry of Health of Ukraine [6-12]. However, as clinical trials of medical devices are not regulated with Order #690 of MoH of Ukraine [13], and Order #616 [14] lost its force on March 28, 2017, it presents the gap in current regulation in Ukraine and current practices follow the regulatory

framework of the country(ies), in which the investigated medical device is to be marketed.

For the European regulations on clinical trials, Scavone et al. [15] mention regulatory aspects (implementation of Directive 2001/20/EC), which together with the economic crisis has led to a slowdown in the number of clinical trials in the European Union along with increasing the attractiveness of non-European countries. Directive 2001/20/EC, despite the aim of optimizing clinical trials in the European Union, this regulation has negatively affected the attractiveness of European countries for the clinical trial industry, increased requirements for sponsors, insurance, administrative costs.

The article by Markus K. Labude and Tsung-Ling Lee [16] it was stated that the Council Regulation (EC) following Directive 2001/20/EC 536/2014 of 16 April 2014 on clinical trials on medicinal products for human use and repealing Directive 2001/20/EC needed to reduce administrative pressure on Sponsors by unifying the submission and evaluation of research applications together with short and expected review times. At the same time, this regulation does not allow extending the deadlines for reviewing the application for a clinical trial by ethics commissions, which may interfere with adequate ethical evaluation of the study.

Concerning regulations on medical devices, in the comparative study of such regulations in the United States and the European Union [17] authors state that prior to the changes in regulatory process in European Union, US FDA employed more restrictive regulatory approach. Even though it led to faster progress in clinical development in Europe, it entailed the device failures to present efficacy and safety on market. These facts provoked European regulators to adjust the approach to more stringent.

Another comparative study of medical device regulations in European Union, USA, and Japan [18] concluded that there are substantial international differences between medical device frameworks. These differences have a tendency to be abated by voluntary global harmonization. However, the author pinpoints the implementation of harmonized norms is influenced by the national and supranational regulatory rules, practices, and politics.

The aforementioned harmonization is embodied in the modified medical device regulation of the CE marking applications of the medical device in European Union. These regulations imply that clinical investigation requirements will be obligatory to produce solid clinical data on the clinical benefits of the device [19].

However, there are currently no modern comprehensive studies on the influence of the regulatory system, primarily Medical Device Regulation [20-23], on the state-of-the-art management of clinical trials conducted in Ukraine and in European Union. Lack of publications on good study design and data management practice leaves a number of issues unresolved and controversial.

Thus, the urgency of the problem, its lack of development in the theory and practice of management the need to solve urgent problems related to improving the process of study design and data management practices, the need to update the testing of modern pharmaceutical innovations led to the choice of dissertation research topic.

THE AIM

To review real-life regulatory-dependent study design and data management practices of post marketing multicenter studies of medical devices conducted in 2021 in Ukraine and Poland.

MATERIALS AND METHODS

STUDY STRUCTURE

The study consisted of three subsequent stages. Firstly, the selection of study objects. For the purposes of this research the following criteria were applied to determine the sample: 1. The author took part in the clinical trial design and data management procedures. 2. The study was post marketing and multicenter study of medical device for Medical Device Regulation procedures. 3. The study was conducted in Ukraine and in European Union. These criteria were chosen predominantly to obtain real-world state-of-the-art knowledge on regulatory-dependent study design and data management practices of post marketing multicenter studies of medical devices. Secondly, available materials of eligible studies were cleared of any information confidential information comprising commercial secret of all parties involved. Thirdly, the methods listed below were applied in order to achieve the study aim.

METHODS

This article presents the case study of 4 post marketing multicenter studies of medical devices conducted in 2021 in Ukraine and European Union. Synthesis, abstraction, generalization, systematic analysis, and comparative method were used to identify Ukrainian and European regulatory practices for clinical trial management, to specify key issues of clinical trial management through the prism of the regulatory system, to highlight the potential of the regulatory system in clinical trial management.

Applying the analytical method, the key trends in the regulatory system of Ukraine for the organization and conduct of clinical trials were considered.

The dialectical and synergetic methods were used to prove the need to innovate the regulatory system in Ukraine.

RESULTS

In all 4 studies, the Sponsor employed 3 contractors: CRO for clinical operations in Poland, CRO for clinical operations in Ukraine, CRO for study design (medical writing and statistics) and data management provider.

The CROs were clearly divided in responsibilities and areas of coverage, whereas the Sponsor carried out coordination. Thus, either duplication of efforts or gaps in service provision were avoided.

The author was the technical employee of the CRO for study design (medical writing and statistics) and data management provider.

The study design should have satisfied the following points to be accepted by Sponsor:

- Writing and statistics must be compliant with both European Union and Ukrainian regulations.
- The study documents must be accepted by both European Union and Ukrainian notified bodies.
- The study design and data collection planning must address both safety and efficacy claims of investigated medical devices manufacturer.
- The data collection planning must not be dependent on local language.

If final versions of study documents had been amended due to the comments from local notified bodies, documents would have been resubmitted to all notified bodies. This outcome should have been avoided whenever possible because of tight project budget and short time frame for the study conduct.

For little was known about best practices for study design in this type of studies, the accessible guidance was taken literally. Taking into account previous experience of submissions to notified bodies of all parties involved, the documents should have present maximum possible compliance given the study aims, manufacturer claims, clinical development stage and risk-benefit ratio.

At the study documents drafting stage, the Ukrainian notified bodies decision on that the study is out of current regulatory scope could not be obtained.

Therefore, the study design followed primarily the ICH E6: Good Clinical Practice: Consolidated Guideline [24]. The study documents were drafted in line with Medical Device regulation [20-23], and order #690 [13] concurrently following the guidance and structure of the ISO 14155:2020 International Standard [25]. Whenever the regulation presented stricter limitation, this regulation was applied and referenced in the document. Consequently, development of the specific regulation on medical devices in Ukraine or adoption of the European regulation, would have led to more clear document flow and contributed to realistic planning of this type of studies in Ukraine.

Considering the post marketing stage of clinical development, the statistics section aimed to present low-risk statistical models in order to corroborated acceptable efficacy of the investigated medical devices. The good practice to apply in statistical section was strict compliance with ICH E9: Statistical Principles for Clinical Trials [26]. Consequently, the minimal sample size was reached through thorough justification of the outcome measures and anticipated effect sizes. As well, the wording of study hypotheses was aligned with the anticipated clinical benefits and manufacturer's claims.

The study documents were developed in English and therefore translated into local languages for domestic notified bodies whenever required.

To avoid delay in study data collection, processing, and analysis and to ensure the appropriate level of compliance, the electronic data capture with electronic case report forms was used for all studies. The case report form was developed and deployed in English, translations into local languages were done for the Investigator's ease of reference (not regulatory-driven decision).

Given that electronic data capture used for these studies was compliant to 21 CFR Part 11, Computerized Systems Used in Clinical Investigations [27], and General data protection regulation [28], only general compliance with the corresponding European Union regulations was checked. As the data management procedures and software followed stricter regulations, no additional measures to ensure regulatory compliance were introduced. This fact laid behind the relatively short electronic data capture start-up (2-3 weeks).

Electronic data capture start-up usually was carried out in parallel with the data processing and analysis planning. Development of statistical analysis plans, plans for data exports and statistical reports shells development at this stage is utmost beneficial for the study results reporting. However, it was not a case for neither of these studies as the data collection was planned to be launched as soon as regulatory approval was obtained.

DISCUSSION

Despite the fact that regulations are published in open access sources, practices of their implementation in real life are not usually published in peer-reviewed literature [1-9]. Details of study design and data management practices of post marketing multicenter studies of medical devices are not published independently of study results. Therefore, we found it difficult to retrieve any solid data on real-life regulatory-dependent clinical trials conduct in Ukraine and European Union.

CONCLUSIONS

The case study lets us draw only several conclusions on common features of study design and data management practices of post marketing multicenter studies of medical devices in Ukraine and in European Union.

- Regulatory framework and practice in Ukraine may be perceived as externally driven due to gaps in medical devices regulations, lack of capacities of domestic notified bodies and business interests of Sponsors (registration of medical device under Medical Device Regulation procedure).
- Gaps in medical devices regulations in Ukraine impede imposition of the context-specific clinical trials managerial and technical solutions for biotech industry in Ukraine.
- The cross-border cooperation might assist the advancement of clinical trials industry in Ukraine.
- Publications on real-life regulatory-dependent clinical trials conduct might be essential to innovate the regulatory system in Ukraine.

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ORIGINAL ARTICLE

OSTEOCHONDRAL AUTOLOGOUS TRANSPLANTATION VERSUS ARTHROSCOPIC DEBRIDEMENT WITH DRILLING IN THE TREATMENT OF TALAR OSTEOCHONDRAL LESIONS AND DEFECTS

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ABSTRACT

The aim: To conduct a comparative analysis of the results of arthroscopic debridement with drilling (ADD) versus osteochondral autologous transplantation (OAT) in the treatment of talar osteochondral lesions and defects (OHLD) based on the assessment of the function of the ankle joint, the level of pain and changes in the range of movements (ROM) in the affected joint.

Materials and methods: The study included 40 patients with OHLD, with an average area of 3.14 cm^2 and a depth of 1.15 cm, located in the posterior and middle medial part of the talus block. In the group 1 performed ADD. In group 2 – OAT. The results were evaluated before surgery, at 12 and 24 months. The level of pain to VAS, the function to AOFAS, the ROM in the joint were studied.

Results: After treatment, there was a significant reduction in pain with the best result in group 2 ($p<0.05$). AOFAS showed that after 12 and 24 months the functional state of the joint in group 2 was better than in group 1 ($p<0.01$). After 12 months, ROM increased significantly in both groups. After 24 months, there was no increase in ROM in group 1, and in group 2 the growth was statistically significant ($p<0.01$), which confirmed the higher prospects and stability of the result when performing OAT.

Conclusions: OAT is better than ADD for talar OHLD, provides maximum recovery of the joint surface, significantly reduces pain and improves ankle function.

KEY WORDS: ankle, osteochondral lesions, osteochondral transplantation

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INTRODUCTION

Osteochondral injuries and defects of the talus in the vast majority of cases have a traumatic origin, in 6.5% of cases complicate the course of inversion-eversion injuries of the foot and ankle joint [1]. To denote this condition in the literature, various terms are used: dissecting osteochondritis, osteochondral lesion of the talus, osteochondral fracture, transchondral fracture. Damage to the articular cartilage and subchondral bone is manifested by their partial or complete destruction, which causes pain during exercise, episodes of synovitis, restriction of movement and blockage of the joint. All this sometimes significantly limits daily activities, production and sports activities.

One of the first reports of dissecting osteochondritis belongs to F. Koenig and M. Kappis, who in 1922 described the features of transchondral lesions of the ankle joint. In 1959, Berndt A.L. and Harty M. proposed a classification of stages of osteochondral lesions and defects (OHLD), based on the radiological picture, which is relevant and most widely used to date [2]. The most common localization of OHLD of the talus is the posterior medial part of the dome of the talus (over 60%), which is mainly due to the inversion mechanism of ankle injury. About 40% of OHLD of the talus are localized in the anterolateral part of the thalamic dome and are the result of eversion-extensor damage to the ankle joint [3].

Early diagnosis of osteochondral lesions has increased with the advent of computed tomography (CT) and magnetic resonance imaging (MRI), when even in recent cases of injuries in the ankle joint can be detected damage based on radiological signs of trabecular bone edema. This injured area may in the future develop into subchondral bone destruction and cartilage destruction. Other important features that determine the prognosis and treatment tactics are the size of the lesion (area and depth), the presence of articular cartilage detachment, topography of subchondral bone changes, the presence of cystic remodeling or sclerotic edges in the defect [4, 5].

Treatment of osteochondral lesions of the talus includes a wide range of conservative measures (drug injections, PRP, bone marrow puncture, stem cells) and surgical methods (open or arthroscopic debridement of the affected area,

antegrade or retrograde tunneling, bone grafting or local metal implant – "patch", etc.). Among them, osteochondral autologous transplantation (OAT) and arthroscopic debridement and drilling (ADD) of the osteochondral defect area are surgical procedures that are most often used in the treatment of this category of patients. On the one hand, OAT of the defect with the restoration of bone and cartilage structure is most consistent with the concept of restoring the dynamic load on the talus. On the other hand, for the ankle joint, the procedure of OAT involves performing arthrotomy, osteotomy and removal of the transplant from another unaffected joint, which increases the trauma of the operation and the risk of complications. Therefore, it is important to determine the critical size of the osteochondral defect of the talus and to establish the limit of this size for the optimal choice between ADD and OAT. Also an issue that is not reflected in the literature is the amplitude of ankle movements and its dynamics after arthroscopy and osteochondroplasty.

THE AIM

To conduct a comparative analysis of the results of arthroscopic debridement with drilling (ADD) versus osteochondral autologous transplantation (OAT) in the treatment of talar osteochondral lesions and defects (OHLD) based on the assessment of the function of the ankle joint, the level of pain and changes in the range of movements (ROM) in the affected joint.

MATERIALS AND METHODS

The study was conducted on the basis of the Department of Traumatology and Orthopedics Bogomolets National Medical University and the Department of Foot Pathology and Complex Prosthetics of the State Institution «Institute of Traumatology and Orthopedics of the National Academy of Sciences of Ukraine».

The study included 40 patients with osteochondral lesions and defects of the talus, who underwent surgical treatment in the period from 2015 to 2020. The design and methodology of the study approved by the Committee on Bioethics State Institution «Institute of Traumatology and Orthopedics of the National Academy of Sciences of Ukraine». Informed consent was obtained from all patients.

Criteria for inclusion in the study: the presence of a symptomatic OHLD of the articular surface of the talus, which includes chondral and bone tissue.

Exclusion criteria: radiological signs of osteoarthritis of the ankle joint stage 2 – 4 according to Kellgren-Lawrence, axial deviations of the hind foot, systemic autoimmune lesions of the musculoskeletal system, diabetes mellitus, previous infectious history of the foot and/or ankle.

The age of patients was 28.9±2.7 years (21 – 41 years), there were 29 men and 11 women. The duration of symptoms before surgery ranged from 6 to 12 months.

All patients were divided into two groups, identical in sex-age composition, size and location of osteochondral damage. The average area of osteochondral defects or lesions was 3.14 ± 0.8 cm^2 (1.9 cm^2 – 4.7 cm^2), the depth of damage – 1.15 cm (0.7 cm – 1.6 cm). All patients included in the study groups had osteochondral lesions in the middle or posterior part of the medial dome of the talus.

In the first group, which included 20 patients, arthroscopic debridement of the affected area was performed, followed by microdrill. In the postoperative period, immobilization for 2 weeks and unloading of the operated joint for 4 weeks were used.

In the second group, which included 20 patients, OAT was performed using specialized instruments and surgical techniques [6]. During surgical treatment, arthrotomy and osteotomy of the medial ankle bone were performed, which provided access to the affected area. After removal of the damaged cartilage and bone tissue within the unaffected tissues, the defect area was closed with an autolochic osteochondral column of appropriate size, taken from the unloaded area of the lateral condyle of the femur of the same limb. In all cases, specialized tools allowed to completely restore the joint surface and tightly fix the transplanted osteochondral autograft by the method of press fit. After restoration of the articular surface of the talus performed stable-functional osteosynthesis of the medial ankle bone according to Weber. In the postoperative period, the operated joint was immobilized for 4 weeks and unloaded for 8 weeks.

The topography and size of the osteochondral lesion/defect were studied in detail by CT and MRI.

In patients of both study groups before surgery, 12 and 24 months after surgery, an assessment of the functional state of the ankle joint was performed according to AOFAS, and the level of pain syndrome was assessed according to VAS. The dynamics of changes in the range of motion (ROM) in the affected joint was also determined.

The range of motion (ROM) in the ankle joint was measured using the 0-pass method using a standard orthopedic goniometer by triple determination of the amplitude of movements with subsequent calculation of averages. Measurements were performed in the supine position with extension in the knee joint. The point of the axis of rotation was the intersection of the long axes of the tibia and the 5th metatarsal bone, the fixed shoulder was located along the axis of the tibia, the movable shoulder along the axis of the 5th metatarsal bone.

X-ray examination included radiography of both ankle joints in frontal and sagittal projections with body weight load (standing). Patients with varus/valgus deviation of the posterior part of the foot above 10 degrees and changes in the horizontal talus-mold angle, which exceeded ±5 degrees, were excluded from the study.

Statistical analysis was performed using nonparametric methods and the Mann-Whitney U-test; the difference between the parameters was considered significant at $p < 0,05$.

RESULTS

Complications after surgery were not observed in any case. In group 2, in all patients, full integration and restructuring of the osteochondral graft occurred on average after 3.4 ± 0.8 months (2.2 – 5 months). There were no

Table I. Comparison of the results of arthroscopic debridement with drilling (Group 1) versus osteochondral autologous transplantation (Group 2)

Index (M ± σ)	Before surgery		12 months after surgery		24 months after surgery	
	Group 1	Group 2	Group 1	Group 2	Group 1	Group 2
Pain (VAS, cm)	5,7±0,3	5,7±0,8	1,1±0,1	1,1±0,2	0,9±0,1	0,5±0,2
	p > 0.1		p > 0.1		p < 0.05	
Function (AOFAS, points)	57,8±1,4	59,4±1,2	86,7±1,7	91,2±1,8	90,3±1,2	94,9±1,1
	p > 0.1		p < 0.01		p < 0.01	
Foot extension, degrees	13,9±1,3	14,0±0,9	18,1±0,7	17,9±0,6	18,0±0,4	19,5±0,5
	p > 0.1		p > 0.1		p < 0.01	
Acceleration gain, degrees	Group 1		Group 2		before surgery / 12 months after surgery	
	4,2±0,6		3,9±0,4			
	p > 0.1					
	Group 1		Group 2		12 months / 24 months after surgery	
	0,1±0,04		1,6±0,1			
	p < 0.01					
Foot flexion, degrees	23,0±1,1	22,9±1,2	27,8±0,9	27,6±1,0	28,0±0,8	30,7±0,9
	p > 0.1		p < 0.05		p < 0.01	
Acceleration gain, degrees	Group 1		Group 2		before surgery / 12 months after surgery	
	5,2±0,7		4,4±0,5			
	p > 0.1					
	Group 1		Group 2		12 months / 24 months after surgery	
	0,2±0,05		3,1±0,09			
	p < 0.001					

cases of transplant instability or migration, as well as an increase in degenerative changes in the ankle joint during the observation period. There were no problems with the removal of the transplant from the knee joint. There were no complications or inflammatory-degenerative diseases of the donor joint. Data on the results of treatment of patients in the observation holes are shown in table I.

When comparing the results of treatment of patients in groups 1 and 2, it was found that at a similar baseline level of pain (p>0.1), characterized by VAS as pain of moderate or severe intensity, 1 year after treatment in both groups there was a significant its reduction to insignificant or weak, however, the difference in the observation groups was not found (p>0.1; table I). After 2 years, it was noted that the intensity of pain in both groups decreased from no to insignificant, and there was a statistical difference between the observation groups with the best result in group 2 (p<0.05; table I), where it was used OAT.

Assessment of the functional state of the posterior foot and ankle joint by AOFAS showed that 12 months after surgery, the functional state of the affected joint from «satisfactory» improved to «good», but the dynamics of functional growth was significantly better in group 2 (table I). The results of the assessment of the functional state of the affected joint after 24 months showed that there was a further increase in function in both groups, the statistical difference in the groups remained (p<0.01), although the dynamics of growth was significantly lower. In group 2, the average result for AOFAS approached the score «excellent» (table I).

According to the analysis of the dynamics of the volume of movement in the operated joint, it was found that 12 months after surgery, both extension and flexion of the ankle joint in the postoperative period significantly increased in patients of both observation groups. There was no statistical difference between the groups (p>0.1; table I). After 24 months, it was determined that in group 1 further increase in the amplitude of movements does not occur, and in group 2 the dynamics of growth was statistically significant (p<0.01; table I), which proved higher prospects and stability of the result when performing osteochondroplasty with restoration of subchondral bone and hyaline cartilage of the articular surface of the talus.

DISCUSSION

The arsenal of surgical techniques for OHLD over the past decades has significantly expanded and is represented by

debridement of the affected area (curettage, drilling, microfracturing) and transplant techniques (bone grafting, autochondrocyte implantation, allo- and auto-osteochondral transplantation). There are a lot of publications on the effectiveness of OHLD treatment and it is sometimes difficult to compare them. One of the reasons for this state of affairs is that the choice of technique depends on the size of the cartilage and bone defect, the preferences and qualifications of the doctor. Despite the low effectiveness of conservative treatment according to systematic reviews [7-9], in certain cases it can be successful. Candidates for conservative treatment or relatively minimally invasive procedures such as tunneling (ante- and retrograde), chondrocyte transplant, etc. there may be patients with a low level of physical activity, age-related or somatically burdened.

OAT involves the use of one or two cylindrical osteochondral grafts, which are removed from the least loaded peripheral part of the condyle of the femur and thereby restore the structural and mechanical properties of the talar articular surface.

It is believed that the indication for OAT are defects of the articular surface with an area of at least 1.5 cm^2, which are not amenable to conservative treatment and, especially, with cystic bone changes [8]. At the same time, in a systematic review of the literature presented by Dahmen J. et al. [7], covering the period 1996 – 2017, it is indicated that the area of the defect ranged from 1.0 to 2.4 cm^2. We believe that in establishing the indications for surgical treatment of OHLD is important not only the area of damaged articular cartilage, but also the depth of the bone defect. With the integrity of the subchondral bone, the restoration of congruence occurs due to the replacement of the hyaline cartilage defect with coarse fibrous tissue, which in most cases helps to restore the slippery function of the talar articular surface. Disruption of the integrity of the subchondral bone causes a number of hydrodynamic effects that increase the area of trabecular bone oedema and create conditions for the formation of cysts [5]. Because of this, OAT has priority in active patients, as it allows you to simultaneously restore damaged or lost structure of cartilage and bone tissue.

Data on the effectiveness of OAT in the literature are very encouraging. Then, Verhagen et al. [10] report 94 % of successful OAT outcomes (systematic review, one source, 36 cases); Zengerink et al. [9] gives 74 – 100 % of successful OAT results (systematic review, nine sources, 243 cases). The results of OAT in our patients coincide with the results of other authors. There was a significant reduction of the pain and the function improvement, which was 80 – 100 points by the AOFAS scale (average 94.9 ± 1.1).

The question of the dynamics of the ankle ROM remains open not only after OAT, but also after any treatment of OHLD in general. This requires further research due to the lack of relevant data in the literature. Thus, Jurina A. et al. [3] reported complete recovery of movement after arthroscopic debridement of anterolateral OHL of the tallus in two patients who did not reach skeletal maturity, but no numerical data are available. In the publication Seo [11], which is devoted to the conservative treatment of OHLD of the tallus, the registration of the ROM in the ankle is only annotated. Numerical data on the dynamics of the ankle ROM is given in the article by Gu W. et al. [12], which is devoted to the use of bone grafting and PRP-scaffold in OHD of the tallus. They showed a clinically significant increase in the range of extension from 8.0 ± 3.4^0 ($0 – 12^0$) to 17.2 ± 3.1^0 ($12 – 22^0$).

Our patients also showed a statistically significant increase in the range of movements, but if we abstract from the statistical assessment of the averages, the increase in the volume of extension by 4.2^0 and the volume of flexion by 7.5^0 from a clinical standpoint does not look very convincing.

The accuracy of angular measurements in ankle goniometry depends on many factors: the position in the knee joint, the neutral position of the heel and forefoot in all phases of the study, the location of reference points, etc. Assessing the reliability of various methods for measuring motion in the ankle continues to be the subject of research [13], but consensus on this issue should not be expected soon.

There is no doubt that the main complaint that forces a patient with OHLD to see a doctor is pain. In our opinion, it is the analgesic effect of OAT that is the main factor determining the success of treatment. The pathogenesis of the pain in patients with OHLD and analgesic effect of OAT remains unknown. From our point of view the most probable explanation of pain origin at the OHLD is abnormal hydrodynamics in the talar bone which was proposed van Nike VanDijk et al. [5]. The replacement of the combined tissue defect with identical tissues by "press-fit" method to normalize the hydrodynamics of the bone and prevent its further destruction.

The weakest point of osteochondroplasty some authors consider the problems of the donor site, manifested by pain and instability, and reach 11% [14]. However, other authors point out that these problems are a consequence of too large parapatellar incision and rough suturing of the capsule [15]. In a series of our observations, the problems of the donor site were noted in one case, which manifested itself in periodic pain after excessive physical exertion.

CONCLUSIONS

Osteochondral injuries and defects of the talus in most cases occur as a result of ankle injury and are potentially dangerous in terms of development and progression of deforming osteoarthritis. The main complaints that force the patient to seek medical help are persistent pain and swelling. Despite the wide range of different treatments, only OAT allows you to simultaneously and completely restore the structural integrity of the damaged joint of the talus. At medium defects, OAT is more effective than arthroscopic debridement and drilling, as the latter does not close the defect, which further causes overload of articular cartilage and the development of degenerative processes in the joint.

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REVIEW ARTICLE

THE ROLE OF A FAMILY DOCTOR IN SOLVING THE PROBLEMS OF FAMILY PLANNING

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ABSTRACT

The aim: To analyze the problem of family planning and highlight possible ways to solve them in the practice of a family doctor.

Materials and methods: Bibliosemantic, statistical, and method of structural-logical analysis. The materials of the study were the data of statistical reports for the period 2014-2020.

Conclusions: In Ukraine, with the existing system of family planning with fairly standardized technologies, there are serious problems, which cause reproductive health disorders of the population. The integration of family planning services into the practice of the family doctor, provided that he/she is trained, will increase their availability, quality, and efficiency.

KEY WORDS: reproductive health, adolescents, women, sexually transmitted infections, abortion

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INTRODUCTION

The FP system is the basis of strategy to improve children's health by improvement of the parent's RH. In 1968, the United Nations (UN) first proclaimed the inalienable right of every citizen to FP and personal responsible parenthood. In 1974, the right of every country to engage in FP at the state level was recognized [1]. In 1994, an important UN event on population and development was the Program of activities was adopted by the Cairo International Conference on Population and Development. According to the World Health Organization strategy that a child is born healthier in the healthy parents, and the child's health is formed before his birth, which was recognized by domestic and foreign scientists and leaders of public policy in the field of RH in the 60's years of the last century, initiated the introduction of this issue to the level of state influence. Ukraine ratified this document in 1995 [2], adhering to the international standards on RH. By the early 2000s, all of the existing items recommended in the Program of Activities had been fully or partially implemented, emphasizing the importance of the participation of non-governmental organizations in human rights activities [3-7], in particular women and children.

THE AIM

The aim of the study is to analyze the problem of family planning and highlight possible ways to solve them in the practice of a family doctor.

MATERIALS AND METHODS

Materials and methods: bibliosemantic, statistical, and method of structural-logical analysis. The materials of the study were the data of statistical reports for the period 2014-2020.

REVIEW AND DISCUSSION

The analysis of the statistics for the period 2014-2020 revealed a high incidence of STIs and abortions among adolescent girls and women of reproductive age as the reason of RH disorders.

According to the basic international documents on the protection of RH, FP is considered the main method of preserving the health of women and men, and also it belongs to the category of fundamental human rights [8] as a guarantee of stability of the demographic situation in Ukraine [9].

The priority of maternity and childhood protection, including FP, is determined primarily by the international documents:

- the Convention on Human Rights [10, 11];
- the Convention on the Rights of the Child [12] of 1989;
- the Program of Activities which was adopted by the Cairo International Conference on Population and Development [1].
- the Beijing Declaration and Platform for Action adopted by the IV World Conference on Women [13].

The modern approaches to solving the problems of motherhood and childhood, including FP, are defined in the Global Strategy for Women's and Children's Health [14]. In 2014, an updated "Global Strategy for Women's, Children's and Adolescents' Health" was presented to achieve ambitious sustainable development goals by 2030 [15] and also includes adolescents as a special age group, helps the

adolescents to realize their rights related to health, and will contribute to the opportunity to fully develop their abilities in adulthood.

One of the tasks of strategic solution of maternal and child health problems should be used in building a system of the integration of obstetrical and gynecological services at the level of primary health care (PHC).

In Ukraine, the FP service was established as the result of the "National Family Planning Program" (1995-2000) [16]. The aim of the program was to influence the solution of RH problems. The ideological basis of the "National Family Planning Program" was the necessity to change radically the imagination and attitude of each person, each family.

The established structure of the FP service provided four levels of medical and counseling help to the population [17]: the first level involved the active participation of the district doctors, who later became family doctors (FD) through reorganization.

The functional responsibilities of the first level of the FP system include the provision of FP counseling services provided by FD: the information to the population on types and methods of preventing unwanted pregnancies, and information is spread both as individually and through lectures, speeches and media, as well as during home visits of family members. However, the sectoral order of the Ministry of Health of Ukraine dated 19.03.2018 N 504 "On approval of the procedure for primary health care" [18] these functions of the FD are not provided.

An extremely important issue in the activities of the FD is the providing of the obstetrical and gynecological services to women with extragenital pathology, which may complicate the pregnancy course and childbirth, and are indicated in the resolution of the Cabinet of Ministers of Ukraine N 144 "On the implementation of Article 281 of the Civil Code of Ukraine" [19]. Such women should be the subject of special attention both in the direction of providing with effective methods of FP and monitoring by the FD. However, according to the main branch order in the field of family medicine dated 19.03.2018 N 504 "On approval of the procedure for providing primary health care", these functions of the FD are also not provided, so they are not performed. The integration of obstetrical and gynecological services into the PHC system will help to prevent the serious conditions of women associated with pregnancy.

According to the global approaches to the organization of the reproductive rights of women and men, the formation of RH in adolescents is a basic technology that is closely associated with the measures to plan the birth of the desired child in each family and provide the necessary medical care for children in PHC [20].

The main indicators that affect RH and the implementation of reproductive law were analyzed to determine the effectiveness of health prevention services in the formation of RH [21]. According to scientists, the health of adolescent girls, who will become mothers in the future, is deteriorating [22, 23]. At the same time, 75 % of girls with diseases of the still undeveloped reproductive system are diagnosed 2-3 chronic extragenital diseases [24]. Inflammatory diseases of the genital organs are the most common pathological conditions in adolescent girls (60-70%), which determine their future RH. Disorders of hormonal status and menstrual function, mostly due to STIs can lead to infertility in the future.

Abortions are one of the most serious negative factors in the future RH of girls-adolescence. There is an unstable situation regarding the level of abortions among pediatric patients [23]. Thus, in 2016 there was an increase rate (0.06 per 1000 girls of the appropriate age) compared to 2015 (0.05), and in 2018 (0.05) compared to 2017 (0.04) [23]. In 2020, this figure dropped to 0.03, and 35 girls did abortion, which in developed countries is not registered at all. That is, the problem of abortion, which has a devastating impact in the future on RH, is still not sufficiently addressed in the country, which indicates a lack of educational activities among adolescents on the culture of sexual relations [23].

In girls 15-17 years old, the number of abortions decreased from 1111 in 2014 to 538 cases in 2020, the indicator – from 1.83 to 0.96 per 1.000 girls of the corresponding age [25-29].

These data indicate an insufficient level of preventive work among adolescents on safe and secure sexual intercourse, prevention of unwanted pregnancies, use of contraceptive methods and means, which may have negative consequences for future RH. The integration of abortion eradication services should be an integral part of the FD activities.

The prevalence of STIs in the world has become epidemic [30]. Every day, more than 1 million cases of STIs occur in the world. It is estimated that 374 million new cases of one of the four STIs occur each year – chlamydia, gonorrhea, syphilis, or trichomoniasis. STIs directly affect sexual health and RH, lead to infertility, cancer, and complications during pregnancy, and increase the risk of human immunodeficiency virus (HIV) infection.

As for viral STIs, including HIV, HSV, hepatitis B and C virus, HPV and human T-cell lymphotropic virus type 1 (HTLV-1), they are either incurable or treatment options are limited. [30, 31].

Undoubtedly, in the world and in Ukraine, STI prevention is one of the main tasks of the FP system, as a factor not only in RH disorders but also in serious somatic diseases and genetic problems.

The incidence of STIs in girls aged 15-17 years is one of the main problems of RH disorders, as evidenced by the analyzed indicators in the dynamics of five years from 2014 to 2018 (Fig. 2) [25-29].

These indicators decreased: the incidence of syphilis among girls 15–17 years decreased in 2.83 times and amounted to 2.86 per 100 thousand girls of the corresponding age, gonococcal infection – 3.28 times and amounted to 2.67 per 100 thousand girls of the corresponding age, chlamydial infection – 2.52 times and amounted to 9.36 per 100 thousand girls of the appropriate age, trichomoniasis – 1.7 times and amounted to 59.97 per 100 thousand girls of the appropriate age, urogenital mycoplasmosis – 1.93 times and was 21.01 per 100 thousand girls of the appro-

Table I. Dynamics of abortion rates in Ukraine, 2016–2020

Year	Number of abortions	The frequency of abortions				
		per 1000 women of reproductive age	per 100 pregnancies	per 100 births	per 100 live births	per 100 live and dead births
2020	61 048	6.24	17.81	21.67	21.53	21.39
2019	74 606	7.55	20.36	25.56	25.36	25.21
2018	81 448	8.15	20.48	25.75	25.55	25.40
2017	88 844	8.78	20.46	25.73	25.54	25.39
2016	96 242	9.38	20.35	25.55	25.39	25.24

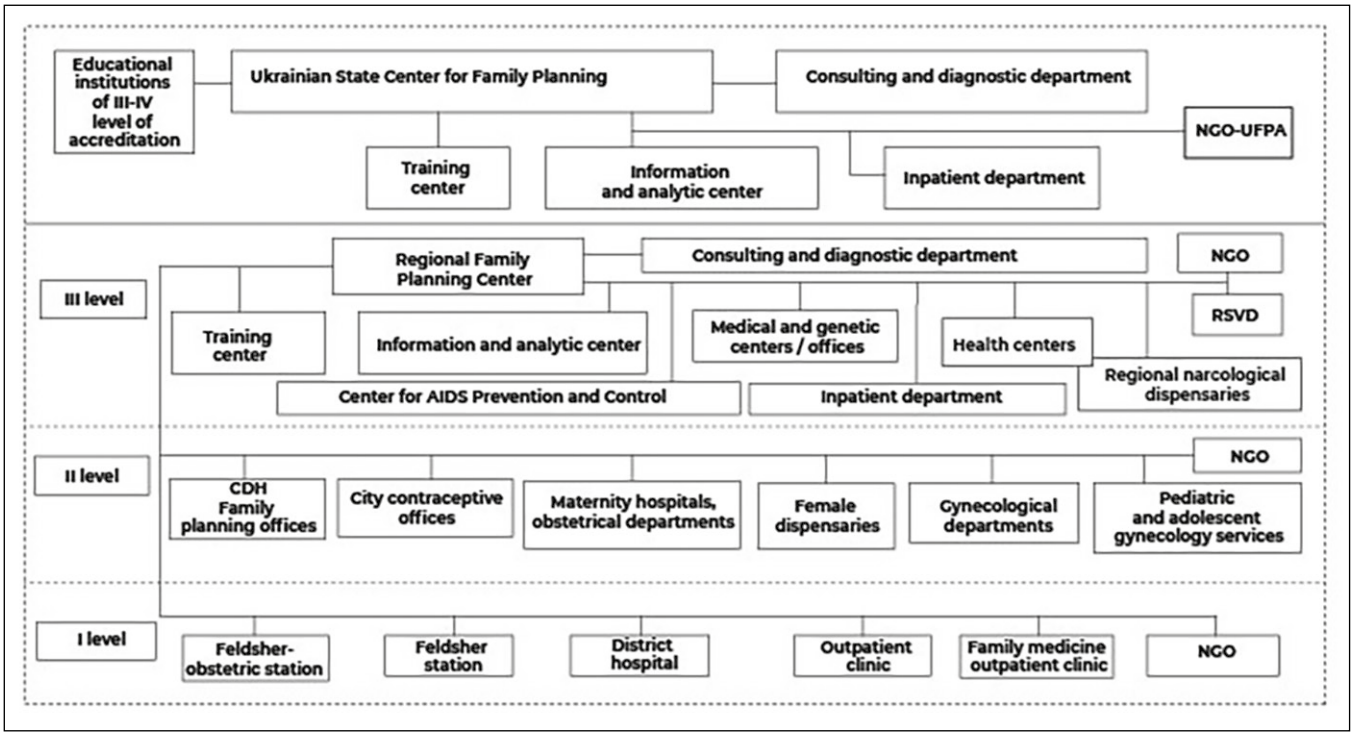

Fig. 1. The structure of the family planning service in Ukraine

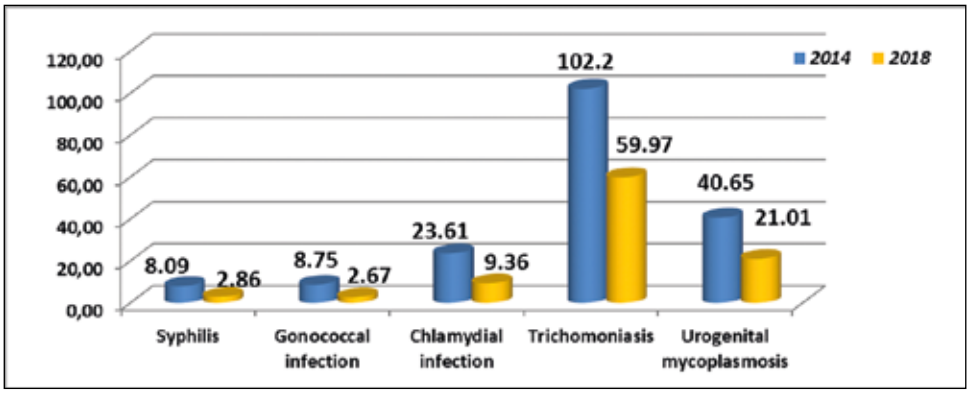

Fig. 2. Incidence of girls 15–17 years old with STIs, 2014 and 2018 (per 100,000 girls of the corresponding age)

priate age [23]. But these indicators demonstrate an insufficient work with adolescents on safe sexual relations.

However, trichomoniasis and urogenital infection are more common (34 and 17 cases, respectively), given the peculiarities of the latent course, which leads to the chronic course of the process and infertility in the future. In adolescents the level of these infections is 4-5 times higher than in girls under 14 years of age.

Despite the reduction, high levels of abortions and STIs are present among adolescent girls in Ukraine [23] that requires the public health service and the FD to strengthen the preventive work to form in adolescents a safe sexual behavior and the formation of RH.

The situation with artificial abortions among adult women in Ukraine is evidence that FP services are not available to a significant number of women [32].

The frequency of abortions among women of reproductive age in Ukraine in 2020 is 6.24 per 1000 women of reproductive age and more than 60 thousand women resort to birth control by abortion.

The number of abortions has decreased significantly due to the implementation of the National Reproductive Health and FP Programs, but according to the results of the International Medical and Demographic Surveys in Ukraine, the abortion rate remains high [30].

The rates of abortions per 100 births, per 100 live births and 100 live and dead births are high and indicate a significant reduction in the number of births in Ukraine. This is confirmed by the comparative characteristics of abortion rates in Ukraine for the period 2016-2020, when the rate of abortions per 1,000 women of reproductive age decreased by 33.5 %, or in 1.5 times (in 2016 – 9.38 per 1,000 women of reproductive age, in 2020 – 6.24) [30].

This situation indicates the necessity for systematic educational work of the FD, both individually and at the community level, which is confirmed by one of the main indicators of FP – the spread of STIs as a serious public health problem in Ukraine. About 400,000 new cases of syphilis, gonorrhea, chlamydia, herpes, urogenital mycoplasmosis, genital candidiasis, and trichomoniasis are registered in Ukraine each year, accounting for 30 to 40 % of STIs [33]. This is undoubtedly due to the spread of false practices of unprotected sex, as well as the increase in latent forms of sexually transmitted diseases. That is why at least 2 million people in Ukraine annually register patients with STIs [33].

In 2020, the incidence of syphilis in the female population was 2.9 per 100,000 women, gonorrhea – 2.5, chlamydia – 20.9, trichomoniasis – 71.4, urogenital mycoplasmosis – 39.3, which indicates a fairly high incidence of women on diseases caused by STIs [30].

It is well known that the analyzed diseases are the result of a conflict with social normal parameters of patient behavior. Unprotected sex is also a consequence of insufficient awareness of safe sexual behavior and the use of prevention tools. The significant hopes for the improvement of the STIs situation are set on the activity of the FD, which should use the knowledge and skills to promote a healthy lifestyle in their work.

In the context of health care reform, when its priority is the development of PHC based on the general practitioners-family doctors [34, 35, 36], the FD should play a leading role in informing the population about the prevention of these infections, diagnosis and treatment with the introduction of rapid testing methods according to WHO recommendations [37, 38].

At present, the normative regulation of the activity of the FP service is at a sufficient level, if to implement it according to the order of the Ministry of Health of Ukraine dated 20.12.2013 N 1030/102 "On improving the system of family planning and reproductive health in Ukraine" [39]. The order of the Ministry of Health of 21.01.2014 N 59 "On approval and implementation of medical and technological documents for standardization of medical care for family planning" approved "The Unified Clinical Protocol of primary, secondary (specialized), tertiary (highly specialized) medical care "Family Planning" [40].

The introduction of standardized provisions in the practice of the FD will allow to have the effective medical care of FP, which will have a positive impact on both the formation and maintenance of RH.

CONCLUSIONS

In Ukraine, with the existing system of family planning with fairly standardized technologies, there are serious problems, which cause reproductive health disorders of the population. The integration of family planning services into the practice of the family doctor, provided that he/she is trained, will increase their availability, quality, and efficiency.

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ABSTRACT BOOK

SCIENTIFIC-PRACTICAL CONFERENCE WITH INTERNATIONAL PARTICIPATION FOR THE WORLD HEALTH DAY 2022

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Venue of the conference - Bogomolets National Medical University, Kyiv, Ukraine
The date of the conference has been postponed from April 5, 2022 to the fall of 2022 due to the martial law in the country.

WHO OFFICIAL INFORMATION

7 April is World Health Day
It is celebrated annually and each year draws attention to a specific health topic of concern to people all over the world.
The date of 7 April marks the anniversary of the founding of WHO in 1948.
World Health Day 2022 7 April 2022 Our planet, our health

In the midst of a pandemic, a polluted planet, increasing diseases like cancer, asthma, heart disease, on World Health Day 2022, WHO will focus global attention on urgent actions needed to keep humans and the planet healthy and foster a movement to create societies focused on well-being.
WHO estimates that more than 13 million deaths around the world each year are due to avoidable environmental causes. This includes the climate crisis which is the single biggest health threat facing humanity. The climate crisis is also a health crisis.
Our political, social and commercial decisions are driving the climate and health crisis. Over 90% of people breathe unhealthy air resulting from burning of fossil fuels. A heating world is seeing mosquitos spread diseases farther and faster than ever before. Extreme weather events, land degradation and water scarcity are displacing people and affecting their health. Pollution and plastics are found at the bottom of our deepest oceans, the highest mountains, and have made their way into our food chain. Systems that produce highly processed, unhealthy foods and beverages are driving a wave of obesity, increasing cancer and heart disease while generating a third of global greenhouse gas emissions.
While the COVID-19 pandemic showed us the healing power of science, it also highlighted the inequities in our world. The pandemic has revealed weaknesses in all areas of society and underlined the urgency of creating sustainable well-being societies committed to achieving equitable health now and for future generations without breaching ecological limits. The present design of the economy leads to inequitable distribution of income, wealth and power, with too many people still living in poverty and instability. A well-being economy has human well-being, equity and ecological sustainability as its goals. These goals are translated into long-term investments, well-being budgets, social protection and legal and fiscal strategies. Breaking these cycles of destruction for the planet and human health requires legislative action, corporate reform and individuals to be supported and incentivized to make healthy choices.

Source: https://www.who.int/campaigns/world-health-day

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OBSTETRIC CARE TRENDS FOR WOMEN IN CHILDBIRTH AND POSTPARTUM PERIOD

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Introduction: Maternal and child health care is a priority of health care systems. In recent decades, the world has made significant progress maintaining and improving maternal health. Despite this progress, maternal deaths globally remain unacceptably high and were about 295,000 in 2017. It is known that most maternal deaths are preventable by timely and high-quality medical care. Therefore, the quality of obstetric care is extremely important.

The aim: Analysis of medical care indicators for women in childbirth and postpartum period in 2014-2019.

Materials and methods: The study methodology was based on the use of information and analytical, as well as medical and statistical methods. The data of the Center for Health Statistics of the Ministry of Health of Ukraine for 2014-2019 on resource provision and results of medical care for women in childbirth and postpartum period were analysed.

Results: The analysis of statistical data on the obstetrics and gynaecology service resources showed that during the five-year period the absolute number of obstetricians decreased by 7.8%, the coverage of the population with obstetricians reduced by 5.3%. The number of maternity hospitals reduced by 4.1% and the number of maternity beds decreased by 13.6%, which was in line with demographic trends and optimization processes in the health care system. From 2014 to 2019, the number of births in the country decreased by 34%. At the same time, the share of complicated births slightly increased (31.6% to 36.2%).

The evaluation of the medical care provision to women giving birth revealed decreased frequency of certain complications, which is an evidence of good management of pregnancy and childbirth. Thus, during five years postpartum haemorrhage decreased by 11.6%, late toxicosis reduced by 24.0%, complicated birth due to urinary tract infection decreased by 5.9%.

At the same time, an increased frequency of other complications in childbirth and postpartum period was found. In particular, the frequency of bleeding at delivery increased by 8.7%, the frequency of labour complications increased by 14.4% due to the circulatory diseases, and by 20.7% due to anaemia. Labour abnormalities increased by 7.3%, perineal ruptures 3-fold, uterine ruptures 4-fold, birth sepsis 2.5-fold and venous complications by 15.9%. Negative tendencies of increasing frequency of childbirth and the postpartum complications require an in-depth study of causes, impact factors and ways of their prevention.

The study of surgical management in obstetric care revealed an increase in the frequency of caesarean sections over a five-year period by 35.8%, vacuum extraction by 49.4%, and a decrease in the prevalence of forceps deliveries by 40.1%.

Conclusions: The analysis of medical care indicators for women in childbirth and postpartum period in 2014-2019 disclosed some positive trends while maintaining a number of negative tendencies associated with reduced obstetric service resources. The current situation requires an in-depth study of causes of the trends identified to justify preventive measures.

KEY WORDS: maternal health, obstetric care, resources, childbirth and postpartum complications.

OBSERVATION OF DORSALGIA IN THE WORKING-AGE ADULTS

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Introduction: Physical inactivity and sedentary lifestyle have been related to all-cause mortality, to lower quality of life and to a higher risk of obesity, diabetes, hypertension and musculoskeletal disorders. Dorsalgia is a disorder characterized by marked discomfort sensation in the back region, acute or chronic pain located in the posterior regions of the cervical, thorax, lumbosacral region, or the adjacent regions. People with prolonged static sitting in the workplace have high risks dorsalgia and demand timely prevention interventions.

The aim: This work analyzes the cases of dorsalgia in the in working-age adults for propose the most effective means of prevention program.

Materials and methods: A survey of 572 worker adults were conducted, examination - height, weight, body mass index, sedentary time in the workplace, dorsalgia was evaluated by using the Visual Analogue Scale.

Results: All subjects 572 (73 % females and 27 % males) with an average age of 40,6 years (23–67 years), a height of 1.73 m (1.60–1.87 m) and a weight of 79.1 kg (52–105 kg), body mass index of females was 26.3 kg/ m^2, body mass index of males was 24.2 kg/ m^2. Above 78% subjects had prolonged static sitting in the workplace. Average sedentary time which spend in the workplace females was 7,8 h, males was 6.2 h. Percentage dorsalgia in females was 56%, in males was 48%, intensity pain by the Visual Analogue Scale in females was 44 mm, in males was 62 mm. Among females lumbalgia was - 42%, cervicalgia was 38%, thoracalgia was -20%. Among males lumbalgia was - 61%, cervicalgia was 25%, thoracalgia was -14%.

Conclusions: Hight level dorsalgia had females but males had hight level intensity pain, females had average percentage cervicalgia and lumbalgia, males had more percentage lumbalgia,

KEY WORDS: sedentary lifestyle, cervicalgia, thoracalgia, lumbalgia.

O.V. KORCHAK-CHEPURKIVSKY'S (1857-1947) ROLE IN THE DEVELOPMENT OF TEACHING SOCIAL HYGIENE AT THE HIGHER MEDICAL SCHOOL

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Introduction: O.V. Korchak-Chepurkivsky's activity as a teacher of Social Hygiene is still insufficiently researched.
The aim: The aim is to find out O.V. Korchak-Chepurkivsky's role in the appearance of Social Hygiene as a subject of teaching in the curricula of medical higher educational institutions of Ukraine.
Materials and methods: Published historical sources; method – historical.
Results: In 1898, Ovksentij Vasilyovich Korchak-Chepurkivsky defended his dissertation for the degree of Doctor of Medicine at the meeting of the Medical Faculty of the University of St. Vladimir. This gave him the right to apply for the position of Private docent. He was elected and then approved in this position by the Department of Hygiene and Medical Police of the named University in 1903. Private docent courses, as opposed to the disciplines taught by professors, were optional for students. Only willing students enrolled in them. Private docents did not receive a salary for teaching these courses. However, the years of being a private docent were included in the teaching experience, which was important for receiving a pension. In general, private docents were an important stage in the academic career of the future professor. In the first half of the 1903-1904 academic year private docent Korchak-Chepurkivsky taught a course in Epidemiology. In the second half of the same academic year, in addition to the course in Epidemiology, he also taught a course in Sanitary Statistics. In later years he continued to teach these two courses. Before the start of the 1907-1908 academic year private docent Korchak-Chepurkivsky partially changed the names of his courses. Epidemiology remained, and instead of Sanitary Statistics, "Public Medicine" appeared. In later years, he continued to teach both Epidemiology and Public Medicine at the same time. The concept of "public medicine" in the Russian Empire was invested in a completely different concept than now. The course "Medical Police", that the professor was supposed to teach, was a discipline of the state (public, imperial) healthcare system. By the beginning of the 20th century, the city and especially the zemstvo (i.e. municipal, in modern terms) system of providing medical care and preventive measures had received significant development in the Russian Empire. Private docent Korchak-Chepurkivsky devoted his course just to this segment of the national health care system. It is important for us to emphasize that in the course of Public Medicine he also dwelled on some issues of Social Hygiene which appeared then in Western Europe. This is the doctrine of population, Malthusianism and neo-Malthusianism, heredity and degeneration, the sexual question, marriage, prostitution.
In 1918, the Ukrainian State University with a Faculty of Medicine was established in Kiev. O.V. Korchak-Chepurkivsky became a professor at this University, taking the Department of Hygiene. Attendance at professorial courses was mandatory for all students, as opposed to private docent courses. So, it is necessary to single out the next (second) stage in the formation of teaching Social Hygiene.
In 1920, the Soviet government merged the Medical Faculties of Kiev Universities (Ukrainian State and St. Vladimir ones) and the Women's Medical Institute with the creation of the Kiev Institute of Health. The latter was renamed Kiev Medical Academy the following year, which was then renamed Kiev Medical Institute. At the Kiev Medical Institute O.V. Korchak-Chepurkivsky headed the Department of General and Social Hygiene. For the first time, the name of the discipline "Social Hygiene" appeared in the name of the Kiev Department, which marks the third stage in the development of teaching this academic discipline in Ukraine. And the latter is also associated with O.V. Korchak-Chepurkivsky's teaching activity.
In December 1922, O.V. Korchak-Chepurkivsky was dismissed from the position of the head of the Department of General and Social Hygiene of the Kiev Medical Institute. He was exiled to Vyatka (now Kirov, Russian Federation), where he was in exile for about a year; in January 1924 his case was reviewed and he was allowed to return to Kiev. In 1923, it was decided to organize a separate Department of Social Hygiene at the Kiev Medical Institute, but the head of this Department was not Professor Korchak-Chepurkivsky, but a member of the Communist Party (Bolsheviks) of Ukraine, Solomon Solomonovich Kagan (1894-1965).
Conclusions: We have identified three stages of O.V. Korchak-Chepurkivsky teaching Social Hygiene in medical higher educational institutions in Kiev. He should be considered the founder of teaching Social Hygiene in higher medical school.

KEY WORDS: teaching in medical Universities, Ukraine, early 20th century.

SELENOPROTEIN P METABOLISM AND LIVER FUNCTIONAL CONDITION IN PATIENTS WITH NAFLD AND CONCOMITANT HYPERTENSION

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Introduction: Nonalcoholic fatty liver disease (NAFLD) is chronic diffuse disease of liver, with increased risk of progressing under presence of comorbidity, especially hypertension (HTN). Among metabolites, which are synthesized by liver, hepatokine Selenoprotein P (Sel P) is one of the studied as it includes almost 60 % of organism's Selenium, which participates in regulation of vascular tone via support of redox balance. Hepatic dysfunction, which gradually develops in patients with NAFLD, may contribute to the development of deviant selenium metabolism with the formation of the corresponding consequences, which determined this study.

The aim: To study Selenoprotein P levels and liver function in patients with NAFLD and concomitant hypertension.

Materials and methods: We examined 100 patients with NAFLD. 49 patients (33 (67,3 %) women and 16 (32,7 %) men) with comorbid course of NAFLD and HTN (main group; MG). Comparison group (CG) included 51 patients with isolated NAFLD (30 (58.8 %) women and 21 (41.2 %) men). Control group included 20 healthy individuals. Median age in MG was 51,0 [45,0; 56,0] years; CG — 52,0 [47,0; 54,0] years; controls —51,0 [45,0; 55,5] years (p=0,564). NAFLD and HTN diagnosis was made according to international and local guidelines and recommendations. Body mass index was calculated as ratio of body mass (kg) to height in meters squared. All patients underwent assessment of alanine aminotransferase (ALT) and aspartate aminotransferase (AST) providing by kinetic method. Levels of Sel P were assessed by ELISA (ElabScience Human Sel P ELISA kit). The de Ritis coefficient was calculated as ratio of AST to ALT. Mann-Whitney test was used to compare two quantitative independent samples; Pearson chi-square was used to compare qualitative variables and Spearman rank correlation was used to assess relations between variables. IBM SPSS 25.0 for Windows was used to perform calculations.

Results: Median BMI was the lowest in controls – 24,5 [23,5; 24,8] kg/m^2 ($p = 0,007$); highest — in isolated NAFLD and NAFLD+HTN group: 24,5 [23,5; 24,8] kg/m^2 and 24,9 [24,2; 25,9] kg/m^2 ($p = 0,008$) respectively. Median systolic (SBP) and diastolic blood pressure (DBP) were highest in main group (150,0 [145,0; 158,0] mm Hg and 90,0 [85,0; 90,0] mm Hg ($p< 0,001$)). SBP in comparison and control group was 125,0 [115,0; 130,0] mm Hg and 120,0 [110,0; 120,0] mm Hg (p=0,012); median DBP did not differ in those groups and was equal: 80,0 [70,0; 80,0] mm Hg ($p = 0,918$).

Liver indices were higher in patients of MG compared to isolated NAFLD patients (ALT: 45,0 [43,0; 47,5] U/l and 36,0 [34,0; 39,0] U/l ($p < 0,001$); AST: 53,0 [51,0; 56,0] U/l and 41,0 [40,0; 45,0] U/l ($p < 0,001$)). Median de Ritis index was significantly ($p<0,001$) lower in controls (0,87 [0,76; 0,99]) but did not differ in main and CG: respectively 1,16 [1,11; 1,24] and 1,14 [1,08; 1,21] ($p = 0,167$). Sel P levels were significantly higher in controls (71,0 [54,3; 76,1] ng/ml), compared to main (19,7 [8,0; 26,7] ng/ml, $p < 0,001$) and CG (43,1 [41,3; 45,4] ng/ml, $p< 0,001$). In patients of main group ALT and AST significantly correlated with Sel P ($\rho = -0,432$ ($p = 0,002$) and $\rho = -0,296$ ($p = 0,039$)). However, ALT/AST ratio did not show significant correlation. In patients with isolated NAFLD only ALT levels correlated with Sel P levels ($\rho = -0,426$; $p = 0,002$). No significant correlations between Sel P and AST and de Ritis index were found. Sel P is chain of antioxidant system, which can be significantly depleted under chronic inflammation. Described mechanisms determine additional decrease of Sel P levels in hypertensive NAFLD patients vs. non-hypertensive. Moreover, this also explains reverse correlation of ALT and AST with Sel P in such patients.

Conclusions: The course of NAFLD is accompanied by a significant inhibition of the synthesis of Sel P, levels of which show significant reversible correlation with the activity of hepatic transaminases. Combined NAFLD and HTN course is associated with a statistically greater increase in these deviations. The obtained data suggest using Sel P as possible marker of the liver functional state in NAFLD.

KEY WORDS: non-alcoholic fatty liver disease, selenoprotein P, liver metabolism.

FOLLOW-UP CHANGES AFTER INTERNET-DELIVERED LOW-INTENSITY CBT FOR PEOPLE WITH SOCIAL ANXIETY DISORDER IN A PERIOD OF COVID-19

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Introduction: Quarantine restrictions and the global pandemic impact on the mental health and stress response of vulnerable groups in a pandemic. Recent studies indicate that low-intensity CBT is effective in pandemic-related anxiety and depression. Internet-delivery low-intensity cognitive behavioral therapy for social anxiety disorder could be helpful for reductions in the severity of functional and social impairment and preventing relapse during a pandemic setting.

The aim: The research aims to study follow-up changes after internet-delivered low-intensity CBT for people with social anxiety disorder in a period of COVID-19.

Materials and methods: The search participants and studies were conducted in 2020-2021. All participants (18-35 years) gave informed consent to participate in the study. They were divided into two intervention subgroups: the first subgroup (ISgr1, n=53) engaged in low-intensity CBT, and the participants of the second subgroup (ISgr2, n=53) were assigned to the waiting list with the following engaging in the same program and control group (n=116). To assess the mental health state were used International Neuropsychiatric Interview (MINI) and a set of IAPT scales. Additional scales and questionnaires were: Social phobia rating scale (SPRS; Wells, 1997) and Acceptance and Action Questionnaire (AAQ-II; Bond, et. al., 2011). Analyses of outcomes by mixed ANOVA considered levels of pre-post therapy effect sizes and clinically significant improvement of symptoms and distress. To determine the impact of use of safety behaviors, negative maladaptive beliefs and experiential avoidance on anxiety and depressive symptoms was conducted hierarchical multiple regression analysis. Statistical analyses were conducted using SPSS Version 23.0 (SPSS Inc., 2019).

Results: At the follow up 1 month the participants of the intervention subgroups achieved a reduction in severe dysfunction by social anxiety disorder in both subgroups of interventions (ISgr1: 3.6 [95% CI, 2.8 to 4.4], $p = 0.000$; effect size (95% CI) 0.5; ISgr2: 2.9 [95% CI, 1.2 to 4.5], $p = 0.001$; effect size (95% CI) 0.2), compared to control groups. The level of distress and tendency to avoid social situations showed a significant decrease against the background of growth of self-consciousness (all p-values <0.001) than those in the control group. Pre-post changes among the participants of the intervention group showed a statistically significant reduction in metacognitive beliefs and the use of safety (all p-values between 0.011 and 0.002). Additionally, the study indicates improving flexibility (less cognitive fusion or experiential avoidance) in both subgroups of interventions (ISgr1: 11.4 [95% CI, 8.7 to 14.1], $p = 0.000$; effect size (95% CI) 0.4; ISgr2: 9.2 [95% CI, 6.3 to 12.2], $p = 0.001$; effect size (95% CI) 0.3), compared to self-help guide psychological care as usual. A reduction in the comorbid level of depression (ISgr1: 5.3 [95% CI, 3.8 to 6.8], $p = 0.000$; effect size (95% CI) 0.4; ISgr2: 5.0 [95% CI, 3.4 to 6.6], $p = 0.001$; effect size (95% CI) 0.3) and generalized anxiety (ISgr1: 4.0 [95% CI, 3.2 to 4.8], $p = 0.000$; effect size (95% CI) 0.5; ISgr2: 3.6 [95% CI, 2.7 to 4.4], $p = 0.001$; effect size (95% CI) 0.5). The results of hierarchical multiple regression analysis indicate that the reduction of maladaptive beliefs of the loss of control over the situation and own thoughts, obsessive attempts to control the situation and their behavior, and reduced experiential avoidance in the intervention group displayed explanatory powers of 92.8% of the level of distress associated with social phobia ($p = 0.001$) and 34.8% of the severity of generalized worries ($p = 0.032$). While obsessive attempts to relax, maladaptive beliefs that they don't like other persons and reduced experiential avoidance explained 62.4% of depressive symptoms ($p = 0.002$).

Conclusions: This research has shown a reduction in the severity of exhaustion from general distress, avoidance, restriction of corrective social interaction experiences, changes in self-consciousness and awareness of their needs and capabilities, use of safety behavior, and emotional burden of negative beliefs in persons with social anxiety disorder. Obtained changes in self-consciousness and negative metacognitive beliefs suggested that these aspects can be significant indicators. Improved psychological flexibility, reduced safety behavior, and experiential avoidance result from enhanced awareness and changes in typical beliefs associated with decreasing rate of comorbid depression and worries. Accordingly, the behavioral aspect of change reinforces strategies to deter relapse. These results demonstrated that low-intensity online interventions based on CBT were helpful for persons with a social anxiety disorder during the COVID-19 pandemic at the follow-up one month after the intervention.

KEY WORDS: unguided online therapies; quarantine restrictions; social impairment.

INFLUENCE OF VITAMIN D DEFICIENCY OR INSUFFICIENCY ON COVID-19 SEVERITY

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Introduction: Vitamin D belongs to the fat-soluble group of vitamins. Widespread use of vitamin D for the prevention and treatment of COVID-19 is primarily related to its immunomodulatory and indirect-virucidal effect. A number of studies in 2021 indicated that low blood serum levels of 25-hydroxyvitamin D (vitamin D) were associated with an increased risk of severe COVID-19 and higher mortality.

The aim: The aim of our study was to identify a possible association between COVID-19 severity and vitamin D deficiency or insufficiency in hospitalized patients of different sex and age groups and to substantiate the potential benefit of vitamin D intake for the prevention and treatment of COVID-19.

Material and methods: We have analyzed the health records of 118 COVID-19 patients who were hospitalized in the private clinic "Oberig", Kyiv, Ukraine. All these patients at hospitalization were tested for vitamin D – $25(OH)D_3$ initial level. The group included 118 patients with a mean age of 60.9±15.7 years, including 40.7 % of women (n=48) with a mean age of 62.1±15.1 years and 59.3 % of men (n=70) with an average age of 60.1±16.1 years. According to COVID-19 severity, three subsets were identified for further analysis, in particular: moderate severity patients accounted for 36.5 % (n=43), severe and critical patients accounted for 38.1 % (n=45) and patients who have not survived were 25.4 % (n=30).

Results: It was found that 73.7 % (n=87) of the total number of patients had a deficiency or insufficiency of vitamin D. Deficiency or insufficiency of vitamin D was observed: (a) in 76.8 % (n=33) moderate severity patients; (b) in 66.7 % (n=30) severe or critical COVID-19 patients; (c) in 80.0 % (n=24) of patients who died from COVID-19. Multiple comparisons (using analysis of variance) did not reveal any statistically significant difference in vitamin D levels in patient's group with vitamin D deficiency or insufficiency (n=87) in clusters according to the severity of the disease (p=0.435). The particular attention was paid to the calculation of the mean difference and 95% CI of the difference in mean vitamin D levels between the subgroups of patients with moderate COVID-19 (group "Medium") and patients who did not survive (group "Deceased") and all of whom were vitamin D deficient or insufficient. The differences in the mean values of vitamin D levels in the subgroups "Medium" and "Deceased" for both men and women together were 1.9 (95% CI -1.1–5.0) and separately for men 2.2 (95% CI -2.7–7.1) and for women 1.9 (95% CI -2.4–6.1). The difference is not statistically significant, however, further analysis shows that the average values of vitamin D in the group "Medium" are 9.8-11.1 % higher than in the group "Deceased", which may indicate a positive effect of vitamin D on reducing the risk of death due to COVID-19.

Conclusions: We identified difference in the mean values of vitamin D between the subgroups "Medium" and "Deceased" according to COVID-19 severity. These data may be important for clinical interpretation and planning of further studies. These data also suggest the effectiveness of preventing of vitamin D deficiency or insufficiency in order to reduce the risk of severe COVID-19 and death. Further research in this area will deepen the understanding of the role of vitamin D deficiency or insufficiency as a potential risk factor for severe COVID-19.

KEY WORDS: COVID-19, disease severity, risk factors, vitamin D.

ASSESSMENT OF PRACTICAL SKILLS IN THE ORGANIZATION OF HEALTHCARE DURING THE OBJECTIVE STRUCTURED PRACTICAL (CLINICAL) EXAM (OSCI) AS A COMPONENT OF THE CERTIFICATION OF FUTURE DOCTORS

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Introduction: Future masters of medicine face important tasks in mastering the theoretical foundations and acquiring practical skills in providing medical care and organizing the treatment and diagnostic process. Verification of these competencies in the course of attestation of graduates is carried out within the framework of the standardized test state exam «Krok-2» and the objective structured practical (clinical) exam (OSCI).

The aim: Substantiation of the content and program of the objective structured practical (clinical) exam on the organization of health care and development of the station passport.

Materials and methods: The research methodology was based on the application of information-analytical method and content analysis. The national educational standards regulating the requirements for the training of masters of medicine, normative and legal documents of the Ministry of Health and the Ministry of Education and Science of Ukraine, etc. were analyzed.

Results: The analysis of the legal framework allowed determining the basic requirements for the practical training of masters of medicine. According to the order of the Ministry of Education and Science of Ukraine «On approval of the standard of higher education in the specialty 222 Medicine for the second (masters) level of higher education» defined special (professional, subject) competencies, which must be able by the graduate. The list of special (professional) competencies includes the ability to maintain medical records, including electronic forms of documents. As a result of the training of higher education applicants defined by the Standard, the ability to keep medical records of the patient and the population on the basis of regulatory documents is provided. According to the Handbook of Qualification Characteristics of Workers' Professions (issue 78 Health Care), approved by the order of the Ministry of Health of Ukraine, the qualification characteristics of general practitioners - family doctors provide knowledge of the rules of medical documentation.

The OSCI-2 station in the discipline «Health Care Organization» is dedicated to testing these knowledge and skills as part of a doctor's training.

The educational purpose of the organization of the station is to assess the ability to choose and fill out forms of documents required by the doctor to record the health of the population and its activities in different situations, which must be demonstrated by students. The passage time of the station is 5 minutes.

Several variants of tasks have been developed to test the ability to choose and fill in document forms. They included demonstrations by graduates of the ability to choose and complete the forms of documents required for a particular diagnosis with coding of diagnoses according to the International Statistical Classification of Diseases and Related Health Problems, X revision. Several variants of diagnoses of socially significant and socially dangerous diseases were selected, including cancer, active tuberculosis or its recurrence, infectious disease, food or acute occupational poisoning, unusual reaction to vaccination, and fixation of causes of death.

In addition, instructions were developed for the teacher-observer, for the student, tickets, student check-list, exam program developed and videos created to help the student prepare for the OSCI station on the organization of health care.

Conclusions: Substantiation of the content and program of the objective structured practical (clinical) exam (OSCI) on the organization of health care allows to introduce an objective test of practical skills of future masters of medicine in the framework of state certification of graduates of medical universities.

KEY WORDS: practical skills, selection and completion of medical documents, objective structured practical (clinical) exam (OSCI), health care organization.

RELATIONSHIPS BETWEEN CASPASE-8 LEVELS AND RESPIRATORY FUNCTION IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Introduction: Chronic obstructive pulmonary disease (COPD) is fourth leading cause of mortality worldwide. Smoking is considered primary risk factor for COPD, followed by environmental and occupational hazards. On the other hand, COPD patients often present with numerous comorbidities including hypertension (HTN), heart failure and diabetes. Subclinical inflammation is known pathogenetic mechanism of COPD development. Given the above oxidative stress and apoptosis can be the consequence of chronic inflammation. Production of pro-inflammatory cytokines and releasing of reactive oxygen species mediate the bronchial epithelium apoptosis. Caspase-8 (Cas-8) is the part of extrinsic apoptotic pathway, which triggers apoptosis under the influence of exogenous factors. Recent researches show that apoptosis should be considered as a fourth pathogenetic mechanism of COPD. It is hypothesized that intensive apoptosis in bronchial wall and lung parenchyma is not compensated by proliferation. Above-mentioned mechanism leads to continuous destruction of lung tissue and development of emphysema.

The aim: The aim of study is to assess the correlation of Cas-8 levels and respiratory parameters in COPD patients with and without concomitant hypertension.

Materials and methods: We have examined 93 patients with COPD. 47 patients had isolated COPD and were included into main group (median age — 62.0 [52.3; 65.8] years; 33 (70.2 %) males and 14 (29.8 %) females). 46 patients had comorbid COPD and HTN and were included into comparison group (median age — 60.0 [58.0; 62.8] years; 29 (63.0 %) males and 17 (37.0 %) females). Control group included 30 individuals with no history of COPD and HTN (median age — 63.0 [55.5; 65.0] years; 18 (60.0 %) males and 12 (40.0 %) females). Diagnosis of COPD was established according to GOLD guidelines and local protocols; HTN was diagnosed according to European society of cardiology guidelines and local protocols. Cas-8 levels were assessed by ELISA (ElabScience Human Caspase-8 ELISA kit). Respiration function was assessed by spirometry with calculation of forced expiratory volume for 1 s (FEV_1) and reversibility of obstruction (RO). Quantitative data were presented as Median [lower and upper quartiles] and compared using Mann-Whitney U-test. Qualitative data were presented as n (%) and compared using Pearson's Chi-squared test. Spearman Rank correlation was used to assess relationship between quantitative data. Logistic regression was used to assess association with binary outcome. Statistical analysis was performed using IBM SPSS 25.0 for Windows.

Results: Median FEV_1 in main group was significantly higher than in comparison group: 61.0 [58.0; 64.0] % vs. 57.0 [54.3; 60.8] % ($p<0.001$); RO did not differ significantly between groups: 3.1 [1.7; 3.5] % vs. 3.2 [3.0; 4.1] % respectively ($p=0.176$). Cas-8 levels were lowest in controls: 2.8 [2.5; 3.0] ng/ml. In patients with COPD and concomitant HTN levels of Cas-8 were significantly higher than in COPD only patients: 3.7 [3.5; 3.8] ng/ml vs. 3.3 [2.8; 3.7] ng/ml ($p<0.001$).

No significant correlation between FEV_1 and Cas-8 was observed in control group ($p=0.640$). Reverse significant correlation was found between FEV_1 and Cas-8 in main group ($\rho=-0.559$; $p<0.001$) and was also significant in comparison group ($\rho=-0.445$; $p=0.002$). Noteworthy that RO in all studied patients did not show significant correlation with Cas-8 levels.

Conclusions: Obtained results show that Cas-8 levels correlate with the obstruction grade (FEV_1) but not reversibility of obstruction, which reflects the intensity of apoptotic process in such patients and allows using Cas-8 as noninvasive predictor of COPD severity.

KEY WORDS: apoptosis, respiration, obstruction.

INTERRELATION BETWEEN ECONOMIC AND MEDICO-SOCIAL COMPONENTS OF THE HUMAN DEVELOPMENT INDEX AS A COMPLEX INDICATOR OF HUMAN POTENTIAL

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Introduction: Human potential is the aggregate ability of society, the state and individuals to use human resources and productive human qualities for any socially useful activity. The components of human potential are directly (socio-demographic potential) or indirectly (socio-economic, socio-cultural, activity potential) related to the state of health of the population. An integral indicator of human potential is the Human Development Index (HDI), the informativeness of its components is unequal. The possibility of improving the further use of this indicator in the planning of strategies and programs of socio-economic development in Ukraine needs to be studied.

The aim: Analyze the relationship between economic and medical and social components of the human development index as a comprehensive indicator of human potential.

Materials and methods: We analyzed the economic (by the example of gross national income (GNI) per capita) and medical-social (by the example of life expectancy at birth) components of the HDI in Ukraine for 1990-2019 using statistical, bibliosemantic, systematic approach and analysis.

Results: HDI includes indicators of education, longevity and living standards. However, HDI does not reflect the health of people throughout life. Environmental pressures are an important factor in determining health inequalities, and even consumption patterns that harm the environment can also contribute to deteriorating health in noncommunicable diseases. The determinants of the disease are complex and multifaceted and affected by the COVID-19 pandemic.

The economic component of HDI is also a source of disagreement. As Jean Drèze and Amartya Sen (Oxford University, 1990) have shown, "including income in the HDI has been criticized as encouraging unaimed opulence — that is, "attempting to maximize economic growth without paying any direct attention to the transformation of greater opulence into better living conditions. Unaimed opulence is generally a roundabout, undependable and wasteful way of improving the living standards of the poor". Income by itself does not mean guaranteed prosperity, but it is an extremely important prerequisite for realizing other opportunities. An important feature of the including income indicators in the HDI is their applied role, which weakens with increasing income. Thus, the revenue component should be considered as an index of opportunities indirectly related to health care. Our correlation analysis showed for Ukraine in 1990-2019 the presence of a positive statistically significant correlation between life expectancy at birth and GNI per capita (constant 2017 Purchasing power parity (PPP) $). Pearson correlation coefficient was 0.658, $p = 0.0001$. At the same time, the trend towards stabilization of HDI in Ukraine during the first decades of the 21st century with a simultaneous increase of life expectancy at birth from 67.3 (2000) to 72.1 years (2019) and GNI per capita from $7025 (2000) to $13216 (2000) is insufficiently embodied in the achievements in public health area.

Conclusions: Thus, we drew a conclusion that there is a need for coordinated consolidated activities of the state, society, individual stakeholders, aimed at developing and maintaining economic growth. Such activities should include actions to increase the standard of living and health of the population as a leading component of the HDI and a marker of economic growth.

KEY WORDS: Human potential, human development index, life expectancy at birth, gross national income, economic growth.

MODERN EHEALTH TECHNOLOGIES AND PATIENT-CENTERED APPLICATIONS USABILITY

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Introduction: The defining trend in the evolution of healthcare in the coming years is the comprehensive development and scalability of the eHealth system. Innovative technologies that meet the wide range of Healthcare 4.0 Technology Standards are conducive to building a better and more efficient healthcare system, and open up new opportunities for personalized medicine. The evolution and construction of an innovative eHealth Ecosystem, the transition to integrated models of health care in accordance with the requirements of Healthcare 4.0 are becoming significant. Ensuring patient usability, efficiency and security is important to maximizing the benefits of patient-centered eHealth applications.
The aim: Our study is focused on possibilities of modern eHealth technologies to improve patient health care, considering possibilities of digital solutions to maximize the potential of eHealth in Patient-Centered Systems with ensuring their usability, efficiency and safety.
Material and methods: PubMed and TRIP databases searches for eHealth technologies studies were conducted and limited to those published from 2000 to 2021. 2041 publications in PubMed and 1677 publications in TRIP were found and used for further selection of associated systematic reviews and meta-analyzes. To study innovative solutions in the eHealth Ecosystem according to Healthcare 4.0 Standards, the "Concept of development of digital economy, society and electronic health care system of Ukraine (2018-2020)", International framework strategies for eHealth development (21 frameworks), statistical methods and usability evaluation were applied.
Results: We have found that most systematic reviews show (or at least suggest promising evidences) that eHealth interventions are effective and rewarding, could improve the quality of care, reduce health care costs, improve cognitive-behavioral therapy for patients. The number of evidences confirms the effectiveness of eHealth technologies such as Web-Based Solutions, Telemedicine, eHealth Record, Virtual Clinics, smart-phones apps, mHealth, Telehealth, Virtual Assistants and ChatBots. The analysis of PubMed and TRIP search results proves that there are significant potential for ChatBots in the key arias such as: (a) automate routine processes in clinical practice, (b) plan patient admissions, diagnose, screen, (c) check symptoms before a doctor's appointment and make a preliminary diagnosis with the ability to enter data into an electronic medical record, (d) support clinical evidence-based decision making, (e) health monitoring and medication tracking, (f) mental health support and counseling, (g) health promotion coaching and patient awareness in the field of medicine. The number of PubMed and TRIP publications suggest that eHealth have to supplement traditional hospitals with virtual ones (such as The Virtual Gastroenterology Clinic) with an expanded ecosystem of patient care capabilities. Evolutionary technology development and transition to Healthcare 4.0 Standards expand and complement the eHealth ecosystem with innovations such as The Internet of Medical Things (IoMT), wearable devices, Artificial Intelligence (AI), Machine learning, Virtual and Augmented reality, Sensors, Big data analytics, Robotic Systems, Natural language processing, Blockchain systems, 3D and 4D printing, human-machine interfaces (HMI), etc. These innovations will further improve the health care system, promote the concept of Patient Participation, which will give patients a more active role in managing their health through the use of various eHealth computer applications, support the development of individual digital plans for prevention and treatment, including on the basis of genomic analysis, which is the driving force for Personalized and Precision Medicine. The introduction of technologies with support for AI, IoMT, VR, AR, HMI, Blockchain will implement new features, enhance functionality, usability and security in Patient-Centered Systems (Virtual Assistants, mHealth, Virtual Clinics, patient electronic medical cabinet, electronic medical examinations, etc.).
Conclusions: The analysis of eHealth's International framework strategies (21 frameworks) has highlighted the importance of ensuring eHealth Patient-Centered Applications usability, ease of use, functionality, design, visibility, user satisfaction and security. Structured Usability Engineering methods could facilitate the application development and ensure efficiency in the design of relevant eHealth Patient-Centered Applications, thus maximizing the benefits of these technologies for personalized health care.

KEY WORDS: eHealth's International framework, Healthcare 4.0, Patient-Centered Applications.

ASPECTS OF CHILDREN'S DISABILITIES RELATED TO INJURIES

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Introduction: Children's disability in the world is seen as an indicator of economic success of society, social protection and quality of care for children. Studying the issue of the formation of children's disability related to injuries, finding ways to improve the effectiveness of rehabilitation of this group of people with disabilities remains an urgent medical and social problem. The urgency of the problem of disability from childhood is also due to the fact that 25% of people with disabilities under the age of 50, disability is due to diseases transmitted in childhood. The issue of prevention of child injuries, finding medical and social solutions should be one of the important areas of public health.
The aim: The aim of the study was to study and analyze the state of disability of children, including injuries and poisonings, depending on the city of residence, age and gender at the regional level.
Materials and methods: The materials of the research were statistical data of sectoral and regional reporting for 2011-17. The statistical and bibliosemantic method was used in the research.
Results: The study found that the number of children with disabilities in the Zaporozhye region during the study period increased by 12%, with a positive decrease in the number of children with disabilities aged 0-17 years in Ukraine. The highest rates of disability were in children aged 7 to 17 years. These include 80% of people with disabilities from the total number in the region. About 60% of disabled people are boys. The share of children's disability from injuries and poisonings is insignificant and is only 1.5% in the region (1.9% in Ukraine), but injury prevention, organization of medical care and rehabilitation will not only reduce disability rates among children and adolescents, but and improve their quality of life and provide them with social protection.
Per 10,000 population, the prevalence of disability of children aged 0-17 years increased from 226.6 to 233.9 (in Ukraine from 201.6 to 205.0 in 2017).
The tendency to increase the disability of children aged 0-17 in the Zaporizhia region is noteworthy, mainly due to urban residents, the figure among which in 2017 is 25% higher than in Ukraine and 10% higher than in the region. The growth of children's disabilities in the region occurs mainly among the age groups from 3 to 6 years and from 7 to 14 years.
Our analysis showed that in the structure of children's disabilities from 0 to 17 years, in the first place congenital defects, in the second – mental and behavioral disorders, in the third - diseases of the nervous system. Injuries and poisonings are in tenth place. Comparing the structure of children's disability with 2011, it is necessary to note changes in the structure of disability due to mental disorders (from third to second), injuries and poisonings moved from 11th to 10th place.
Of concern is the growth of children's disabilities in the age group of 3-6 years from birth defects and mental disorders that require detailed analysis by obstetricians and gynecologists with the development and adoption of measures for their prevention.
Conclusions: The analysis of disability indicators reveals regional and gender differences that need to be taken into account when designing and implementing disability prevention programs, especially for injuries and poisonings. Preventing child injuries, deaths and disabilities due to external causes should be an important part of public health. The results require health care providers and local authorities to develop and implement measures to prevent injuries, provide quality care, and create conditions for rehabilitation after severe disabling illnesses. This is possible only with intersectoral cooperation.

KEY WORDS: children's disability, injuries, prevention.

SHORT CHAIN FATTY ACIDS CHANGES IN PATIENTS WITH ATHEROSCLEROSIS AND ATRIAL FIBRILLATION

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Introduction: Gut microbiota composition is an important characteristic of the human health. It influences at atherosclerosis (AS) and atrial fibrillation (AF) through its metabolites. Short chain fatty acids (SHFA) are produced in processes of fermentation and decomposition of dietary fibers. SHFA includes acetates, propionate and butyrate, but also valerat, caproate, isobutirat, isovaleriat can be checked.

The aim: To check changes in fecal SHFA in patients with AS and AF.

Materials and methods: 300 patients were investigated. All investigated were divided into 3 groups: control group (CG) – 27 patients without AS and arrhythmias; mean group – 149 patients with AS but without arrhythmias; comparable group – 124 patients with AS and AF paroxysm. Fecal SHFA composition were determined by gas chromatography with mass electron detection.

Results: The CG is characterized the significant lower level of acetates (0,52±0,21 vs 4,57±0,37 and 5,53±0,42, mg/g of feasus, $P<0,05$) and higher level of butyrate (1,66±0,18 vs 0,70±0,13 and 0,46±0,15, mg/g of feasus, $P<0,05$) compared with mean and comparable groups. Also, in the patients of mean and comparable group were detected isobutirat and isovaleriat, that were not common for healthy controls. In the comparable group compared with the mean group significant decreasing of the butyrate level was revealed (0,46±0,15 vs 0,70±0,13, mg/g of feasus, $P<0,05$), also significant increasing of isobutirat level was detected (0,17±0,03 vs 0,11±0,03, mg/g of feasus, $P<0,05$). It was not any significant changes between valerat and caproate levels in investigated groups.

Conclusions: The current study revealed the significant changes in SHFA synthesis in patient with AS and AF. That can be an important therapeutic goal for further pathogenetic treatment and prevention of development AS and AF.

KEY WORDS: atherosclerosis, atrial fibrillation, short chain fatty acids

DYNAMICS OF CHILDREN'S HEALTH INDICES: CHALLENGES OF HEALTH CARE REFORM

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Introduction: The current three decades in Ukraine have been accompanied by ongoing reforms in the health care system amid socio-economic unrest, administrative reform, declining population's incomes, hostilities in the east, and outbreaks of infectious diseases that have affected key health indices of children.

The aim: Determining the dynamics of the key indices of child health, changes in certain indicators of the health care system during the period of Ukraine's independence in order to identify possible ways to improve the organization of child healthcare in the country.

Materials and methods: The analysis of statistical data of the Ministry of Health of Ukraine and the systematic assessment of indices dynamics of the child health service for the period 1990-2020.

Results: The number of children under 17 was decrease from 13.3 million in 1990 to 7.46 million in 2020 amid considerable reduction in the resources supplying of the organization medical care for children. During this period, the number of children's departments (rooms) decreased from 3,532 to 999, the number of children's beds in hospitals - from 90,600 to 33,700, and coverage decreased from 81.7 per 10,000 child population to 44.8 respectively, with an increase beds in day hospitals from 1.9 to 6.2 per 1,000 child population. The number of pediatricians decreased from 21,800 to 9,500, including district pediatricians from 8,700 to 2,100, which reduced the level of coverage by them from 2.0 to 1.05 per 1,000 children and 0.79/0.28, respectively. At the same time, the number of general practitioners / family doctors has increased to 14,800, which currently does not satisfy the necessary needs for primary health care in population. The training of family physicians in pediatrics is inadequate. The family doctor's work has been changed to remote format; children at home are practically not served by medical persons. During the COVID-19 pandemic, the total number of doctor visits (mostly at the reception) by children aged 0-17 until 2018 was 9.5-11.6 per 1 child per year, and in 2020 decreased to 6.9. The coverage completeness by preventive examinations also decreased to 94.3%, the frequency of treated children in day hospitals decreased by about 4 times and was 6.2 per thousand children, the hospitalization rate of children in inpatient hospitals during this period also decreased almost twice to 107.8 per thousand children.

The positive achievements of the healthcare system for children are: increasing the breastfeeding rate; reduction in the child morbidity in the first year of life from 1415.1 to 1219.7 per thousand children of the appropriate age. In the country, statistical reporting on the morbidity of children under 17 has been abolished since 2018. At the same time, the total disability of children increased from 95.7 per 10,000 children in 1992 to 216.3 in 2020, which may be due to the extension of the list of medical indications that give the right to receive social assistance for children with disabilities, as well as poor children's health, reducing the quality and accessibility of primary health care.

The mortality rate of children under 5 decreased 2.2 times during 1990-2020 (from 17.3 to 7.95 deaths under the age of 5 per 1,000 live births), and infant mortality from 12.8 per 1,000 live births in 1990 to 6.7 in 2020. The reduction in mortality was achieved during this period due to both neonatal (from 6.7‰ to 4.45‰) and postneonatal mortality with an increase in the neonatal mortality ratio from 52.3% to 66.4% (with a reference optimal value of 65-70%). However, the infant mortality rate according to the world ranking (2018) remains high in Ukraine and ranks 61st among 193 countries.

Conclusions: The results of this study indicate shortcomings in the organization of primary health care; the rapid collapse of pediatric care causes negative trends in children's disability and may be the basis for management decisions to optimization of medical care, especially preventive, for children.

KEY WORDS: children, health, infant mortality, disability.

ROLE OF BUSINESS MODEL OF GENETIC LABORATORIES FOR PRECISE DIAGNOSIS BY NGS

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Introduction: Nest Generation Sequencing (NGS) is a powerful method of genetic testing. However, genetic laboratory business models have created conditions where doctors of any specialty or patients themselves can send a biosample for testing. That being said, the lack of understanding by doctors and patients of thetesting principles and the testing accessibility creates a misconception regarding the simplicity of the diagnosis and can lead to critical errors when conducting bioinformatics processing. Errors may include the derivation of an excessive number of variants without clinical significance which will make genetic counseling too difficult, can lead to false-negative results and/or misdiagnosis. To what extent is the fullness and detail of the description of a patient's clinical presentation

The aim: The aim of reseach is to analyze if the ignoring of description of the fullness and detail of the description of a patient's clinical presentation critical to ensure the precise diagnosis by NGS?

Materials and methods: Retrospective bioinformatics reanalysis of raw sequencing data (RAW data) for patients seeking genetic counseling to clinically interpret Whole exome sequencing (WES) by NGS results in case of negative results (no mutations identified) (2020-2021).

Group A – patients (24 cases, full clinical information collection, patient phenotyping, HPO-coding when referring to WES).

Group B – patients (12) who underwent WES only with a diagnosis. Group C – patients (15) who underwent WES with clinical information, but without a description of the phenotype.

Participants/materials, setting, methods: The study included cases of negative WES results in the case of examinations of children with undifferentiated neuropsychiatric retardation aged 1 to 5 years for whom clinical interpretation of WES results was performed independently of the WES implementing laboratory. For all negative results, RAW data bioinformatics re-processing was performed in an independent laboratory. For groups B and C – after full clinical information collection, phenotype description, and HPO coding.

Results: Bioinformatics re-analysis in an independent laboratory in the group with a full patient description (A) allowed to identify 2 positive cases out of 24 previously negative ones (8.3%). In group B – 5 cases out of 12 (41.7%) after full clinical information collection, phenotype description, and HPO-coding. In group C, with full phenotype description and HPO coding, – 3 cases out of 15 (20%). Overall chi-sq (2;N=51)=5.64 p=0.059 Group A vs B: chi-sq (1;N=36)=5.67 p=0.017 (significant at $p \leq 0.05$) Group A vs C: chi-sq (1;N=39)=1.12 p=0.28 (not significant at $p \leq 0.05$) Group B vs C: chi-sq (1;N=27)=1.05 p=0.22 (not significant at $p \leq 0.05$)

Limitations, reasons for caution: The study results and the evaluation of statistical significance criteria are limited to a small sample with negative WES results, and also apply only to children with undifferentiated neuropsychiatric retardation aged 1 to 5 years.

Conclusions: A full clinical presentation and description of a patient's phenotype are critical to reduce the incidence of false-negative results at the WES bioinformatics processing stage. The study results may serve as a basis for modifying the requirements of genetic laboratories for the description of a clinical case during referral for diagnosis by WES. Such modifications will allow geneticists to find a precise diagnosis and provide reproductive family planning, including preimplantation and prenatal testing procedures.

KEY WORDS: precise diagnosis, business model, NGS, WES, reproductive family planning.