REVIEW ARTICLE

PECULIARITIES OF THE PREVALENCE OF INTRAUTERINE INFECTIONS AT THE PRESENT STAGE

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ABSTRACT

The aim: According to the literature sources to summarize statistics on the prevalence of intrauterine infection and its impact on pregnancy and the condition of newborns at the present stage.

Materials and methods: The article analyzes 35 literature sources (scientific publications) from 2000 to 2021, indexed in international scientometric database and covers the incidence of intrauterine infections in countries with different income levels, as well as their impact on pregnancy, childbirth and the condition of newborns.

Conclusions: The main task of obstetrics and gynecology at the present stage is to reduce reproductive losses, which necessitates further study of the etiology of IUI, especially in low- and middle-income countries. The screening for IUIs during pregnancy is cost-effective because treatment of the effects of IUIs requires disproportionately greater resources.

KEY WORDS: Intrauterine infections, perinatal infections, perinatal morbidity and mortality, neonatal period, congenital pathology

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INTRODUCTION

An urgent problem of today's medicine is the steadily increasing number of intrauterine infections (IUIs) of the fetus and newborn. According to modern literature, one of the leading places among the causes of the pathological course of pregnancy and childbirth is occupied by intrauterine infectious pathology. This creates not only medical but also social problems due to the fact that in many cases, children who have undergone IUI require lifelong help [1].

Intrauterine infection is a disease of the fetus caused by hematogenous (transplacental) predominantly viral or toxo-infection with fetal damage or clinical manifestations of infection after birth, i.e. results from intrauterine infection implementation. Intrauterine infection reflects the fact of invasion of the microorganism into the body of the fetus, which does not always lead to the development of pathological changes. Intrauterine infection occurs much more often than the development of clinical manifestations of the disease, and therefore this term is not used as a diagnosis [2].

Perinatal infections are infections that can be transmitted from mother to child during fetal development (intrauterine, or congenital, infections), during childbirth (actually perinatal or intranatal infections) or immediately after childbirth (postnatal infections) [3].

THE IAM

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MATERIALS AND METHODS

The article analyzes 35 literature sources (scientific publications) from 2000 to 2021, indexed in international scientometric database and covers the incidence of intrauterine infections in countries with different income levels, as well as their impact on pregnancy, childbirth and the condition of newborns.

REVIEW AND DISCUSSION

According to the World Health Organization, more than 5 million perinatal deaths are reported worldwide each year, including 2.7 million neonatal deaths and 2.6 million stillbirths [4]. Elimination of preventable infant mortality and stillbirth remains one of the main goals of international health efforts [5]. Comprehensive assessment of the causes of neonatal death and stillbirth is required to develop treatment and prevention programs aimed at improving basic care for every woman and every child born, determining the risk of perinatal death in subsequent pregnancies and thus, reducing this risk. A special place in the structure of causes of perinatal mortality is occupied by IUI, caused by infection of the fetus before birth or during birth. IUI can be considered a preventable cause of perinatal mortality and serve as a significant reserve for its reduction [6]. Infectious effects during pregnancy have become more frequent and difficult due to immigration, international travel (*ZIKA virus, hepatitis*, COVID-19), increased viral morbidity (*H1N1 influenza virus, Ebola*), reduced primary vaccination and annual vaccination against influenza and children infections (*rubella, chickenpox, measles*) [7, 8].

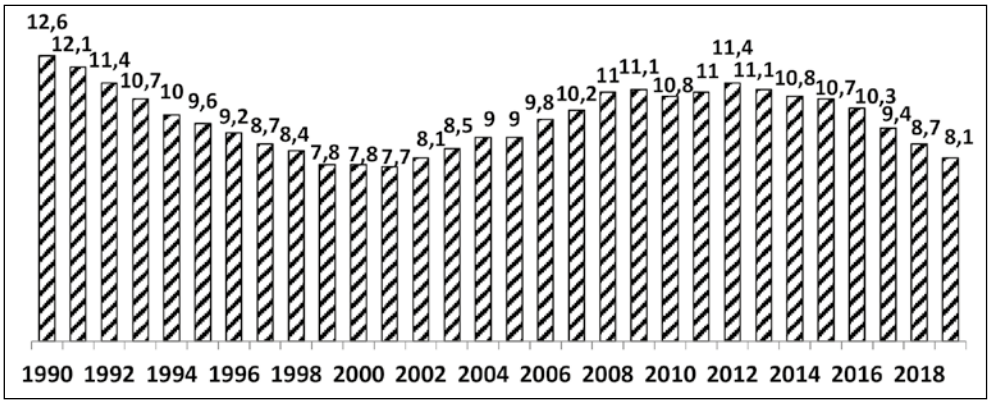

Fig. 1. Birth rate in Ukraine in 1990-2019.
According to the official website of the State Statistics Service http://www.ukrstat.gov.ua /

Currently, there is no reliable data on the frequency of IUI, as IUI diagnosis is associated with certain difficulties, and there is no total screening for IUI in any country in the world. Most of the infectious diseases of pregnant women, leading to intrauterine infection, occur in a subclinical form or asymptomatically, which significantly complicates the diagnosis of IUI. In 50% of cases, infectious pathology among newborns is hidden behind such diagnoses as intrauterine hypoxia, ante- or intranatal asphyxia, pneumopathy, sepsis, birth trauma, malformations, etc. It has been established that only 15-20% of congenital abnormalities are diagnosed during the neonatal period. The majority of congenital abnormalities are detected only in the first year of life or at a later age [9].

The incidence of IUI varies from 2.0 to 58%, reaching 70% among premature infants. Among the causes of perinatal mortality, IUI is up to 45%, ranking third [10, 11]. At the same time, the publications provide indicators without taking into account the differences between intrauterine infections and intrauterine infection implementation.

The number of stillbirths caused by IUI varies in countries with different income levels: in developing countries, more than 50% of stillbirths and fetal deaths are due to infection in the mother, in developed countries this number reaches 10-25% [12]. Thus, in 2014 in the UK, perinatal infections caused 3.1% of stillbirths and 7.3% of neonatal deaths [13]. In the United States, there is 1 stillbirth per 1,000 births caused by IUI, due to the implementation of a number of strategies to reduce the risk of stillbirths associated with infection [14].

Measles, mumps, rubella, and *chickenpox* have once again attracted attention in connection with IUI. In economically developed countries, only a few cases of IUI caused by these viruses have been reported. According to the literature, 96.9% of pregnant women in Italy had antibodies against measles [15], 91.1% against chickenpox [16], and 98.6% of pregnant women in Norway were seropositive for *chickenpox virus* [17]. Despite effective vaccination strategies, unfortunately, there is currently a trend of mistrust and fear of vaccine safety, and the spread of misconceptions related to vaccine science has led to a relative resurgence of these infectious diseases in economically developed countries [18].

Herpesviridae viruses are of particular interest because they are often the cause of IUI, influencing the course and outcome of pregnancy. In pregnant women, the most common viruses of this family are *herpes simplex virus* (HSV) types 1, 2 and 6 and *cytomegalovirus* (CMV) [19, 20]. According to the WHO, 1–10% of pregnant women suffer from genital herpes caused by HSV-2 [21], according to other researchers, this figure reaches 7.6–8.4% [22]. In the United States, approximately 22% of pregnant women are infected with HSV-2, and 2% of women become infected during pregnancy [23]. 3% of Italian women become infected with HSV-2 during pregnancy, which can cause antenatal fetal death, intrauterine growth retardation and premature birth [24].

Among the causes of IUI, one of the important places is CMV, which is detected in 0.2–3.0% of live births [25, 26]. In socially and economically developed countries, congenital CMV infection is detected in 0.3–2.4% of all newborns [27]. Vertical transmission of CMV infection is the cause of the development of its most severe forms. Thus, among the non-genetic causes of neurosensory deafness, congenital CMV infection ranks first, and is also the leading among the known viral causes of mental retardation. In about 10–15% of newborns, congenital CMV infection is accompanied by clinical symptoms, more often it is neurosensory deafness, increase in the size of internal organs, intracranial calcifications and chorioretinia [28, 29].

Currently, toxoplasmosis is considered the second most common type of IUI accounting for 0.6-1.7 per 1000 pregnant women [30]. *Toxoplasmosis* is spread in the world inhomogeneously, which is explained by the religious and socio-economic characteristics of the regions. Thus, the number of *toxoplasmosis*-infected pregnant women in South America is in the range of 51–72%, 54–77% in Africa, 10% in the UK and 55% in France and Greece [31, 32]. In neonates, manifestations of congenital toxoplasmosis may include hydrocephalus, microcephaly, intracranial calcifications, strabismus, blindness, epilepsy, psychomotor, and mental retardation [33].

An assessment of the basic statistical indicators of the perinatal period has been carried out on the example of Kharkiv region (Ukraine).

According to the Ministry of Health of Ukraine, the birth rate in Ukraine has decreased by 40% over the past five years. The State Statistics Office provides annual data on the birth rate per 1,000 total population (Fig. 1).

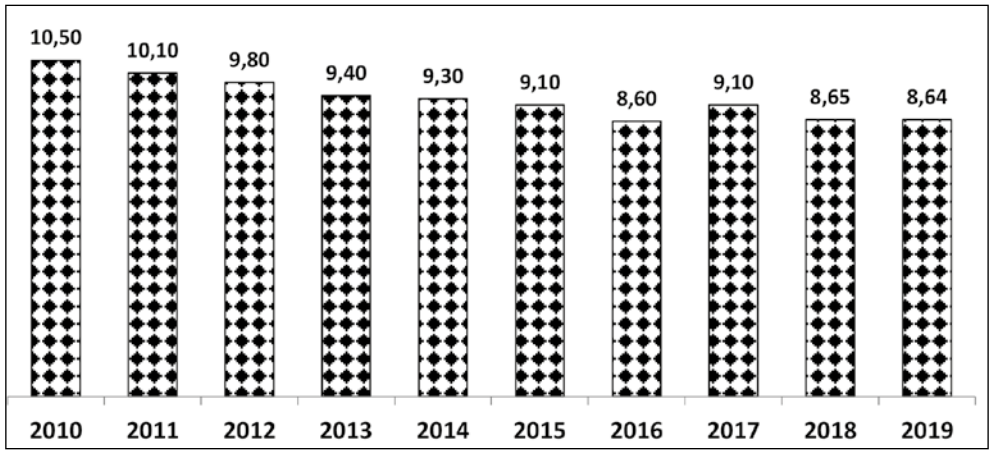

Fig. 2. Perinatal mortality in Ukraine. According to the official website of the State Statistics Service http://www.ukrstat.gov.ua/

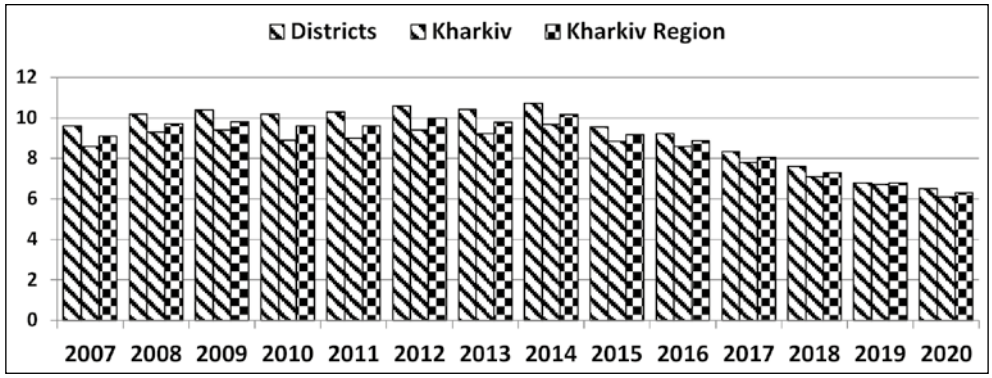

Fig. 3. Birth rates by district, in Kharkiv and Kharkiv region, ‰.
According to the Main Department of Statistics in Kharkiv region

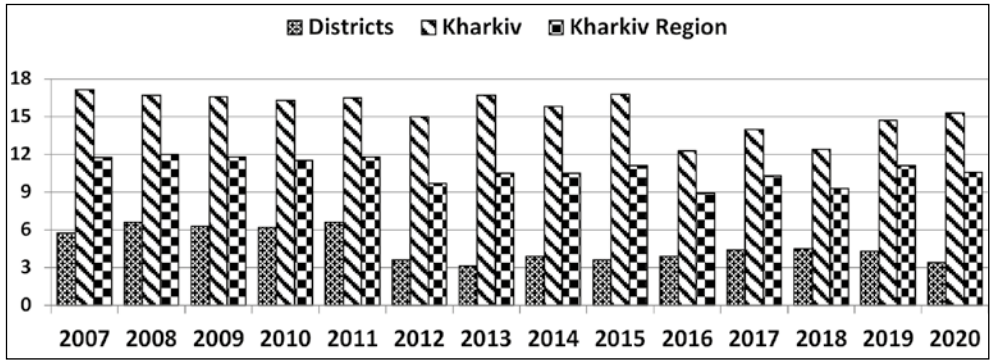

Fig. 4. Indicators of perinatal mortality by districts, in Kharkiv and Kharkiv region, ‰.
According to the Main Department of Statistics in Kharkiv region

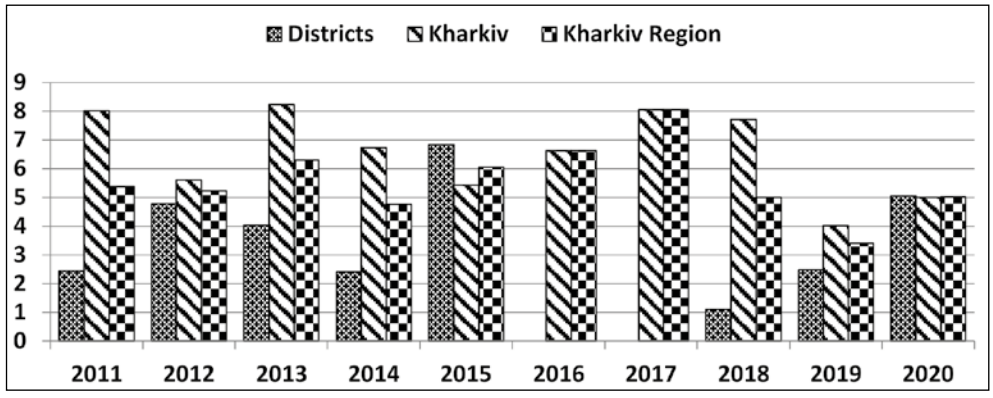

Fig. 5. Indicators of causes of death associated with infections, specific for the perinatal period, by districts, in Kharkiv and Kharkiv region, 0/000.
According to the Main Department of Statistics in Kharkiv region

In 2013–2019, the birth rate decreased from 11.1 to 8.1, i.e. by 22% in five years, while in 2001–2012 it increased from 7.7 to 11.4 (by 48%).

Perinatal mortality is one of the main markers characterizing the state of obstetric and gynecological care in the country. According to the State Statistics Service, for the period 2000–2010, this indicator in Ukraine had a negative trend and ranged from 10.11 in 2000 to 10.5 in 2010 per 1,000 live births and deaths. Given that different criteria were used to determine perinatal mortality in these years, the data of analysis and dynamics are not sufficiently correct. Until 2007, perinatal mortality in Ukraine included fetuses that died between the 28th full week

of fetal development and the 7th full day after birth. Since 2007, Ukraine has been using WHO recommendations that the perinatal period begins with the 22nd full week of fetal development. Recalculation of this indicator according to the new criteria shows that the level of perinatal mortality in Ukraine from 2000 to 2010 decreased 2.6 times (from 27.1 in 2000 to 10.5 in 2010 per 1,000 live and stillbirths). According to the European Health for All Database, in 2017 this figure in Ukraine was 9.1 per 1,000 live and stillbirths, while in the European region it did not exceed 7.2, and in the EU no more than 6.1 (per 1000 live and stillbirths) [34, 35].

Thus, the highest perinatal mortality rates in Ukraine per 1,000 live births were registered in 2010–2013 and comprised 10.5–9.4 per 1,000 live births and deaths. From 2014 to 2019, this indicator was slightly lower and remained stable (Fig. 2).

As for the birth rate and perinatal mortality in the districts, city of Kharkiv and Kharkiv region, according to the Kharkiv Regional State Administration, for 14 years (2007-2020) the highest birth rate was observed in the districts of Kharkiv region (Fig. 3).

The birth rate peaks in 2014 and is 10.72 per 1,000 inhabitants. Since 2014, the birth rate has been declining. The lowest rates were registered in 2020, and the birth rate in Kharkiv in 2020 was 6.1 ‰, while in the districts it was 6.5 ‰ and 6.3 ‰ in Kharkiv region. Fig. 1.3).

The highest perinatal mortality rates were also recorded in Kharkiv. In 2007, they amounted to 17.15 per 1,000 population with a minimum value of 12.3 ‰ in 2016 (Fig. 4).

Among the causes of neonatal mortality caused by certain perinatal conditions, the main ones are infections specific to the perinatal period, which were first detected in Kharkiv in 2011-2014 and 2018-2020. The data for 2016–2017 were not recorded, so the figures for Kharkiv and the region coincide comprising 6.62 and 8.05, respectively, per 10,000 live births (Fig. 5).

Over the last 10 years in Kharkiv, perinatal mortality associated with infections specific to the perinatal period in 2012 and 2018 ranked 2nd among the causes of perinatal mortality, ranking third in 2011, 2013, 2016 and 2017, and fourth in 2014, 2015, 2019, 2020.

Thus, a more complex demographic situation was registered in Kharkiv, where the lowest birth rates were observed against the background of high perinatal mortality rates due to causes related to perinatal infections.

CONCLUSIONS

The main task of obstetrics and gynecology at the present stage is to reduce reproductive losses, which necessitates further study of the etiology of IUI, especially in low- and middle-income countries. The screening for IUIs during pregnancy is cost-effective because treating the effects of IUIs requires disproportionately greater resources.

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The Authors declare no conflict of interest

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