ORIGINAL ARTICLE

EPIDEMIOLOGICAL ANALIYSIS OF PERTUSSIS MORBIDITY IN UKRAINE

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ABSTRACT

The aim: To improve epidemiological monitoring of pertussis by analyzing the disease morbidity during 1995-2017 in Ukraine, to make a prognosis.

Materials and methods: Analysis of the pertussis morbidity during 1995-2017 using the data of the Ministry of Health of Ukraine. The cyclicity was determined by Fourier spectral analysis. The models of prognosis were constructed using polyharmonic regression and an exponential smoothing algorithm. Cartographic analysis and integrated indicators (multiyear index of the prevalence rate, mean square deviation, mean the multiyear pace of the gain in the prevalence rate) were used to determine the areas of risk. Summarized data were used to calculate the generalized coefficient.

Results: The pertussis morbidity cycle has 5 years intervals in Ukraine. The prognosis is for increasing the pertussis morbidity from 4.91-5.54 to 5.48-7.06 per 100.000 people. The generalized coefficient was significantly higher in western part (83.3%) than in central (50.0%) and eastern (16.6%) parts. The study showed that population reproduction rates, natural population increase, and the proportion of people against vaccination were higher in the western part than in other parts of the country.

Conclusions: The pertussis cyclicity depends on the internal mechanisms of interaction in the ecological system. There is a prognosis of worsening the epidemic situation of pertussis spreading. The risk area is the western part of Ukraine, which is characterized by active demographic processes and a greater number of people who are negative about vaccination.

KEY WORDS: whooping cough, morbidity, forecasting, risk factors, Periodicity

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INTRODUCTION

Pertussis is a respiratory infection with the bacterial pathogen *Bordetella pertussis*. It is widespread in all age groups with a high mortality rate in young children [1]. This respiratory infection is characterized by 3-5 years of cyclicity, which is determined by social conditions, vaccination and phases of parasitic systems functioning [2, 3, 4]. Prolonged specific prevention of pertussis contributed to the reduction of pertussis morbidity and mortality [5]. At the same time pertussis is a topical issue in many countries now [6]. Outbreaks and fatal cases are reported among toddlers [7, 8], morbidity among adolescents and adults also increases [9, 10]. Therefore, it is important to identify the causes of worsening the epidemic situation of pertussis. Such causes include attenuation of specific immunity in school-age children and adults [11], using ineffective vaccines [12], mutation of the pertussis agent [6] and low level of public confidence in preventive vaccination [13]. Moreover, increasing of pertussis epidemic rates in the developed countries with high level of vaccination is linked to natural factors such as air temperature, environmental vapor pressure, economic development of territories, and the size of certain groups of population [14, 15, 16]. An increase in the pertussis morbidity may also be the result of quality diagnostics [17].

Ukraine lives in the constant modernization of social, economic and political spheres of society [18], which can have both positive or negative impact on the pertussis morbidity. In the administrative territories within the country, these processes can vary significantly.

Thus, the increase in the pertussis morbidity in the world, the ambiguity of determining the reasons for its increase, and the difficult socio-economic situation in Ukraine during the health care system reform stimulated us to research this topical issue.

In order to improve epidemiological monitoring of pertussis, we conducted the pertussis morbidity analysis in Ukraine during 1995-2017 and made a prognosis. We also identified epidemiological risks of being infected with pertussis taking into account social factors in the western, central and eastern parts of Ukraine and a comparative analysis of pertussis morbidity.

THE AIM

The aim was to improve epidemiological monitoring of pertussis by analyzing the disease morbidity during 1995-2017 in Ukraine, to make a prognosis.

MATERIALS AND METHODS

Ukraine has an area of 603.000 km^2, 24 administrative territories that differ in socio-ecological and economic status [19]. We analyzed the pertussis morbidity and demographic processes from 1995 to 2017 using to official statistics of the Ministry of Health and the State Statistics Service of Ukraine.

The long-term pertussis morbidity was characterized by cyclicity and the tendency allowing to make a prognosis using the constructed model.

Fourier spectral analysis was used to determine cyclicity.

The time series model was defined as

$$y(t) = tr(t) + P(t) + \varepsilon,$$

where *tr (t)* is a linear trend, *P (t)* is a periodic component, and ε is a random error.

A polyharmonic regression model was used for approximation:

$$P(t) = a_0 + \sum_{i=1}^{k}(a_i cos\ it + b_i sinit)$$

$$a_0 = \frac{1}{n}\sum_{j=1}^{n} y_{tj};\ a_i = \frac{2}{n}\sum_{j=1}^{n} y_{tj} cosit;\ b_i = \frac{2}{n}\sum_{j=1}^{n} y_{tj} sinit.$$

where a_0, a_i, b_i are the model coefficients.

The coefficient of determination of the model is calculated by the formula:

$$R^2 = 1 - \frac{\sum_{i=1}^{k}(y_i - \tilde{y}_i)^2}{\sum_{i=1}^{k}(y_i - \bar{y})^2},$$

where $\tilde{y}_i$ is predicted by the indicator model value, $\bar{y}$ is the arithmetic mean of the indicator [20].

The cartographic analysis of the pertussis morbidity was carried out in the administrative territories. According to the results of the analysis we defined the following parts of Ukraine: western (Volyn, Transcarpathian, Ivano-Frankivsk, Lviv, Rivne, Ternopil, Khmelnytsky and Chernivtsi regions), central (Vinnytsia, Zhytomyr, Kirovograd, Kyiv, Mykolaiv, Odessa, Cherkasy and Chernihiv regions) and eastern (Dnipropetrovsk, Donetsk, Zaporizhia, Lugansk, Poltava, Sumy, Kharkiv and Kherson regions).

To establish epidemiological risks (risk areas, risk groups, risk factors), a comparative analysis of pertussis morbidity, social factors and quality of life was conducted in the western, central and eastern parts of Ukraine. We also studied the morbidity of pertussis among children under 12 months, under 17, 18 and older.

A comprehensive assessment of long-term annual morbidity rates in the regions was performed using integral indices, an algorithm of calculation referred to as the "sum of places" method [21]. Integral indices included the sum of places by rank (from minimum to maximum), the multiyear index of the prevalence rate (M), mean square deviation, (σ), and mean the multiyear pace of the gain in the prevalence rate (T). The obtained integral indices allowed calculating the generalized coefficient (GC, in %) by the formula:

$$GC = \left(1 - \frac{S_x - S_p}{S_x - S_y}\right) \times 100\%,$$

where S*x* is the worst sum of places; S*p* is the sum of the places of a specific object; S*y* is the best sum of places.

The generalized coefficient (GC) represents an integrated assessment of the average annual morbidity rate, taking into account the main statistical characteristics describing them.

The quality of life of the population was studied according to the official data of Ptukha Institute of Demography and Social Research of the National Academy of Sciences of Ukraine and the State Statistics Service of Ukraine. The Integrated Human Development Index (HDI) includes 33 indicators, which are combined into 6 blocks (population reproduction, social environment, comfortable life, well fare, well-paid job, and education). The population reproduction unit includes the total reproduction rate, infant mortality, average life expectancy at birth, the probability of men and women surviving from 20 to 65 years [19].

Adsorbed pertussis-diphtheria-tetanus vaccine is used for active immunization. Since 2006 the acellular pertussis-diphtheria-tetanus vaccine has been used. Children under 24 months receive 4 doses of vaccine (3 doses of vaccination and 1 dose of revaccination). To calculate the population distribution by vaccination ratio (positive, neutral, negative), we used the results of a nationwide representative sociological survey of the Ukrainian population on healthy behavior [22].

The differences between the indicators were assessed using the Student's t test.

A systematic search for literature sources on the topic of the study was conducted using the online search service PubMed, EMBASE and the Cochrane Library.

Statistical analysis of the study results was performed using Microsoft Office Excel 2019 and StatSoft Statistics 10 software [23, 24].

RESULTS

Ukraine experienced periodic ups and downs of the pertussis morbidity in the period of 1995-2017. The highest rates were recorded in 2011 (6.42 per 100.000 people), in 2016 and 2017 (7.32 and 5.8 per 100.000 people, respectively). The lowest rates were in 2002 and 2003 (0.8 and 0.63 per 100.000 people, respectively) and 2013 (1.5 per 100.000 people). There was a significant difference between the pertussis morbidity in different administrative territories. The maximum average long-term indicators were above 6.0 per 100.000 people in Vinnytsia, Zaporizhzhya and Ivano-Frankivsk regions, and the minimum indicators were 0.3-0.7 per 100.000 people in Transcarpathian and

Table 1. Calculations according to coefficient cycles of the projection model of the pertussis morbidity rate

Cycles	Years	Model coefficient		
		a_0	a_1	b_1
1	1995-2000	0.296	-0.954	0.350
2	2000-2005	-0.277	2.583	0.118
3	2005-2010	-0.178	0.177	1.619
4	2010-2015	-0.696	0.117	2.183
5	2015-2020	1.425	0.401	1.148
6	2020-2025	1.425	0.401	1.148

Table 2. Pertussis morbidity rate forecasts in Ukraine over the period from 2018 to 2023 (per 100 000 population)

Year	ETS exponential smoothing algorithm	Lower confidence bound	Upper confidence bound	Polyharmonic regression model forecast
2018	4.91	1.79	8.04	5.50
2019	5.02	1.90	8.15	5.64
2020	5.14	2.01	8.26	7.12
2021	5.25	2.13	8.37	6.83
2022	5.36	2.24	8.49	6.95
2023	5.48	2.35	8.60	7.0

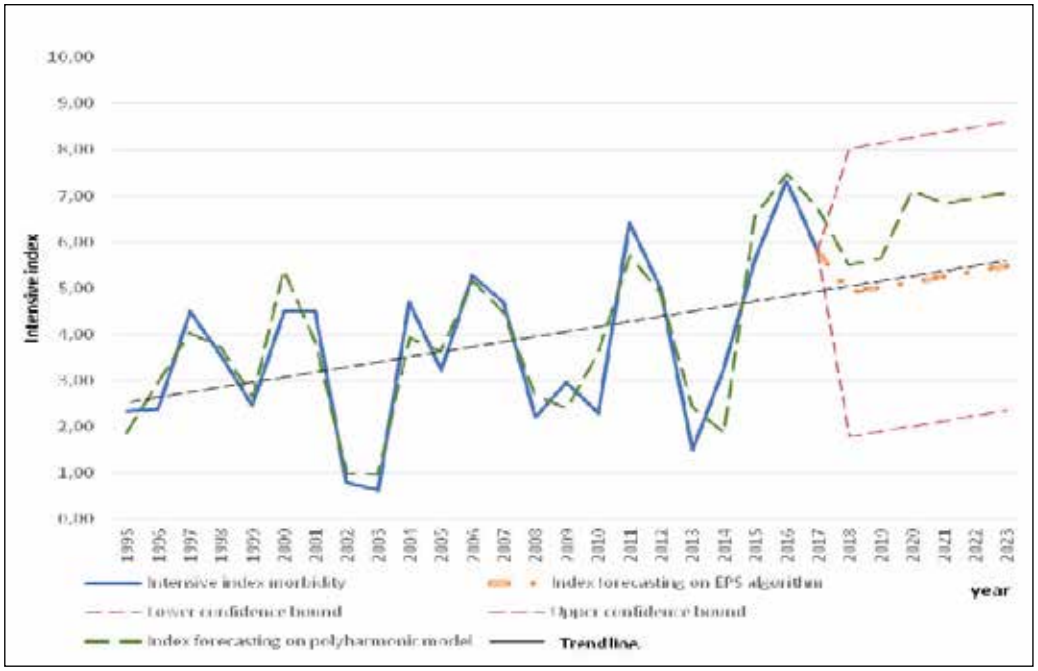

Fig. 1. Long-term pertussis morbidity time-course over the period from 1995 to 2017, calculated trend line and forecasts in Ukraine.

Lugansk regions. The average long-term annual morbidity of pertussis was 3.7 per 100.000 people.

There were regular fluctuations in the morbidity rate in the long-term dynamics of the pertussis morbidity. Fourier Spectral Analysis allowed establishing cycles with an interval of 5 years. The study period was divided into 5-year cycles. We calculated the coefficients of the model of the pertussis morbidity prognosis for each cycle. The coefficient of determination of the model was $R^2 = 0.854453$ (Tab. 1).

The prognosis for 2018-2023 is made in two ways: 1) by the results of the calculated coefficients of the polyharmonic regression model; 2) using the MS Excel 2019 tool *"forecast sheet"* (using the exponential smoothing algorithm ETS). A significance interval is calculated for each of the predicted values of the indicator. All calculations are summarized in table 2.

Having analyzed the obtained results of epidemiological studies, we constructed a diagram that showed a pronounced cyclicity of the pertussis morbidity, comorbidity of actual and theoretically calculated indicators, the tendency of increasing morbidity along the trend line and prognosis (Fig. 1).

Fig. 2. Pertussis morbidity (per 100 000 population) in regions of Ukraine in 2017

According to the constructed prognosis, the pertussis morbidity in Ukraine will increase from 4.91-5.54 to 5.48-7.06 per 100.000 people.

The cartographic analysis showed that the pertussis morbidity in the western region (10.1 per 100.000 people) was 3.6 times higher than in the eastern region (2.8 per 100.000 people), and by almost 2 times higher than in the central (5.4 per 100.000 people) region (Fig. 2).

Comparison of statistical indicators (M, σ, T) characterizing long-term pertussis morbidity in the regions, showed that ICC in the western part (83.33%) was significantly higher than in the central (50.0%) and eastern (16.6%) parts (Tab. 3).

The average long-term pertussis morbidity in children under 17 (21.2-28.3 per 100.000 children) was significantly higher than in adults (0.08-0.1 per 100.000 people). The pertusis morbidity in children under 12 months (120.9-184.4 per 100.000 children annually) was 5-6 times higher than in children under 17. The highest pertussis morbidity in children (28.3), including children under 12 months (184.4) was in the western part of Ukraine.

The indicators of quality of life and reproduction of the population were higher in the western part (3.751 and 0.704, respectively) compared to the same indicators in the central (3.558 and 0.673, respectively) and eastern (3.638 and 0.682, respectively) parts. In Ukraine there is a decrease in population [36]. But the average natural population increase and population density in the western part were (-2.7) % and (84.2 people / km^2), while in the central part these figures were (-7.5) % and (51.5 people / km^2), and in the eastern part these indicators were (-7.0) % and (78.3 people / km^2).

The study results showed that population of the western part had the following attitude to the prophylactic vaccinations: neutral (20.0 ± 1.2) %, negative (16.8 ± 1.1) %, and positive (63.2 ± 1.5) %. In the eastern part, the population attitude to the prophylactic vaccinations was spread in this way: neutral (10.7 ± 1.0) %, negative (7.6 ± 0.9) %, and positive (81.7 ± 1.3) %. The central part of Ukraine showed the following data: neutral (12.7 ± 1.0) %, negative (10.6 ± 1.0) %, and positive (76.7 ± 1.3) %.

DISCUSSION

In Ukraine, the average long-term pertussis morbidity was almost 2 times higher than the maximum and 2-4 times lower than the minimum. This indicates a more pronounced intensity of recessions than rises in the long-term dynamics of pertussis morbidity. A difference of more than 10 times between pertussis morbidity rates in administrative territories may be related to both the pertussis diagnostics and the impact of various environmental factors, which was confirmed by other authors [25].

The long-term dynamics of pertussis morbidity is characterized by short intervals of cyclicity and a tendency to increase. Moreover, 5-year cyclicity was observed during the whole period of the study, despite the variability of

Table 3. Standard and generalized pertussis morbidity rates in regions of Ukraine over the period from 1995 to 2017

Region	Average integral indexes		Standard dispersion		Average growth rate		Rank sum	Integral visual coefficient	
	M	rank M	σ	rank σ	T	rank T	rank S	Cv	rank Cv
West	3.848891	2	2.49222	3	1.09745161	3	8	83.33%	3
East	3.337714	1	1.869375	2	1.002874461	1	4	16.67%	1
Center	3.955672	3	1.651986	1	1.038851935	2	6	50.00%	2

M: mean of the index of the prevalence rate; T: mean of the growth rate; σ: standard deviation

socio-economic processes in Ukraine. Thus, in the 1990s, significant destabilization processes took place in the social, economic and political spheres of Ukraine. Since 2008 vaccination has not reached 95% of the target people, sometimes this indicator was critical (30-40%). At the same time, the cyclic morbidity of pertussis did not change. The pertussis cyclicity is likely to depend primarily on the internal mechanisms of interaction between the pathogen and the susceptible organism, as indicated by other authors [4, 26]. They also highlight the role of feedback mechanisms interacting in the ecological system. However, we cannot exclude the dependence of pertussis morbidity cyclicity on vaccination, social factors and the course of the infectious process [27, 28, 29].

A number of studies [14, 15, 16] proved that the pertussis morbidity depended on socio-environmental factors. A comparative analysis of natural population increase, population density, and population reproduction unit characterizing demographic processes, showed that these figures were higher in the western part than in the eastern and central parts of Ukraine. Therefore, higher ICC (generalized coefficient of long-term annual disease morbidity) and pertussis morbidity rates in children of the western part confirm the impact of these factors on the level of pertussis morbidity.

The fact that prophylactic pertussis vaccinations has a significant effect on its morbidity has been proven [5, 25]. Since 2008, the morbidity of pertussis vaccination has not reached a sufficient level (95.0%) in Ukraine to form the immune layer of 80-90 %, and now it averages 55.4%. There is a statistically higher percentage of the population that was against preventive vaccinations in the western part than in the eastern ($p < 0.05$) and central ($p < 0.05$) parts of the country.

Thus, the social factors and bad vaccination coverage led to significantly higher rates of pertussis morbidity in the western part of Ukraine compared to its central and eastern parts.

CONCLUSIONS

Prognosis of the pertussis morbidity dynamics on the basis of data recorded at fixed time intervals proved to be one of the most practical models. Cyclicity was established with a small interval of 5 years and a tendency to increase the pertussis morbidity in Ukraine. According to our prognosis, the pertussis morbidity may have increased to 7.06 per 100.000 people by 2023 if the vaccination coverage rate remains low.

Using ICC (generalized coefficient of long-term annual disease morbidity) revealed the risk of worsening the epidemic situation of pertussis. Thus, the western part of Ukraine can be attributed to the risk area compared to the central and eastern parts because of long-term pertussis morbidity, more pronounced conditions for spreading this infection (natural population increase and population density, a high percentage of non-vaccinated people, etc.). In the western part of Ukraine, children under 12 months remain at risk for pertussis disease due to its higher morbidity in this part of the country.

In the period of health reform and public health development, it is advisable to improve the system of epidemiological surveillance for pertussis by immediately increasing the coverage of the population with vaccination and introducing a system of social and hygienic monitoring that will identify the leading risk factors in a specific territory.

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The Authors declare no conflict of interest.

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