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**T.M. Kotelevska,
N.O. Pryimenko,
H.M. Dubynska,
T.I. Koval,
O.M. Iziumska,
I.M. Zviagolska**

WEST NILE FEVER IN THE CENTRAL PART OF UKRAINE

Ukrainian Medical Stomatological Academy («UMSA»)

Shevchenka str. 23, Poltava, 36011, Ukraine

Українська медична стоматологічна академія («УМСА»)

кафедра інфекційних хвороб з епідеміологією

(зав. – д. мед. н., доц. Т.І. Коваль)

вул. Шевченка, 23, Полтава, 36011, Україна

e-mail: kotelevska.tetiana@gmail.com

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Ключові слова: *вірус Західного Нілу, гарячка Західного Нілу, арбовірусна інфекція, Полтавська область, центральна частина України*

Ключевые слова: *вирус Западного Нила, лихорадка Западного Нила, арбовирусная инфекция, Полтавская область, центральная часть Украины*

Abstract. West Nile Fever in the central part of Ukraine. Kotelevska T.M., Pryimenko N.O., Dubynska H.M., Koval T.I., Iziumska O.M., Zviagolska I.M. West Nile Fever (WNF) is the most common arbovirus infection with a transmission mechanism caused by West Nile Virus (WNV), present on all continents, except for Antarctica. WNV has a high epidemic potential and is dangerous for health of the population all over the world, due to rapid global spread, the formation of new natural foci and the ability to cause epidemics in endemic areas. Over the past 20 years, there have been numerous epidemic outbreaks of the disease among people, birds and horses, associated with WNV. On the territory of Ukraine WNV was first detected in the 70s of the XX century, but at present clinical and epidemiological aspects have been understudied. This study analyzed the epidemic situation regarding WNF in Poltava Region in 2011-2018, and clarified the epidemiological and clinical manifestations of serologically confirmed cases of acute WNF. This is the first actual survey of WNF cases in Poltava Region, its results indicate the prevalence of WNV in the central part of Ukraine. The aim of the study was to study the epidemiological and clinical characteristics of West Nile Fever in Poltava Region. The cases of WNF in Poltava Region in 2011-2018 have been analyzed, according to the annual reporting forms of the Ministry of Health of Ukraine. A serological study of pair blood sera for specific IgG-class antibodies to WNV of 232 patients with febrile conditions, requiring screening for WNF, was conducted. The clinical course was studied in a retrospective analysis of 14 case histories of patients with WNF under treatment in the Poltava Regional Clinical Infectious Diseases Hospital. The analysis demonstrated that in Poltava Region in 2011-2018 35 serologically confirmed cases of acute WNF were registered, with the largest number (14) in 2012. Serologic examination of the specific markers of WNV in 232 patients with febrile conditions allowed to detect 57 (24.6%) seropositive patients. Acute WNF was diagnosed in 35 (15,1%) patients, past WNF – in 22 (9,5%) persons. Analysis of case histories of patients with acute WNF showed that the most susceptible ones were females (64,1%), and the average age of the persons was 46.28 ± 0.30 years old. According to the epidemiological history, the city residents dominated among the patients (71,4%), all of them (100%) marked mosquito bites, and the disease was of a seasonal nature, with the largest (78,6%) number of cases in July-August. The clinical course of WNF in all (100%) patients was moderate-severe and characterized by polymorphism of clinical manifestations. The leading clinical syndromes were: intoxication (100,0%), fever (100,0%), catarrhal (50,0%), allergic (42,8%), dyspeptic (35,7%) syndromes and lymphadenopathy (28,5 %). Thus, the conducted researches have shown that there are all conditions for formation of a natural center of WNF on the territory of Poltava Region. WNF was characterized by a typical course of the disease.

Реферат. Гарячка Західного Нілу в центральній частині України. Котелевська Т.М., Прийменко Н.О., Дубинська Г.М., Коваль Т.І., Ізюмська О.М., Зв'ягольська І.М. Гарячка Західного Нілу (WNF) – найбільш розповсюджена арбовірусна інфекція з трансмісивним механізмом передачі, викликана вірусом Західного Нілу (WNV), що присутній на всіх континентах, за виключенням Антарктиди. WNV має високий епідемічний потенціал, становить загрозу для здоров'я населення в усьому світі завдяки швидкому глобальному розповсюдженню, формуванню нових природних осередків і здатності спричиняти епідемії в ендемічних регіонах. За останні 20 років зареєстровано численні епідемічні спалахи хвороби серед людей, птахів та коней, пов'язані з WNV. Вперше на території України WNV виявлений в 70-х роках ХХ століття, проте на сьогодні клінічні та епідеміологічні аспекти залишаються вивчені недостатньо. У цьому дослідженні проаналізовано епідемічну ситуацію щодо WNF в Полтавській області за 2011-2018 рр., з'ясовані епідеміологічні та клінічні особливості серологічно підтверджених випадків гострої WNF. Це перший актуальний огляд про випадки WNF в Полтавському регіоні, результати якого свідчать про розповсюдженість WNV в центральній частині України. Мета дослідження – з'ясувати епідеміологічні та клінічні прояви гарячки Західного Нілу в Полтавській області. Проаналізовано випадки WNF в Полтавській області за 2011-2018 рр., згідно з річними звітними формами МОЗ України. Загалом серологічне дослідження парних сироваток крові на специфічні антитіла класу IgG до WNV проведено 232 хворим із гарячковими станами, що потребували обстеження на WNF. Клінічний перебіг вивчали при ретроспективному аналізі 14 історій хвороб пацієнтів з WNF, які знаходилися на лікуванні в Полтавській обласній клінічній інфекційній лікарні. Установлено, що в Полтавській області впродовж 2011-2018 рр. зареєстровано 35 випадків гострої WNF, з найбільшою кількістю – 14 осіб у 2012 році. Серологічне обстеження на специфічні маркери WNV 232 хворих із гарячковими станами дозволило виявити 57 (24,6%) серопозитивних пацієнтів. Гостра WNF діагностована в 35 (15,1%), перенесена – у 22 (9,5%) осіб. Аналіз історій хвороб пацієнтів з гострою WNF показав, що найбільш вразливими виявилися особи жіночої статі (64,1%), а середній вік обстежених становив $46,28 \pm 0,30$ року. Згідно з епідеміологічним анамнезом, серед хворих переважали жителі міст – 71,4%, усі (100%) відмічали укуси комарів, захворювання мало сезонний характер з найбільшою (78,6%) кількістю випадків у липні-серпні. Клінічний перебіг WNF в усіх (100%) хворих мав середньотяжку форму та характеризувався поліморфізмом клінічних проявів. Провідними клінічними синдромами були: гарячковий (100,0%), інтоксикаційний (100,0%), катаральний (50,0%), алергічний (42,8%), диспепсичний (35,7%) та лімфаденопатія (28,5%). Таким чином, проведені дослідження показали, що на території Полтавського регіону є всі умови для формування природного осередку гарячки Західного Нілу. Західнонільська гарячка мала типовий перебіг.

West Nile Virus (WNV) is a viral pathogen from the Flavaviridae family which is able to impose a great threat to the health of the population all over the world, due to rapid global spread, the formation of new natural foci and the ability to cause epidemics in endemic areas. WNV is the most common flavivirus that is registered on all continents, except for Antarctica [11].

For the first time the virus was isolated in 1937 from a febrile woman living in the West Nile area in the Northern Province of Uganda during an epidemiological examination of the endemic focus of yellow fever [4]. However, after the emergence of WNV in the United States and Canada in 1999, where the dramatic outbreak of this disease developed among people with severe and fatal consequences, the world medical community realized that WNV had a high epidemic potential and imposed a major threat to society. Over the past two decades, after numerous epidemic outbreaks in the countries of Europe and the Mediterranean basin, the Middle East and North America, WNV has gained global significance [12].

Nowadays WNV circulation has been confirmed in 20 European countries, including close to Ukraine – Poland, Russia, Romania, Slovakia and Hungary. According to experts from the European Center for Disease Control, during the last decade the proportion of seropositive persons to West Nile Fever (WNF) among the population of the European Union varies from 2.1% to 10.6% [13].

The earliest reports of cases of WNV circulation in humans and birds in Ukraine belong to the 70s of the XX century. In 1974 cases of neuroinvasive forms of WNF among humans and the detection of specific antibodies in wild birds and farm animals in the southwestern region of Ukraine were first described [10]. In 1985 in Zakarpattia region 38 cases of illness among people were registered, 16 of them – with neurological manifestations [1]. At the same time, the WNV strain was detected in the blood and internal organs of wild birds (Rook, *Corvus frugiles*) in the Black Sea area. In recent years the prevalence of arbovirus infections, including WNF, among people in natural foci of the northwest of the Black Sea region (Odesa, Mykolayiv, Kherson regions and the Crimea), western and eastern regions of Ukraine has been studied [1]. In 2010-2011 the most comprehensive study on the detection of specific anti-WNV antibodies in horses was conducted for the first time in Ukraine. Screening of more than 300 blood serum samples from healthy horses in 14 regions of the country has shown that WNV is circulating among animals in Zaporizhia, Poltava, Kharkiv, Kirovograd, Luhansk,

Kyiv and Khmelnytsky regions, which are located in the forest-steppe zone, with the seropositivity level of 13.5% [14].

Most of the territory of Ukraine according to its geographical (rivers, wetlands and lowlands) and climatic conditions (wet winter, hot summer), flora and fauna characteristics (variety of birds, animals and a wide range of mosquitoes) is favorable for the formation of ecological complexes, necessary for circulation of WNV in the wild [1, 5]. In addition, Ukraine is located within the international transcontinental corridors of migratory birds linking Africa and the Middle East with Eurasia, which causes the circulation of WNV in our country. It is also relevant for Ukraine that in the anthropogenic (urban) foci of WNF there is a violation of the functioning of the drainage system of open water bodies due to improper basic sanitation (flooded cellars of dwellings, basements, stables, etc.), which may contribute to the breeding of mosquitoes infected by WNV in the cold season [1, 3, 14].

The range of WNV owners is wide: the virus is found in more than 65 types of mosquitoes and ticks, 225 species of birds and 29 species of mammals [7]. However, in natural foci the virus is maintained in the enzootic cycle between ornithophile mosquitoes and some species of wild birds, whose seasonal migrations provide intercontinental distribution of WNV.

The leading mechanism for transmitting WNV to a human is the transmission due to bites of mosquitoes and ticks. For a long time it was believed that this transmission route had been the only one, and the person in the epizootic-epidemic process had been a “dead-end owner” until new mechanisms for its transmission were discovered [9]. Today the possibility of transmitting WNV through blood transfusion, transplantation of organs, through placenta and breastfeeding has been proved, as well as laboratory cases of infection have been described.

The disease is caused by WNV as human infection is West Nile Fever, in the overwhelming majority, up to 80-90%, it runs asymptomatic, about 20% of patients develop fever and less than 1% have neuroinvasive disease in the form of meningitis, encephalitis or acute flaccid paralysis [6]. Other manifestations of the disease have also been described – hepatitis, pancreatitis, chorioretinitis, myocarditis, myositis and orchitis. Predictors of neuroinvasive disease development are a combination of factors of the pathogen (type of the involved WNV strain) and the patient: age over 60, alcohol abuse, presence of concomitant diseases (hypertension, diabetes mellitus, history of cancer, chronic renal failure, HIV infection, etc.) [8].

Since WNV was not found on the territory of Poltava Region before, the characteristic of the first laboratory-confirmed cases of WNF is of great interest.

The aim of the study is to find out the epidemiological and clinical characteristics of West Nile Fever in Poltava Region.

MATERIALS AND METHODS OF RESEARCH

The epidemiological situation regarding WNF in Poltava Region in the dynamics (2011-2018) is analyzed, according to the annual reporting forms of the Ministry of Health of Ukraine.

A serological study of pair blood sera for specific IgG-class antibodies to WNV of 232 patients hospitalized into infectious units of health-care institutions of Poltava Region with fever conditions, requiring screening for WNF, was conducted. Blood sampling of patients with WNF serum markers was carried out 2-3 times with an interval of 7-10 days, the first one at hospitalization, which coincided with the 3rd-12th day of illness.

The diagnosis of West Nile Fever was established according to the ICD-10 (WHO, 1998) on the basis of epidemiological, clinical and anamnestic

data, and confirmed by the detection of specific IgG antibodies to WNV in the blood of patients by the ELISA and immunofluorescence technique with an increase by 4 or more times in their titre in dynamics providing the exclusion of other etiological factors of fever, including arboviruses.

The clinical course was studied in a retrospective analysis of 14 case histories of patients with WNF under treatment in the Poltava Regional Clinical Infectious Diseases Hospital.

Statistical processing of the results was performed using descriptive statistics methods by one-dimensional analysis. The results were calculated on a personal computer using Statistica for Windows and Microsoft Excel 7.0 licensed software [2].

RESULTS AND DISCUSSION

The analysis showed that according to the official statistical reporting documentation for certain infectious and parasitic diseases in Poltava Region in 2011-2018, 35 serologically confirmed cases of acute WNF were detected, with the largest number (14 patients) in 2012, which coincided with the indicators around Ukraine (Fig. 1).

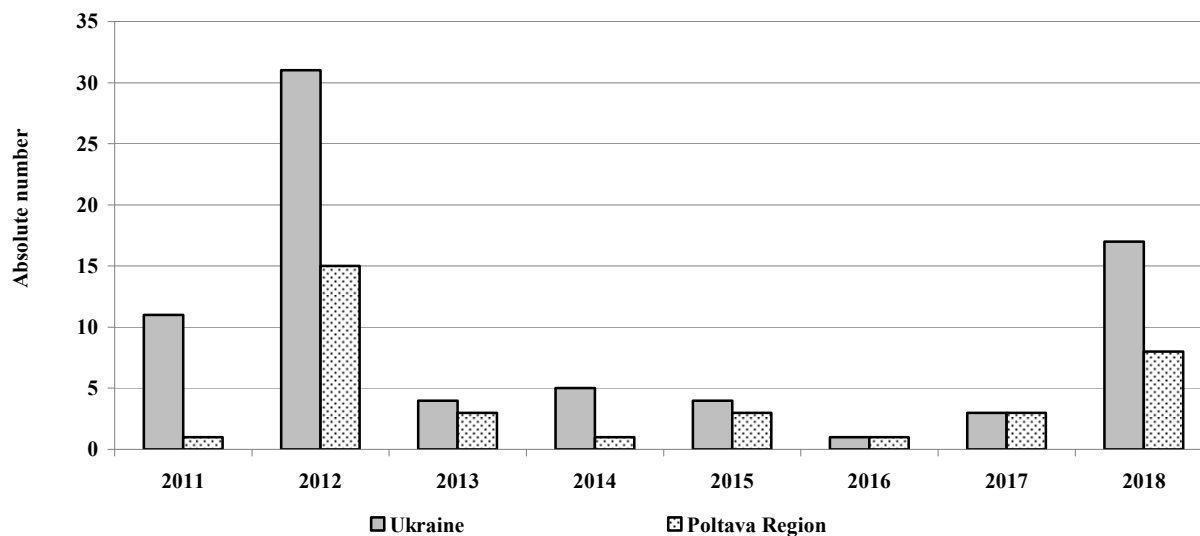


Fig. 1. The number of cases of West Nile Fever in Poltava Region in 2011-2018

It should be noted that the peak of WNF registration in 2012 is probably related to the introduction of specific diagnostics and the maximum number of the examined.

Blood sampling for specific WNV markers in patients with febrile conditions was carried out only in selected districts of the region, as shown in Fig. 2.

As can be seen from Fig. 2, with the same access to the laboratory examination of patients with WNF, only in certain districts doctors were alert for this

disease. In general, in 2011-2018 in Poltava Region 232 patients with a diagnosis, which did not rule out the presence of WNF, were examined, 57 of them (24,6%) were seropositive. At the same time, 35 (15,1%) patients in paired sera an increase in the titre of specific IgG antibodies to WNV by 4 or more times was marked, indicating an acute infection, 22 (9,5%) – without an increase in their dynamics, which did not rule out the past WNF.

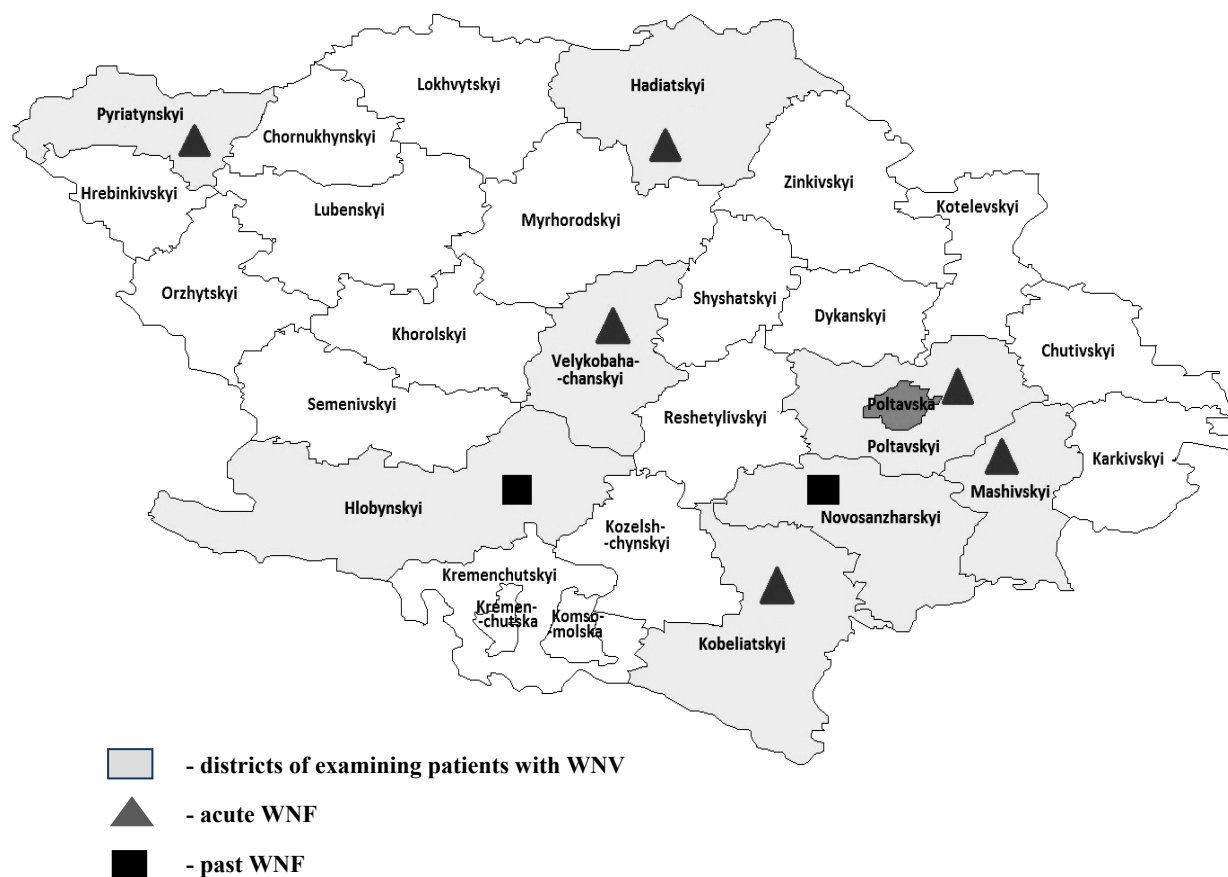


Fig. 2. Map of districts of Poltava Region with examination of WNF patients

Analysis of case histories of patients with acute WNF showed that there were 35.7% males, 64.3% females aged 15-71 (mean age is 46.28 ± 0.30). The distribution of patients by age was as follows: 15-24 years old – 3 (21.4%), 25-44 years old – 3 (21.4%), 45-60 years old – 4 (28.6%), 61-75 years – 4 (28.6%).

According to the epidemiological history, city residents dominated among the patients – 71.4%, 6 of them (42.9%) lived near water. All of them (100%) in the incubation period marked bites of mosquitoes, and 1 (7.1%) additionally pointed to the suction of the tick. All cases of WNF were seasonal and recorded from June to October, with the vast majority (78.6%) in July-August.

Patients with WNF were hospitalized on the 2nd-14th days of the disease (on average on 6.43 ± 2.80). At the initial treatment, the diagnoses were as follows: fever of unclear genesis – 42.9%, acute respiratory viral infections – 35.7%, acute gastroenterocolitis – 21.4%. Acute onset of the disease was noted by 12 patients (85.7%), gradual – by 2 (14.3%). All patients (100%) had the moderate-severe form of the disease which was characterized by polymor-

phism of clinical manifestations. The leading clinical syndromes were: intoxication (100.0%), fever (100.0%), catarrhal (50.0%), allergic (42.8%), dyspeptic (35.7%) syndromes and lymphadenopathy (28.5%).

Intoxication syndrome was manifested by general weakness – 14 (100.0%), headache – 12 (85.7%), chills – 11 (78.6%), body aches – 10 (71.4%) and dizziness – 5 (35.7%) in the examined. The duration of the intoxication syndrome was from 5 to 30 days (on average 12.43 ± 4.78).

The fever in the overwhelming majority of cases – 8 (57.1%) was febrile, in 3 (21.4%) – hectic, in 2 (14.3%) – subfebrile, and in 5 (35.7%) – diphasic one. At the same time, the second wave of fever occurred repeatedly on the 6-7th day after complete normalization of body temperature. The duration of febrile syndrome ranged from 5 to 30 days (on average 12.14 ± 4.90 days) and in 50.0% of patients it was more than 10 days.

In half of patients catarrhal syndrome was recorded as: pharyngitis – in 3 patients (21.4%), tonsillitis – in 2 (14.3%), bronchitis – in 2 (14.3%). Febrile catarrh persisted from 5 to 9 days (on average – 6.85 ± 1.55).

Allergic syndrome was diagnosed in 6 patients (42.8%) and manifested by a rash on the trunk and limbs: spotty-papular – 4 (28.6%), urticarial – 2 (14.2%). The rash appeared on the 2nd-3rd days of the disease, persisted from 3 to 10 days (on average 5.83 ± 2.17) and disappeared without pigmentation and peeling.

Dyspeptic syndrome was characterized by decreased appetite and nausea in 5 (35.7%), vomiting – in 4 (28.6%), heaviness and/or pain in various abdominal areas – in 4 (28.6%), diarrhea – in 2 (14.3%) patients. Dyspeptic disorders lasted from 2 till 7 days (on average 4.8 ± 1.2). In 2 (14.3%) patients hepatosplenomegaly was marked.

Moderate regional lymphadenopathy (cervical and axillary) occurred in 4 (28.6%) patients with a rapid reverse regression on the 2nd-3rd days.

In 1 (7.14%) patient neurological manifestations were observed: diplopia, shaking hands, stiff neck muscles – quickly disappearing in the dynamics and were associated with toxic encephalopathy.

In the overwhelming majority – in 9 patients (64.3%) at hospitalization neutrophilia was registered in the hemogram, in 4 of them (28.6%) associated with leukocytosis and in 5 (35.7%) – with elevated ESR, 2 patients (14.3%) had thrombocytopenia. In the urogram in 2 patients (14.3%)

leukocytes and protein traces were found out. In the biochemical blood test elevations ALT, AST (less than 3 upper limits of normal) were marked in 2 (14.3%) patients. It should be noted that in the dynamics at discharge in isolated cases in the hemogram there remained: leukocytosis – in 2 (14.3%) patients, elevated ESR (25-33 mm/h) – in 6 (42.9%) patients, and indicators of urograms and biochemical blood tests have come to the norm.

In general, the disease lasted from 8 to 23 days (on average 15.64 ± 3.88).

CONCLUSIONS

On the territory of Poltava Region there are all conditions for the formation of the natural WNF centre. In 2011-2018 in Poltava Region 232 patients with febrile conditions were examined for specific WNV markers, 57 of them (24,3%) were seropositive. Acute WNF has been diagnosed in 35 (15,1%), past WNF – in 22 (9,5%) patients. WNF in all (100%) patients was moderately severe and characterized by polymorphism of clinical manifestations with leading clinical syndromes: intoxication (100.0%), febrile (100.0%), catarrhal (50.0%), allergic (42.8%) ones, dyspepsia (35.7%) and lymphadenopathy (28.5%).

Conflict of interests. The authors declare no conflict of interest.

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