Asian Journal of Epidemiology

ISSN 1992-1462

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OPEN ACCESS Asian Journal of Epidemiology

ISSN 1992-1462
DOI: 10.3923/aje.2018.26.33

Research Article

Estimating the Complication Risk of Epidemic Situation with Diphtheria in Ukraine

Podavalenko Alla Pavlivna

Department of Hygiene, Kharkiv Medical Academy of Postgraduate Education, Epidemiology and Occupational Diseases, street Amosova, 58, 61176, Kharkiv, Ukraine

Abstract

Background and Objective: In the era of globalization, the intensity of the epidemic process of diphtheria can change significantly as a result of the impact of social, environmental, economic and other factors. Therefore, the identification of the causes and conditions for the intensification of the epidemic process of diphtheria is the main task of modern epidemiology. Therefore, the aim of the study was to assess the complication risk of the epidemic diphtheria, taking into account the influence of the environmental factors on the course of the epidemic process of this infection. **Materials and Methods.** The morbidity and prevalence of diphtheria in six oblasts and in general in Ukraine during 1985-2016 were studied. About 28 predictors (social and ecological factors, indices of human development etc.,) were used to construct a mathematical model using binary logistic regression. A correlation analysis between the morbidity of diphtheria and the factors of the life environment was conducted. **Results.** It was established that the indexes of diphtheria incidence were 10 times higher in the period during the marked processes of modernization of political, social and economic spheres in Ukraine, in comparison with the period of their stabilization. It was determined that the probability of intensification of the diphtheria epidemic process can be associated with a decrease in 4.2% of the public immunization, with an increase in 25.3% of emissions of harmful substances into the air, with an increase in 21.0% of natural population growth and a population density in 3.8%. In modern conditions, there is a risk of intensifying the epidemic process of diphtheria due to the low level of vaccination against diphtheria, but decreasing the population and reducing the emissions of harmful substances into the atmosphere is a restraining factor to the prevalence of diphtheria. **Conclusion.** There is a strong downward trend of diphtheria incidence in terms of population decline and emissions of harmful substances into the atmosphere, but the low level of vaccination against diphtheria demonstrateds an unstable epidemic situation with this infection and requires making adequate managerial decisions immediately.

Key words: Diphtheria, morbidity, epidemic situation, social and ecological factors

Citation: Podavalenko Alla Pavlivna, 2018. Estimating the complication risk of epidemic situation with diphtheria in Ukraine. Asian J. Epidemiol., 11: 26-33.

Corresponding Author: Podavalenko Alla Pavlivna, Department of Hygiene, Epidemiology and Occupational Diseases, Kharkiv Medical Academy of Postgraduate Education, Street Amosova, 58, 61176 Kharkiv, Ukraine

Competing Interest: The author has declared that no competing interest exists.

Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

Diphtheria is an infectious disease that is controlled by facilities of specific prophylaxis and is predefined by the action of exotoxin of *Corynebacterium diphtheriae* (*C. diphtheriae*). In a pre-vaccination period, diphtheria was one of the leading reasons of death in children[1]. In the world, levels of morbidity and diphtheria death rate have decreased considerably according to the World Health Organization[2,3]. But, the toxicants of *C. diphtheria* constantly circulate everywhere[4,5]. Therefore, cases of diphtheria are practically registered in all continents[6-9] and there is an epidemic rise in some countries[5,10-16]. There was an epidemic of diphtheria in the 1990s in Ukraine and other countries of the Soviet Union. Over 20 people had diphtheria and more than 700 patients died during a period of epidemic in Ukraine[17-19]. It is considered that the epidemic morbidity rise of diphtheria is connected to the low level of immunization coverage against this infection[20-22]. It is also impossible to exclude the influence of social, ecological and other factors on the movement of diphtheria epidemic process and characteristic of *C. diphtheriae* in the epoch of globalization[6,17,19,23-27]. Detection of the causes and conditions of the intensification of the diphtheria epidemic process and making administrative decisions in time to warn the epidemics is the main task of modern epidemiology.

According to the above-mentioned, taking into account the influence of environmental factors on the epidemic process of this infection, the assessment of the complication risk of the epidemic situation became the goal of the study.

MATERIALS AND METHODS

Materials: The morbidity and prevalence of diphtheria, including in age-related groups, as well as social and ecological factors during 1985-2016 were studied according to data of the Ministry of Health and Statistics services of Ukraine. Taking into account the permanent changeability of social, economic and environmental factors in Ukraine, through formal logic receptions two periods with different level of influence of these factors were detected. The first period (1985-1998) was characterized by the expressed processes of modernization of social (depopulation processes, increases of urbanization, activation of migratory processes), economic (financial crisis, unemployment, poverty increase) and political (change of political system) spheres in Ukraine and the second period (1999-2012) was characterized by stabilizing of these processes[28]. Taking into account the social and ecological factors the forecast of risk complication in diphtheria epidemic situations was made. For the construction of a mathematical model of prognostication, we calculated the median of morbidity in the six areas of Ukraine that differed from state social and ecological factors. The studied areas were divided into 2 groups. Areas that had indexes of morbidity higher than median was a part of the 1st group and areas that had indexes of morbidity below the median were a part of the second group. These data included a binary logistic regression.

For measuring logistic equations 28 indexes were used (Table 1).

Methods: Applying the method of binary logistic regression, the parameters of the regression equation were determined, the prognosis of the probability of influence of a specific factor on the morbidity level of diphtheria was determined. The state of the object (incidence rate) was described by a discrete qualitative sign, in our case, a rank. The role of predictors (harbingers, preconditions and indices of human development) was quantitative.

The probability that an event will occur will count on such a formula:

$$p = \frac{1}{1+e^{-z}}$$

Where:

$$z = B_1{*}X_1+B_2{*}X_2+\ldots+B_n{*}X_n+a$$

X_1 = Meaning of independent variables
B_1 = Coefficients, their calculation is the task of binary logistic regression
a = Constant

The core message of this study is that the incidence of diphtheria was considered as an object (nosological form) and as a qualitative sign with two gradations ((1) Moderate and (2) Severe morbidity). A sign "Pronounced morbidity" was predicted with help of the method of constructing logistic multifactor models of regression.

The relative contribution of forecasters and harbingers of risk (social and environmental) was expressed by the value of Wald's statistics χ^2 (Wald chi-square), as well as the standardized regression coefficient (Standardized Estimate). As a criterion for the coordination of the real distribution of observations for individual gradations (1 and 2 groups) and the forecast based on the equalization of logistic regression, the percentage of indicators correctly classified. The overall

Table 1: Indexes that characterize the epidemic process of diphtheria and can influence on the level of morbidity

Groups 1	Indexes 2	Units of measurement 3
Harbingers of risk	Incidence among children	Per 100 thousand of the age group
	Adult morbidity	Per 100 thousand of the age group
	Morbidity of the villagers	Per 100 thousand inhabitants of the village
	Morbidity of the inhabitants of the city	Per 100 thousand inhabitants of the city
Prerequisites risk		
Social factors	Immunization coverage	(%)
	Degree of urbanization	(%)
	Population density	Persons per 1 sq km
	Mortality	Per 1000 population
	Natural increase	Per 1000 population
	Overall increase	Per 1000 population
	Migration balance	Per 1000 population
Ecological factors	Emissions into the atmosphere from stationary sources	Thousand tons per year
	Emissions into the air from mobile sources	Thousand tons per year
	Emissions into the air from stationary and mobile sources	Thousand tons per year
	Amount of air in the dust	Thousand tons per year
	Amount of sulfur dioxide in the air	Thousand tons per year
	Amount of nitrogen dioxide in the air	Thousand tons per year
	The amount of carbon monoxide in the atmosphere	Thousand tons per year
Human development index	Integral index of human development	Coefficients
	Demographic development	Coefficients
	Material well-being of the population	Coefficients
	Living conditions of the population	Coefficients
	Development of regional labor markets	Coefficients
	Education level of the population	Coefficients
	State and health care	Coefficients
	Social environment	Coefficients
	Ecological situation	Coefficients
	Finding of human development	Coefficients

Contribution of each of the factors in the development and spread of diphtheria were studied

assessment of coordination between the model and the real data was estimated using the Hoster and Lemeshow (Hoster and Lemeshow Goodness-of-Fit Test) test. The part of the aggregate model described by the constructed model was considered sufficient if R^2 Nagelkerka exceeded 0.5. For estimating the regression equation, the method of step-by-step incorporation of predictors (indicators) that ranked signs in accordance with their contribution to the model was used. The level of significance for including of risk factors in the regression equation was set in such a way in order to achieve a significance level χ^2 (Pr>chi-square) for each predictor at the end of the step procedure no more than 5.0%. In order to assess the quality of the model, indicators of its sensitivity, specificity and accuracy were calculated. Sensitivity was defined as the percentage of indicators that really belonged to the group with pronounced intensity of the epidemic process that is true and correct. Specificity as a percentage of indicators that really belonged to the group with moderate intensity of the epidemic process that is true (truthfully) negative. Accuracy points to the percentage of correct performance of the indicators in the model for all factors and it is the aggregate indicator of the informativeness of the selected indicators. In order to assess the degree of the relationship between precursors, risk prerequisites and human development indices, the odds ratio (OR) and its 95.0% probability interval (PI).

There has been a change in the processes of modernization in social and economic spheres during the last 15 years in Ukraine. Currently, there are demographic changes, the activation of external migration processes, the financial crisis in society. In view of this, an assessment of the epidemiological situation was made with diphtheria for 2002-2016, taking into account the identified main risk of forecasting.

By analyzing the incidence and prevalence of diphtheria, the following random parameters were studied: M is the arithmetic mean, Me is median (at interquartile latitude 25-75%) and the magnitude of the oscillations (the difference between the minimum and maximum morbidity rates).

The long-term dynamics of diphtheria morbidity was estimated using a straight line trend. The growth rate (GR) was calculated using the method of least squares, while the decrease (-) or growth (+) was estimated according to the following criteria: From 0 to ±1.0% considered the trend to be moderate, from ±1.1% to 5.0% is stable and more (±5.0%) expressed.

The correlation of diphtheria morbidity was made with the amount of harmful substances released into the atmosphere from fixed and mobile sources (thousand tons per year), the number of most common substances in the atmosphere (thousand tones per year), such as carbon monoxide, dust, sulfur dioxide and nitrogen dioxide, indicators of population density (people per 1 sq. km) and immunization (%) and total population (abs. n.). Correlation analysis was performed using the Spearman rank coefficient (r_s). The value (r_s) to 0.29 indicated a weak link, 0.30-0.69 about the average connection, 0.70-1.0 about a strong connection.

Statistical processing of the results was carried out using the following computer programs: Excel and SPSS-17.

RESULTS

During 1985-1998 (the first period), 19 500 people died of diphtheria, the median incidence was 2.9 per 100 thousand population and the rate of fluctuations was 10.1 per 100 thousand population. During 1999-2012 (second period), 1 848 people died of diphtheria, the median incidence was 0.3 per 100 thousand population and the rate of fluctuation was 0.8 per 100 thousand population.

A correlation analysis between the diphtheria incidence and the environmental factors revealed 42.6% of the correlation pairs, including 30.4% of the pairs of strong forces. In most cases, direct correlations ($r_s = 0.5$, $p<0.05$, $r_s = 0.7$, $p<0.05$, $r_s = 0.8$, $p<0.05$) were established between the indicators of the diphtheria incidence and the population density.

Using a binary logistic regression, a mathematical model for detecting risk factors with a view to taking early steps to deal with complications of the epidemic situation with diphtheria was constructed. Thus, based on the coefficient of regression function (B), including the constant: for environmental factors (1.645), social factors (2.370), human development indexes (-0.308) and risk predictors (-0.259) the correlation of these factors with the intensity of the diphtheria epidemic process was predicted (Table 2).

The constructed model made it possible to classify correctly 73.5% of environmental factors, 66.7% of social factors, 87.5% of human development index and 87.5% harbingers of risk introduced into the model. So, an increase in the content of sulfur dioxide in the atmosphere increases the chances of intensifying the epidemic process of diphtheria by 25.3%, meanwhile specificity of the model was 69.7%, sensitivity -77.3%, accuracy -73.5%.

The decrease in the level of vaccination against diphtheria increases the chances of intensifying the epidemic process of this infection by 4.2%, while the natural population growth by 21.0%, meanwhile the specificity of the model was 61.5%, sensitivity -81.8%, accuracy -76.7%.

The rise in the diphtheria incidence in the city increases the chances of an intensification of the epidemic process by almost 17.0% and can be a predictor of the complicated epidemic situation with this infection in a certain territory, meanwhile the specificity of the model was 83.3%, sensitivity -68.6%, accuracy -65.9%.

Improving living conditions, including increasing population density, increases the chances of intensifying the dip epidemic process of diphtheria by 3.8%, meanwhile the specificity of the model was 88.9%, sensitivity -86.1%, accuracy -87.5%.

For the period 2002-2016, the median of the incidence and prevalence of diphtheria was respectively 0.05 and 0.4 per 100 thousand population and the rate of fluctuations-respectively, 0.59 and 1.56 per 100 thousand population.

At present, the long-term dynamics of morbidity and prevalence of diphtheria infection in Ukraine is characterized by stabilization of these indicators. For the last 15 years, patients with diphtheria were 942 people.

Table 2: Results of the prognosis risk factors of the complicated epidemic situation with diphtheria depending on the environmental factors

Name of factors	Regression coefficient (B)	Standard error	χ^2 walda	Achieved level significance	Relation chances	95% PI for odds ratio
Environmental factors						
Sulfur dioxide	0.226	0.055	16.7	<0.001	1.253	1.125-1.396
Social factors						
Vaccination	-0.043	0.017	6.6	0.001	0.958	0.926-0.990
Natural increase	-0.231	0.061	14.4	<0.001	0.794	0.704-0.894
Generalized environmental factors (indices of human development)						
Living conditions, including population density	0.037	0.009	18.0	<0.001	1.038	1.020-1.056
Expeditors of risk						
Morbidity rate of city residents	0.153	0.063	5.9	0.001	1.166	1.031-1.318

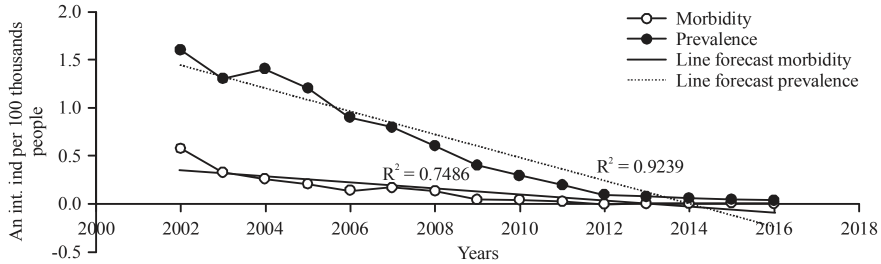

Fig. 1: Dynamics of morbidity and prevalence of diphtheria during 2002-2016 in Ukraine

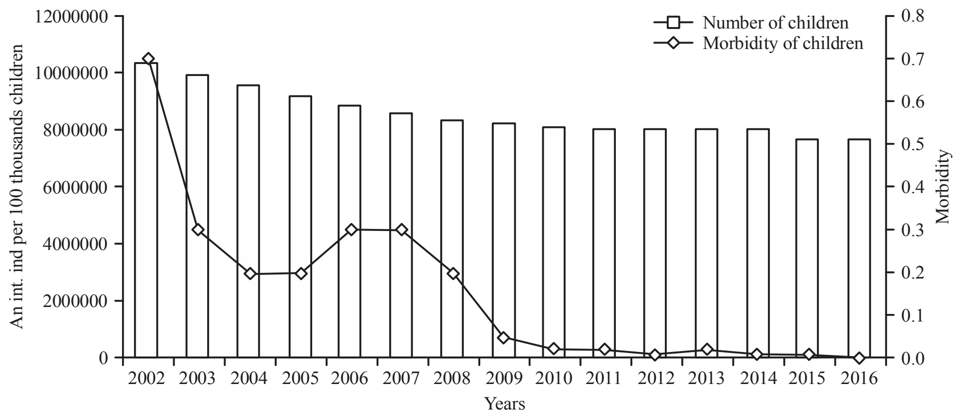

Fig. 2: Dynamics of the morbidity of diphtheria in children and the number of children in Ukraine during 2002-2016

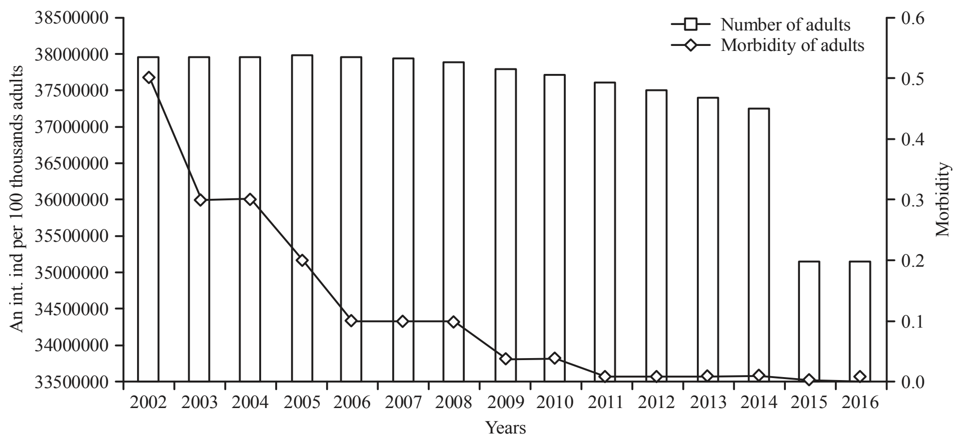

Fig. 3: Dynamics of adult diphtheria morbidity and the number of adult population in Ukraine during 2002-2016

There is a pronounced tendency to decrease the incidence (GR = (-9.8%) and the prevalence (GR = (-16.2%) diphtheria (Fig. 1).

During the last 15 years, the incidence of diphtheria among children was slightly higher than among adults (0.16 and 0.11 per 100 thousand, respectively of certain age group). There has been a decrease number of adult (from 37,933,900-35,145,000 people and child population) and the child population (from 10, 30, 700-7, 614, 700 people).

A strong correlation between the incidence of diphtheria among children and number of children population ($r_s = 0.7$, $p<0.001$) has been established. Figure 2 showed decline in the incidence of diphtheria among children on the background of reducing the child population.

There is a strong correlation between the incidence of diphtheria in adults and the number of adults ($r_s = 0.8$, $p<0.001$). Figure 3 showed a reduction in the incidence of diphtheria among adults in the context of declining in adult population was.

DISCUSSION

The study showed that the diphtheria morbidity and the extent of fluctuations during the period of marked modernization of political, social, economic and other spheres in Ukraine (1985-1998) were, respectively 10 and 12 times higher than during the period of stabilization of these processes (1999-2012). The correlation analysis and the constructed mathematical model have confirmed the dependence of the morbidity level on the environmental factors. Thus, direct correlation between the incidence of diphtheria and population density has been established. According to the forecast, the risk of complicated epidemic situation with diphtheria will increase by 4.2%, with a decrease in the vaccination coverage, by 25.3% with an increase in emissions of harmful substances into the air, by 21.0%, with an increase in population growth and by 3.8% with increasing population density. In the case of an increase in incidence among city residents, the risk of intensification of the diphtheria epidemic process is expected to increase by 17.0%. The research confirmed the hypothesis of the influence of the aspects of globalization (economic, ecological, political, demographic) on the intensity of the epidemic process of infectious diseases, as well as diphtheria[6,17,29,30].

The results of the forecast were used to assess the epidemic situation with diphtheria in modern conditions. A powerful deterrent to the intensification of the diphtheria epidemic process is a high level of vaccination coverage that should be at least 95%. The rate of child vaccination against diphtheria amounted to 55.6% on average, meanwhile adults practically did not receive any dose during the last ten years in Ukraine.

At the same time, the study of many industrial enterprises has been suspended in the country and the number of gas driven vehicles has decreased that led to reducing in 10-30% of harmful atmospheric emissions. The high mortality rate and low birth rate among children, as well as the activation of external migration processes, contributed to a decrease of 5 million 650 thousand population.

So, it can assumed that the state of environmental and social factors has positively influenced the intensity of the diphtheria epidemic process. This is confirmed by low morbidity rate and a pronounced tendency to reduce the incidence of diphtheria (Fig. 2, 3), as well as by strong direct correlation between the incidence rates among children and adults and the number of these age groups. The influence of demographic processes on the incidence of anthropogenic infections[31,32] and in the study of Savylov and Ylyna[27] and Chumachenko[33] it is noted the negative impact of environmental factors on specific immunity that contributes to the formation of susceptible population segments to infectious diseases.

Consequently, the scientific concepts based on the analysis of risk factors, the evolution of the epidemic process have practical confirmation in the study of diphtheria. Thus, the decrease in the percentage of immunization, the crisis in social, economic and political spheres has led to a deterioration of the epidemic situation with diphtheria. This was established by comparing the indicators of diphtheria morbidity in different periods of modernization of social, economic and political spheres in Ukraine and confirmed by established direct correlation relations between the indicators of the incidence and environmental factors. Assessing the results of prediction using mathematical modeling, it can be argued that the diphtheria incidence depends on the complex action of social and environmental factors. A long period of decreasing in the level of immunization can not contribute to the complication of the epidemic situation with this infection without the complex influence of the environmental factors. Under condition of the growth in population size, population density and deterioration of environmental factors in low levels of immunition, an epidemic increase in the diphtheria incidence can be expected. However, in conditions of low level of immunization of the population against diphtheria, the epidemic situation with this infection should be assessed as unsustainable and immediately taking decisions of increasing the level of anti-diphtheria immunity among the Ukrainian population.

CONCLUSION

The complication of the diphtheria epidemic situation occurred during the social, economic and political crisis in Ukraine. It was observed that indicators of diphtheria incidence were almost 10 times higher and 12 times higher the magnitude of their fluctuations. Installed the probability of intensification of the epidemic process, depending on population density, population growth, the level of vaccination and the increase of harmful substances in atmospheric air, as well as the increase in of diphtheria incidence among the urban population was determined. Reducing the population and reducing emissions of harmful substances into the atmosphere has a positive effect on the intensity of the epidemic process of diphtheria, but the low level of vaccination against diphtheria demonstrates the unstable epidemic situation of this infection and requires the prompt adoption of adequate managerial decisions.

SIGNIFICANCE STATEMENTS

This study discovers the risk of intensification in the diphtheria epidemic process, taking into account migration and demographic processes, air pollution, as well as vaccination rate to diphtheria among population that can be beneficial for predict diphtheria in a certain area.

This study will help the researcher to uncover the critical areas of impact of specific social and environmental factors on the epidemic process of diphtheria that many researchers were not able to explore.

Thus, a new theory of the epidemic situation assessment of diphtheria at the regional level may appear, which will help to optimize the system of epidemiological surveillance of this infection.

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