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ЕПІДЕМІОЛОҐІЧНО ЗНАЧИМІ ЧИННИКИ РИЗИКУ ІНФІКУВАННЯ ЛЮДЕЙ ВІРУСОМ ГАРЯЧКИ ЗАХІДНОГО НІЛУ

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Реферат

Гарячка Західного Нілу є актуальним вірусним трансмісивним природно осередковим захворюванням у світі. Захист населення від зараження цим вірусом планують з урахуванням епізооото-епідеміологічної ситуації, оцінювання та аналіз якої базується на стандартах епідеміологічного нагляду щодо трансмісивних інфекцій. Інформаційна база даних включає характеристики циркулюючих штамів, спектр резервуарів, джерел і переносників вірусу, гідрологічний і кліматo-географічний опис, дані моніторингу захворюваності й поширеності захворювання, а також ризики інфікування людей. Визначення останніх вимагає проведення цілеспрямованих описово-оцінювальних й аналітичних епідеміологічних досліджень.

Мета. *Провести статистичне опрацювання й аналіз епідеміологічно важливої інформації за результатами анкетування респондентів із визначенням епідеміологічно значимих чинників інфікування людей вірусом гарячки Західного Нілу, встановити характер взаємозв'язку виявлених чинників ризику в разі їх поєднаного впливу.*

Матеріали і методи. *Проведено систематизацію епідеміологічної інформації 120 респондентів шляхом створення комп'ютерної бази даних. Статистичне опрацювання даних проведено з використанням непараметричних математичних методів: багатофакторного лінійного регресійного аналізу, логістичної регресії, дискримінантного аналізу, методу нейронних мереж (програмний пакет нейромереж Statistica 8.0).*

Результати й обговорення. *Групування і систематизацію даних здійснено на підставі гіпотез щодо впливу чинників на ймовірність зараження вірусом. Епідеміологічну інформацію поділено на смислові блоки для диференціації ризиків за типом: поведінкові, професійні, рекреаційні, тощо. Визначено, що розрахунковий параметр t мав становити 1,979280117 і більше (ступень свободи k (124) при 95 % (P<0,05)). Оцінювання достовірності розбіжності альтернативних ознаки встановило 11 ознак із достовірною різницею (P<0,05). Вивчення поєднаного впливу чинників на інфікування людей вірусом гарячки Західного Нілу з використанням лінійної та логістичної моделі засвідчило відсутність цього ефекту. Застосування нейронних мереж виявило неприйнятний рівень апроксимації вихідних спостережуваних даних (коефіцієнт детермінації R2<0,3).*

Висновки. *Отже, виявлено 11 епідеміологічно значимих чинників ризику інфікування людей вірусом гарячки Західного Нілу. Багатофакторний аналіз заперечив їх поєднаний вплив на інфікування людей: кожна з ознак самостійна і при наявності лише однієї з них є високий ризик зараження людей. Отримані результати засвідчили, що район дослідження є активним природним осередком гарячки Західного Нілу.*

Ключові слова: *гарячка Західного Нілу, чинники ризику, статистичний аналіз*

Abstract

EPIDEMIOLOGICALLY SIGNIFICANT RISK FACTORS OF HUMAN INFECTION WITH WEST NILE VIRUS

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West Nile fever is an important viral transmissible natural focal disease in the world. Protecting the population from infection with this virus is organized considering the epizootic and epidemiological situation, assessment and analysis of which is based on the standards on epidemiological surveillance of transmissible infections. Information database includes characteristics of circulating strains; range of reservoirs; sources and vectors of the virus; hydrological, climatic and geographical description; data of monitoring of incidence and prevalence of the disease; and the risks of human infection. The estimation of the latter requires conducting of targeted descriptive-evaluative and analytical epidemiological research.

Aim. *To perform statistical processing and analysis of epidemiologically important information on the results of survey of respondents with determination of epidemiologically important risk factors of human infection with West Nile virus; to establish the nature of the relationship of identified risk factors in case of their combined impact.*

Materials and Methods. *Systematization of epidemiological information of 120 respondents was performed by creating a computer database. Statistical analysis of the data was conducted using nonparametric mathematical methods: multivariate linear regression analysis, logistic regression, discriminant analysis, neural networks method (neural networks software package Statistica 8.0)*

Results and Discussion. *Grouping and systematization of data are based on a hypothesis about the factors' impact on the likelihood of infection with the virus. Epidemiological information is divided into semantic units to differentiate the type of risk: behavioral, occupational, recreational, etc. It is determined that the estimated parameter t has to equal 1.979280117 and more (degrees of freedom k (124) 95% (P<0.05)). Evaluation of reliability of the discrepancies of alternative features detected 11 signs with significant difference (P<0.05). The study of combined factors' influence on human infection with West Nile virus using linear and logistic models showed no such effect. The use of neural networks showed*

unacceptable levels of initial approximation of the observed data (coefficient of determination R2 <0.3).

Conclusions. *Eleven epidemiologically significant risk factors for human infection with West Nile virus were found. Multivariate analysis denied their combined effect on the infection of people: each of the features is independent, and the presence of only one of them has a high risk of human infection. The results showed that the area of research is the active natural focus of West Nile fever.*

Keywords: *West Nile virus, risk factors, statistical analysis*

Introduction

West Nile fever (WNF) is an actual natural focal transmissible endemic disease caused by a virus of the Flaviviridae family. This is an extremely dangerous infection (EDI) with high epidemic potential, by the recommendation of WHO referred to infections that are subjected to international surveillance [1].

Organization of epidemiological surveillance of WNF at the modern level provides for conducting of epizootic and epidemiological observations blocks with advanced virological monitoring of pathogen among reservoirs and vectors, tracking incidence and prevalence indicators of WNF among vulnerable population, identification of risks and prediction of the situation. Adequate control system using modern information technology can optimize preventive and counter measures to protect all people in peacetime and wartime [2, 3, 4, 5].

A number of objective circumstances influence at the formation and functioning of WNF foci. Despite the fact that in Ukraine there are all conditions for the existence of natural WNF foci, still there are not identified certain spatial and temporal characteristics of foci, the circumstances that contribute to human infection with this pathogen. In our country there are the conditions for the functioning of all types of WNF foci: natural, anthropurgical (in the urban landscape, mostly in closed habitats), mixed - in places changed due to human impact on natural biocenoses. Research in the Northeast region of Ukraine confirmed the existence of stable anthropurgical foci that are active year around [6].

Sporadic incidence of people with WNF is more evidence of imperfection verification of the disease, and the lack of data about the herd immunity cannot estimate the intensity of disappeared WNF epidemic process [7]. It is not held revealing of seropositive people among total population, although it can detect people who have suffered illness in the past with manifest or asymptomatic forms, and those who without clinical manifestations had only immune response to this antigen, that confirms the circulation of this pathogen in particular area [8].

It is important to determine risk factors for human infection, which can be done both during hospital surveillance, and in the case of population studies to assess the immunological structure of the population to WNF. Adequately organized collection of epidemiological information access to evaluate qualitative and quantitative features of epidemic process of the disease, including data of time, territory and risk factors. Questioning of persons involved in the study makes it possible to obtain various information about the living conditions of people, occupational status, conditions of work and rest habits, behavioral characteristics, migration history, etc. [9, 10].

Still are not studied the circumstances that contribute to the probability of human infection with WNV in different types of foci in our country. It should be noted that obtaining information about risk factors and their use in the planning and implementation of measures of anti-epidemic protecting the population substantially increases the efficiency of the latters and is extremely highly profitable given the opportunity to address the use of material and human resources.

Aim. To perform statistical processing and analysis of epidemiologically important information on the results of survey respondents with determination of epidemiologically important risk factors of human infection with West Nile virus, to establish the nature of the relationship of identified risk factors at their combined impact.

Materials and Methods

It is conducted a systematization of epidemiological data of 120 respondents by creating a computer database of surveyed people. At the results of blood serum titration of 120 people, they are divided into two groups with regard to WNV infection: seronegative (100) and seropositive (20).

Calculation of absolute (R), relative (RR) and additional (RD) risk conducted on the table 2x2. The study of combined influence of risk factors was conducted by using mathematical methods: multivariate linear regression analysis, logistic

Table 1

Indicators of absolute, relative and additional risk of human infection with WNV

№	The study alternative ign	Code of sign	Indicators of risk:		
			R_e and R_{ne}	RD	RR
1	Does the patient remember rodents or their tracks?	6.8	R_e=0,1667 R_{ne}=0	0,1667	0,1667
2	Did the patient notice mosquitoes in the house?	6.9	R_e=0,1980 R_{ne}=0	0,1980	0,1980
3	Does the patient remember bites by mosquitoes? (in the residence)	6.10	R_e=0,1667 R_{ne}=0	0,1667	0,1667
4	Did the patient work with feed at the farm (agricultural work)?	8.8	R_e=0,2093 R_{ne}=0,0769	0,1324	2,7217
5	Did the patient walk the cattle or sheep in / near the forest?	8.9	R_e=0,2045 R_{ne}=0,0704	0,1341	2,9048
6	Did the patient work in the apiary?	8.10	R_e=0,3077 R_{ne}=0,0556	0,2521	5,5341
7	Did the patient plant and gather potatoes near the forest?	8.11	R_e=0,1711 R_{ne}=0,0476	0,1235	3,5945
8	Did the patient participate in gathering harvest crops near the forest?	8.12	R_e=0,3333 R_{ne}=0,0625	0,2708	5,3328
9	Did patient bred campfire or collect firewood while working?	8.13	R_e=0,2727 R_{ne}=0,0722	0,2005	3,7770
10	Does the patient remember the presence of mosquitoes? (during agricultural works)	8.16	R_e=0,1667 R_{ne}=0,0526	0,1141	3,1692
11	Does the patient remember bites of mosquitoes? (during agricultural works)	8.17	R_e=0,1667 R_{ne}=0,0526	0,1141	3,1692

regression, discriminant analysis, neural network method. Adequacy and reliability of the processed linear models was performed using Fisher criterion (by comparison with tabulated values for the appropriate number of degrees of freedom) and χ^2, logistic regression - criterion Wald, criterion Nehelkerkena and χ^2 [11]. It was used neural network software package Statistica 8.0, developed by Stat Soft Inc. [12].

Results and Discussion

Determining of risk factors was conducted by the results of cohort researches on studying the prevalence of WNF among the population in rural areas "WB", which included, at the stage of their immediate implementation, obtaining informed consent form to participate in the research, taking of blood from the cubital vein, filling by respondents epidemiological cards of close-open type.

By results of the titration of blood sera in ELISA there were detected antibodies IgG to the WNV in 20 ((5.4±1.2)%) of 120 surveyed participants that allowed to form two comparison groups: seronegative (100) and seropositive (20) persons.

After the laboratory stage of research it was conducted study of questionnaire data of participants. The information contained in epidemiological cards was divided into logical blocks. The first group features included age, sex distribution, occupation, place of work (study) of respondents. The second group concerned the residence, there were taken into account the apartment features, the distance to the forest, the availability of farm and domestic animals (birds), the characteristics of farming. The third group of questions was about participation in agricultural work, the fourth about visiting of cottages (garden, forests); next - holiday and rest. All of groups of except the first, included questions about the presence of mosquitoes, other arthropods and rodents, also bites by mosquitoes or other insects.

To understand the causative-resulting relations of alternative signs it was calculated of R, RR and RD. Totally analyzed 55 pairs of signs, for 23 of them was shown a direct impact of factors at the probability of human infection with the WNV. The most important were 11 circumstances that are presented in table 1.

The next step was held for revealing of discrepancies of alternative indicators studied by comparing the signs in seropositive and seronegative groups of cohort research participants.

Based on the calculated degree of freedom k (124) for our sample at the level of reliability of 95% ($P<0.05$), it was determined that the option Student t-test must match the value 1.979280117 and more. The performed statistical analysis of epidemiological database with definition of Student t-test showed that among a number of signs between two comparable

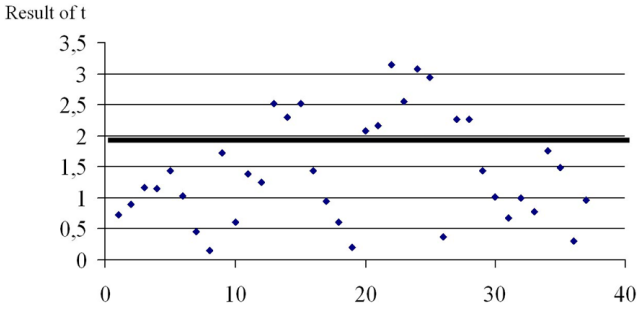

Fig. 1

Distribution of signs by results of Student t-test

groups of people, only 11 of them have a significant difference to the degree of reliability of P<0.05, as shown in Fig. 1

As seen from the graphically presented data from the total reliability calculation of questioned discrepancies of alternative signs, most of them cannot be recognized as epidemiologically significant for analyzed situation.

The table 2 shows details of statistically significant signs that we have seen as risk factors for human infection with the WNV.

The obtained results allowed confirm persons, who have a high risk of infection with WNF: working in the apiary, participating in gathering harvest crops near the forest, collecting firewood and / or breeding campfire, remembering bites and / or the presence of mosquitoes during agricultural work, planting and harvesting potatoes near the forest, remembering bites and / or the presence of mosquitoes in the place of residence, noticing rodents or their tracks, and walking cattle or sheep in the forest and working with feed on farm or agricultural works.

In our opinion, the results may be due to environmental constraints with vectors, including the best breeding sites and mosquito habitats, and additional sources of pathogen of infection (domestic animals - large and small cattle, rodents). In addition, a detailed analysis of all risk factors indicating the existence of active natural focus, where in the future, it is possible to form foci of mixed type.

The study of combined impact of analyzed risk factors for human infection WNV was conducted to ascertain the fact of potentiating the risk of infection in the presence of several signs at the same time, and if the positive answer - the definition of dominating of them.

The obtained results showed that the working mathematical linear and logistic models do not match the degree of reliability, and their test on an existing database indicates low sensitivity and accuracy.

Therefore, to identify complex relationships between input and output parameters, we used process modeling using artificial neural networks. According to obtained information, the application of neural networks gave acceptable (rather low) level of approximation of the initial observed data (coefficients of determination R2<0.3).

Conclusions

Thus, because of statistical processing of questionnaire database of cohort research participants in the area "WB" by using various mathematical methods, it was found 11 epidemiologically significant factors that increase the risk of human infection with the WNV. However, multivariate analysis denied combined impact of the analyzed risk factors for human infection. This indicates that each of the signs is independent and presence only one of them has a high risk of

Table 2

Results for questioned discrepancies of alternative features and their ranking in seropositive and seronegative groups among cohort research participants

The study alternative sign	Code of sign	Student t-test	Ranking signs by:	
			Parameter t-test	Code of sign
Does the patient remember rodents or their tracks?	6.8	2,521814934	3,146596359	8.10
Did the patient notice mosquitoes in the house?	6.9	2,291516864	3,074855124	8.12
Does the patient remember bites by mosquitoes? (in the residence)	6.10	2,521814934	2,936680162	8.13
Does the patient work with feed at the farm (agricultural work)?	8.8	2,077830704	2,268175869	8.17
Did the patient walk the cattle or sheep in / near the forest?	8.9	2,170947994	2,268175869	8.16
Did the patient work in the apiary?	8.10	3,146596359	2,54896487	8.11
Did the patient plant and gather potatoes near the forest?	8.11	2,54896487	2,521814934	6.10
Did the patient participate in gathering harvest crops near the forest?	8.12	3,074855124	2,521814934	6.8
Did patient bred campfire or collect firewood while working?	8.13	2,936680162	2,291516864	6.9
Does the patient remember the presence of mosquitoes? (during agricultural works)	8.16	2,268175869	2,170947994	8.9
Does the patient remember bites of mosquitoes? (during agricultural works)	8.17	2,268175869	2,077830704	8.8

infection the virus. In addition, the results showed that the study area is the natural focus of WNF.

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