DOI: https://doi.org/10.17816/EID636844

Clinical and epidemiological features of the 2019 West Nile fever outbreak in the city of Krasnodar

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ABSTRACT

BACKGROUND: West Nile fever (WNF) is an emerging infectious disease in the Krasnodar region with understudied clinical and epidemiological manifestations. The role of the urban environment in the formation of new endemic foci remains an open question.

AIM: To characterize the main clinical and epidemiological manifestations of WNF and identify potential foci locations within the city of Krasnodar, using the 2019 outbreak as an example.

MATERIALS AND METHODS: A retrospective analysis was conducted on 78 inpatient medical records of patients diagnosed with WNF in 2019, confirmed via enzyme-linked immunosorbent assay (ELISA) and polymerase chain reaction (PCR). Inclusion criteria required patients to have resided within Krasnodar or its suburbs for at least one month prior to symptom onset. Using the online resource Yandex.Maps, we recorded the actual residential addresses of the cases and created a map to identify potential epidemic foci within Krasnodar and adjacent areas.

RESULTS: The 2019 WNF outbreak in Krasnodar region registered between July and September, peaking in August. The mapping of cases in Krasnodar revealed an association with urban water bodies, both natural (lakes, ponds) and artificial (reservoirs, abandoned water bodies), with a lesser degree of association with the Kuban river. In the structure of clinical forms of WNF, the meningeal and meningoencephalitic forms predominated (77.4%, Group 1), while the influenza-like form was observed in 25.6% (Group 2). There were no gender differences between the groups; the mean age was 44.7 ± 0.51 years, with 65% being unemployed or retired. Comorbid conditions were present in 84.5% of Group 1 patients and 35.0% of Group 2 patients, with cardiovascular diseases being the most common (46.1%). Group 1 was characterized by an acute onset with febrile fever, general cerebral and meningeal symptoms, ataxia, and meningitis with moderate lymphocytic pleocytosis. In Group 2, 50% of cases began with low-grade fever, with rash (65%), lymphadenopathy (40%), hyperemia and granular pharyngeal mucosa (75%–50%), and cough (30%) being more frequently observed.

CONCLUSIONS: Mapping of potential infection sites confirmed the importance of urban water bodies and helped identify areas at risk of WNF transmission. Effective WNF prevention in urban environments requires comprehensive surveillance of water bodies, mosquito control, and monitoring of migratory birds. For timely diagnosis, PCR and ELISA testing for West Nile fever markers should be included in the comprehensive diagnostic evaluation of patients presenting with symptoms of meningitis, meningoencephalitis, or fever of unknown origin with catarrhal symptoms, rash, and lymphadenopathy during the summer-autumn period in the southern regions of Russia.

Keywords: West Nile fever; epidemiology; clinical presentation; diagnosis; treatment.

To cite this article:
Avdeeva MG, Kulbuzheva MI, Blazhnyaya LP, Bakhtina VA, Vanyukov AA, Nezhurin AV, Arzumanyan KA, Mishchenko NE. Clinical and epidemiological features of the 2019 West Nile fever outbreak in the city of Krasnodar. *Epidemiology and Infectious Diseases.* 2024;29(5):321–336. DOI: https://doi.org/10.17816/EID636844

Received: 08.10.2024 **Accepted:** 29.01.2025 **Published online:** 18.02.2025

ECO•VECTOR

DOI: https://doi.org/10.17816/EID636844

Клинико-эпидемиологические особенности вспышки лихорадки Западного Нила 2019 года (на примере города Краснодара)

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АННОТАЦИЯ

Обоснование. Для Краснодарского края лихорадка Западного Нила является эмерджентной инфекцией с недостаточно изученными клинико-эпидемическими проявлениями. Остаётся открытым вопрос о роли городской среды в формировании новых эндемичных очагов.

Цель исследования — охарактеризовать основные клинико-эпидемические проявления лихорадки Западного Нила и определить возможное расположение очагов в городе Краснодаре на примере вспышки 2019 года.

Материалы и методы. Проведён ретроспективный анализ 78 карт стационарного наблюдения пациентов, находившихся на лечении в 2019 году с диагнозом «лихорадка Западного Нила», подтверждённым методами иммуноферментного анализа и полимеразной цепной реакции. Условием отбора было нахождение пациентов в пределах города Краснодара и его пригородов в течение месяца до начала заболевания. При помощи электронного ресурса «Яндекс. Карты» отражены данные фактического места проживания заболевших, построена карта для определения возможных эпидемических очагов на территории Краснодара и прилежащих районов.

Результаты. Вспышка лихорадки Западного Нила в Краснодарском крае зарегистрирована в период с июля по сентябрь 2019 года, с пиком в августе. Картографическое распределение случаев на территории Краснодара показало их связь с водными объектами внутри города как естественного (озёра, пруды), так и искусственного происхождения (водохранилище, безымянные заброшенные водные объекты), в меньшей степени отмечена связь с рекой Кубань. В структуре клинических форм лихорадки Западного Нила преобладали менингеальная и менингоэнцефальная формы (77,4%) (1-я группа); гриппоподобная форма отмечена в 25,6% (2-я группа). Гендерных различий в наблюдавшихся группах выявлено не было, средний возраст составил 44,7±0,51 года, 65% относились к нетрудоустроенной группе и пенсионерам. Коморбидная патология присутствовала у 84,5% пациентов 1-й группы и 35,0% пациентов 2-й группы. Преобладала патология сердечно-сосудистой системы (46,1%). Для 1-й группы было характерно острое начало с фебрильной лихорадки, общемозговых и менингеальных симптомов, атаксии, развитие менингита с умеренным лимфоцитарным плеоцитозом. Во 2-й группе заболевание в 50% случаев начиналось с субфебрильной лихорадки, чаще регистрировались экзантема (65%), лимфаденопатия (40%), гиперемия и зернистость слизистой ротоглотки (75–50%), кашель (30%).

Заключение. Картирование вероятных точек заражения людей подтвердило важность водных внутригородских объектов и помогло определению зон риска передачи инфекции. Эффективная профилактика лихорадки Западного Нила в городах требует комплекса надзорных мер за водными объектами внутри населённых пунктов, уничтожения комаров и контроля перелётных птиц. Для своевременной диагностики методы полимеразной цепной реакции и иммуноферментного анализа на маркёры лихорадки Западного Нила необходимо включать в комплексное обследование пациентов с клинической картиной менингитов и менингоэнцефалитов, а также при лихорадке неясного генеза с катаральным синдромом, экзантемой, лимфаденопатией в летне-осенний период в южных регионах России.

Ключевые слова: лихорадка Западного Нила; эпидемиология; клиническая картина; диагностика; лечение.

Как цитировать:
Авдеева М.Г., Кулбужева М.И., Блажняя Л.П., Бахтина В.А., Ванюков А.А., Нежурин А.В., Арзуманян К.А., Мищенко Н.Е. Клинико-эпидемиологические особенности вспышки лихорадки Западного Нила 2019 года (на примере города Краснодара) // Эпидемиология и инфекционные болезни. 2024. Т. 29, № 5. С. 321–336. DOI: https://doi.org/10.17816/EID636844

Рукопись получена: 08.10.2024 **Рукопись одобрена:** 29.01.2025 **Опубликована online:** 18.02.2025

BACKGROUND

West Nile fever (WNF) is a natural-focal arboviral vector-borne infection caused by an enveloped virus of the genus *Flavivirus* (the West Nile virus), first isolated in Uganda in 1937 [1]. The main vectors of West Nile virus (WNV) are mosquitoes of the *Culex and Aedes* genera [2]. The WNV has been identified in 30 mammalian species, 60 mosquito species, and some reptiles, including snakes; however, it is most widespread among birds inhabiting aquatic and wetland ecosystems, which serve as the primary reservoir and amplifying host of the virus [3, 4]. WNV mosquito vectors are widely distributed across the globe, and the known geographic range of WNV transmission has steadily expanded over the past 30 years. Humans, like other mammals, are considered incidental hosts and do not contribute to further transmission, serving as a “dead-end” in the infection cycle. In most cases, WNF is asymptomatic or presents as a mild, influenza-like illness and often remains undiagnosed. Severe forms involving the central nervous system are rare but may result in long-term sequelae or death [5].

In the Krasnodar Territory, WNF is considered an emerging infectious disease, having appeared in a previously unaffected geographic area. WNV was first isolated from mosquitoes in the region in 1988 during arbovirus circulation research. However, human cases were first diagnosed in the region during the first documented outbreak of WNF in the Russian Federation (RF) in 1999 [6, 7]. That year, Russia experienced record-breaking summer temperatures [8], although average summer temperatures in Krasnodar remained within the typical historical range. A dramatic increase in WNF incidence occurred in 2010 (527 cases) and spread to seven regions of the RF, most notably the Volgograd Region (413 cases) [9]. This period also coincided with the occurrence of extreme summer heat [8]. Between 2010 and 2018, only sporadic WNF cases were reported in the Krasnodar Territory [10]. In 2019, WNF incidence rose again across the RF, reaching 2.14 cases per 100,000 population in the Krasnodar Territory compared with 0.02–0.05 per 100,000 between 2016 and 2018 [11].

WNV may be introduced into the RF from countries in Africa, Southwest Asia, and Southeast Asia. The virus is introduced from Africa by migratory birds such as black-headed gulls, quails, swallows, ducks, sandpipers, rooks, starlings, and other species following southern and southwestern flyways. In Western Siberia, species posing a potential risk include geese, ducks, sandpipers, gulls, and passerines that follow similar migratory routes. In Russia, the primary endemic focus is maintained by Eurasian coots and several duck species inhabiting the Kuban and Terek River deltas [12]. In the Krasnodar Territory, WNV antibodies have been detected in 34 bird species [10]. Global climate change has altered migratory patterns of birds and contributed to increased population densities of synanthropic and ornithophilic mosquitoes [6]. In the Krasnodar Territory, rising ambient temperatures contribute to WNV transmission by facilitating the accumulation of effective temperature sums required for viral replication and persistence within mosquitoes [9]. Elevated temperatures accelerate mosquito population growth, shorten the incubation period, and enhance the efficiency of viral transmission to birds [13]. A strong correlation has been documented between extreme heat events and the intensity of human outbreaks [14].

When analyzing the factors contributing to the rise in WNF incidence, particular attention is given to the formation of transmission foci within large urban centers [9]. In Krasnodar, areas at risk for WNV transmission remain underrecognized.

AIM

The work aimed to characterize the main clinical and epidemiological manifestations of WNF and identify potential foci locations within Krasnodar, using the 2019 outbreak as an example.

METHODS

Study Design

It was an observational, cross-sectional, single-center, non-controlled study of the clinical and epidemiological characteristics of WNF.

Medical records of 78 inpatients diagnosed with WNF were selected for the study. All patients received care at the State Budgetary Healthcare Institution “Specialized Clinical Infectious Diseases Hospital” of the Ministry of Health of the Krasnodar Territory. The diagnosis was established in accordance with Sanitary Regulations 3.1.7.3107-13, Prevention of West Nile Fever, based on the detection of WNF-specific IgM and IgG antibodies via enzyme-linked immunosorbent assay (ELISA) and by polymerase chain reaction (PCR). Using the online mapping service Yandex. Maps, a visualization was created to reflect the actual residential addresses of individuals diagnosed with WNF. This mapping aimed to identify potential areas for the formation of WNF transmission foci within the urban territory of Krasnodar.

Eligibility Criteria

Inclusion criteria: a confirmed diagnosis of West Nile fever; age over 18 years; residence within Krasnodar or its suburbs within one month prior to symptom onset.

Exclusion criteria: Given the clinical polymorphism of WNF, differential diagnoses were ruled out using PCR testing of cerebrospinal fluid for conditions with similar symptoms, including: enteroviral infection, Ixodes tick-borne borreliosis, tuberculosis, parvovirus infection, pneumococcal infection, influenza, toxoplasmosis, and herpesvirus infections caused by herpes simplex virus types 1 and 2, human herpesvirus 6, Epstein–Barr virus, cytomegalovirus, and varicella-zoster virus. ELISA testing was used to exclude the presence of specific IgM antibodies to measles, HIV, and rubella.

Non-inclusion criteria: absence of IgG and IgM antibodies to WNV in blood samples; residence outside the Krasnodar Territory.

Study Setting

The study included data from medical records of patients hospitalized in 2019 at the State Budgetary Healthcare Institution "Specialized Clinical Infectious Diseases Hospital" of the Ministry of Health of the Krasnodar Territory.

Study Duration

Medical documentation was analyzed from 2023 to 2024.

Intervention

Patient selection was based on a confirmed diagnosis of WNF, established by ELISA detecting serum IgM and IgG antibodies to WNV in rising titers or via seroconversion, and/or by the presence of WNV RNA identified using PCR in cerebrospinal fluid or blood.

Examination and treatment of patients were performed in accordance with Decree of the Chief State Sanitary Physician of the RF dated January 28, 2021, No. 4, "Approval of Sanitary Rules and Regulations SanPiN 3.3686-21 'Sanitary and Epidemiological Requirements for the Prevention of Infectious Diseases,'" Methodological Guidelines MU 3.1.3.2600-10 "Measures to Combat West Nile Fever in the Russian Federation" (approved by the Chief State Sanitary Physician of the RF on April 19, 2010), and the clinical management protocol for patients with West Nile fever at the State Budgetary Healthcare Institution "Specialized Clinical Infectious Diseases Hospital," which includes performing lumbar puncture with cerebrospinal fluid analysis by PCR.

The primary indicators assessed upon hospital admission included: actual residential address, age, complete blood count and urinalysis, liver enzymes [alanine aminotransferase (ALT), aspartate aminotransferase (AST)], creatine phosphokinase (CPK), lactate dehydrogenase (LDH), C-reactive protein (CRP), urea, creatinine, and bilirubin levels.

Potential zones of anthropurgic transmission risk in Krasnodar were determined using the Yandex.Maps digital platform.

Main Study Outcome

Identification of diagnostically significant manifestations of WNF based on clinical symptoms, complete blood count, biochemistry, urinalysis, and cerebrospinal fluid analysis.

Identification of WNF transmission foci within Krasnodar based on the geographic distribution of diagnosed cases.

Subgroup Analysis

Patients were stratified into two groups according to the clinically diagnosed form of the disease. Group 1 (n = 58) included patients with meningeal or meningoencephalitic manifestations of WNF; group 2 (n = 20) included patients with an influenza-like form of WNF. Each patient's actual residential address was used to determine the administrative district and the presence of nearby water bodies.

Statistical Analysis

Principles of sample size calculation. The sample size was not pre-calculated.

Statistical methods. Statistical analysis was used for comparisons of quantitative variables. Means (M), standard deviations (SD), 95% confidence intervals, and standard error of the mean (m) were calculated. Distribution normality was assessed using the Shapiro–Wilk test. The significance of differences was assessed using Student's t-test; differences were considered statistically significant at $p < 0.05$. Nonparametric statistical methods were used to analyze the results, employing Microsoft Excel 10 (Microsoft, USA) and Statistica 6.0 software package (StatSoft, USA), which were also used for graphical data presentation.

Ethics Approval

The study protocol was approved by the independent ethics committee of the Federal State Budgetary Educational Institution of Higher Education "Kuban State Medical University" of the Ministry of Health of Russia, Krasnodar (Protocol No. 89, dated June 26, 2020).

RESULTS

Participants

The process of sample formation is presented in the study design flowchart (Fig. 1). Initially, medical records of 180 patients with a preliminary diagnosis of "meningitis, fever of unknown origin, WNF?" were screened. A total of 78 inpatient records with a clinical diagnosis of WNF were selected. A total of 102 patients were excluded from the study due to the absence of a confirmed final diagnosis of WNF and residence outside the Krasnodar Territory or recent travel outside the territory within the past month.

Based on the clinical presentation, developed complications, and changes in laboratory parameters, patients were divided into groups according to the clinical form of the disease as established by the final diagnosis: group 1 included meningeal or meningoencephalitic forms; group 2 included influenza-like form.

Primary Results

All patients were admitted to the hospital as emergency cases on average on day 5.9 ± 0.32 of the disease. In terms of sex distribution, among the 78 patients included in the study, 48.7% (38 patients) were male and 51.3% (40 patients) were female. The mean age of the patients was 44.7 ± 0.51 years (18–78 years), individuals under 50 years of age accounted for 57.7% of all cases, with the most affected age group being those aged 29–38 years (29.5%).

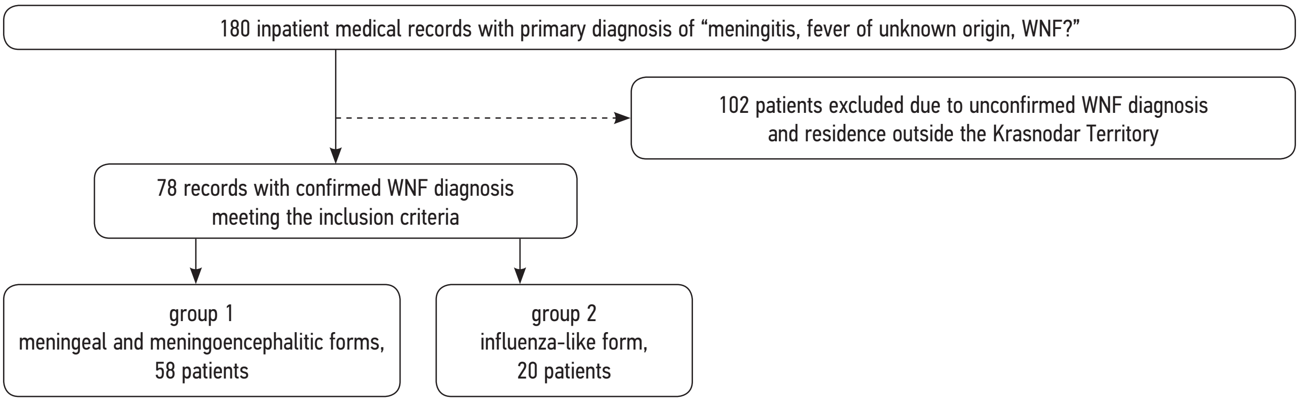

Fig. 1. Study design flowchart. Flowchart developed by the authors (in accordance with STROBE guidelines). WNF, West Nile fever.

The age distribution of patients with WNF is presented in Fig. 2.

The majority of patients were unemployed (44.9%, 35 patients), 34.6% (27 patients) were employed, 17.9% (14 patients) were retirees, and 2.6% (2 patients) were students. The average hospital stay was 14.2 ± 6.71 bed-days.

The most prevalent comorbidities (Fig. 3) included cardiovascular diseases in 36 patients (46.1%), of whom 17 (21.8% of the total) had hypertension. Respiratory disorders were reported in 21 patients (26.9%); genitourinary and gastrointestinal pathologies were reported in 28 patients each (35.9%); nervous system diseases were reported in 25 patients (32.0%); and hematologic conditions were reported in 21 patients (26.9%), including 20 cases of anemia. Cardiovascular pathology was observed in patients over 48 years of age. In group 1, 84.5% of patients had comorbidities of varying severity, most often in combination. Diabetes mellitus, hypertension, immunosuppression, chronic kidney disease, and liver disease were associated with a more severe clinical course, complicated diagnosis and prolonged recovery. In group 2, isolated cases of comorbid pathology were observed in only 35.0% of patients.

WNF cases were recorded from July through September, with a peak in August 2019 (see Fig. 4). The month preceding the increase in incidence—June 2019—was characterized by a moderate rise in precipitation levels (35 mm) compared with 2018 (11 mm), although it did not exceed the levels recorded over the past 10 years. At the same time, precipitation level

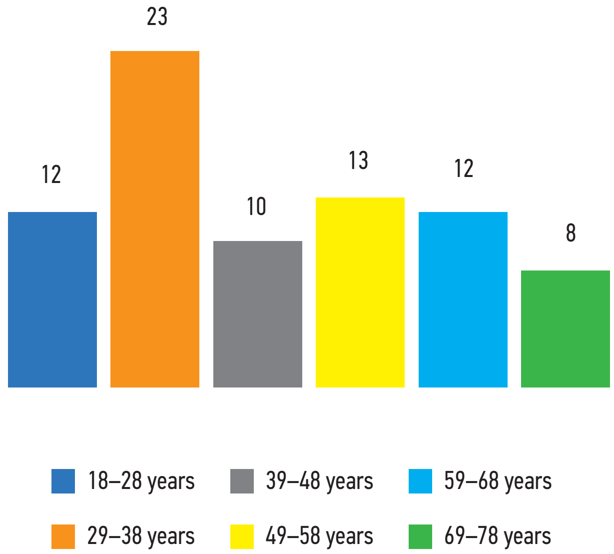

Fig. 2. Age distribution of patients with West Nile fever.

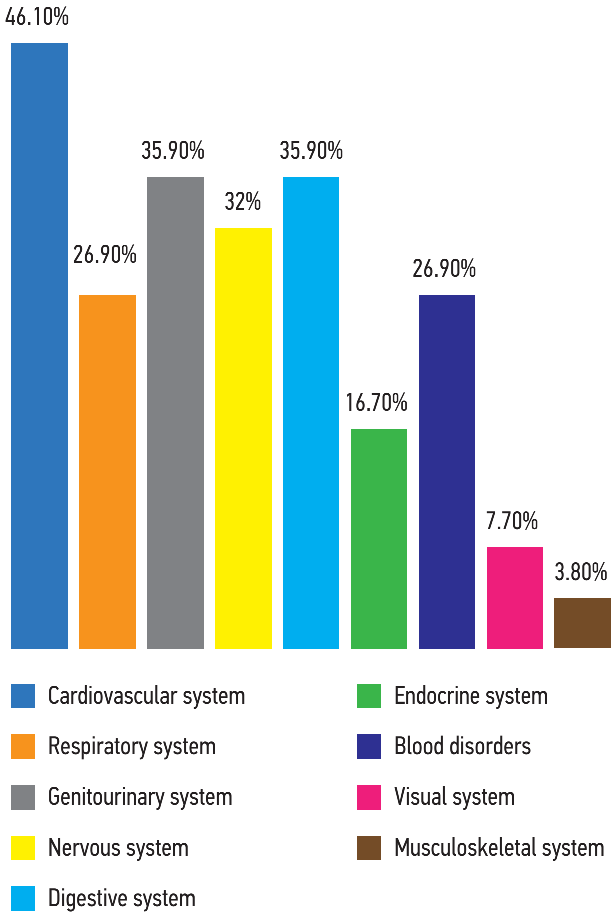

Fig. 3. Comorbidity profile in patients with West Nile fever.

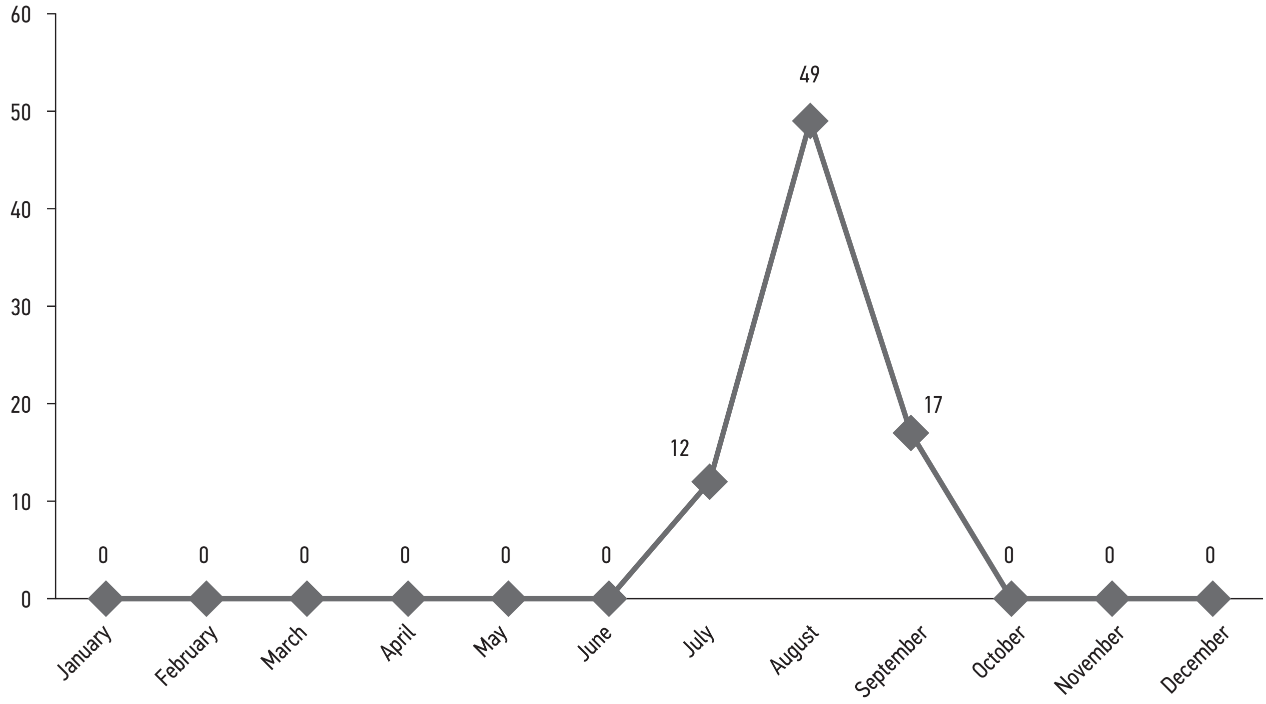

Fig. 4. Seasonal characteristics of West Nile fever in 2019.

in July 2019 reached 132 mm, surpassing the highest level for that month over the past 20 years. A higher precipitation level was recorded only in July 1997, which was 171 mm. August and September, precipitation levels decreased to 38 mm and 41 mm, respectively. The average monthly temperatures in the summer of 2019 remained within 25.3–23.7°C, not exceeding the average values for the decade [15].

Of all examined patients, only 11 (14.1%) associated deterioration in their health with a mosquito bite as a potential risk factor for WNF (see Fig. 5). Meanwhile, 47 patients were unable to precisely identify or speculate on the cause of their disease, reflecting low awareness of possible transmission routes of WNF. The majority of affected individuals were unaware of the existence of the disease.

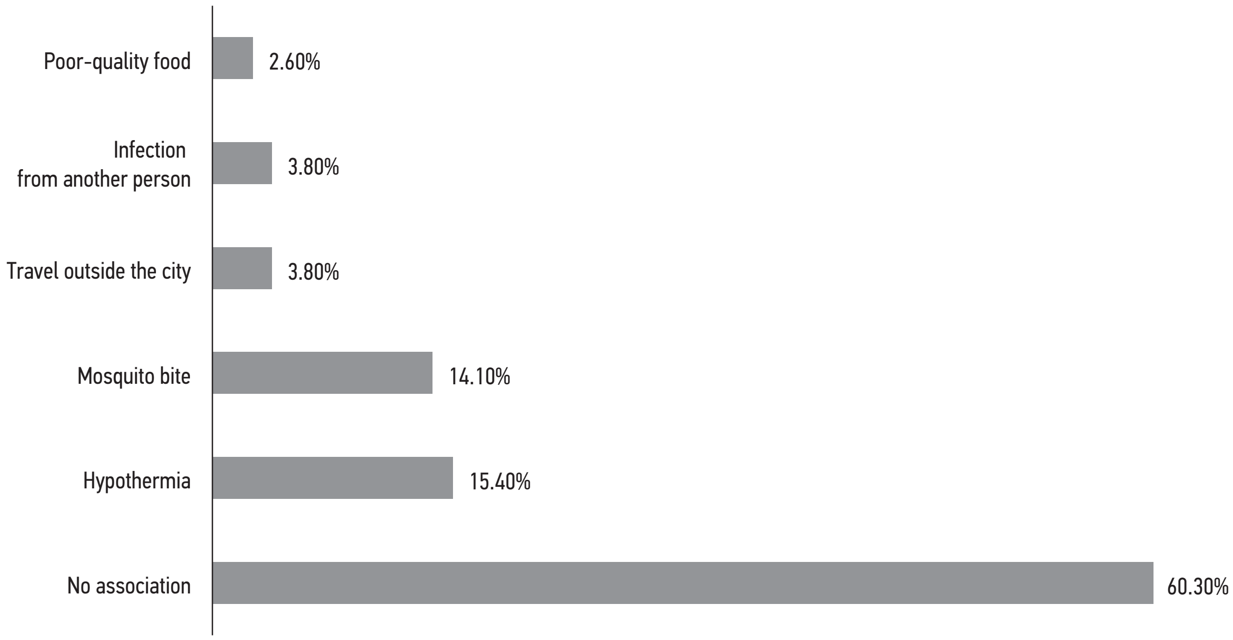

Fig. 5. Results of patient survey on possible sources of West Nile fever infection.

DOI: https://doi.org/10.17816/EID636844

Based on patients' actual residential addresses, a distribution map of registered WNF cases was constructed and analyzed by territorial districts (see Fig. 6). The highest number of cases was found in the Prikubansky District—50.0% (39 patients)—with a predominance of cases near Rossiyskaya Street and Rostovskoe Highway (see Table 1). This district includes the Shapsug Reservoir, Kopanka Lake, Tsaritsyna Lake, and several small water bodies near Kruglikovsky Boulevard, Ekaterininskaya Estate, and the Yuzhny settlement area. Numerous unnamed water bodies and shallow stagnant water ditches were also observed in this district. In the Karasunsky District, 23.1% of cases (18 patients) were registered. This district borders the Krasnodar Reservoir, with foci concentrated along the Karasun Lakes and Kotlovan Lake. In the Central District, 14.1% of cases (11 patients) were identified near the Kuban River, Staraya Kuban Lake, and Verkhnee Pokrovskoe Lake. The Western District accounted for 3.8% of cases (3 patients), and adjacent suburban areas along the Kuban River or its tributaries accounted for 9.0% (7 patients).

Thus, all WNF cases occurred among individuals residing in close proximity to urban water bodies of both natural (lakes, ponds) and artificial origin (reservoirs, unnamed abandoned water bodies). Flowing waters of the Kuban River appeared to have considerably less significance.

In most cases, disease onset was acute with febrile temperatures recorded (55.1%); 11 cases (14.1%) presented with pyretic fever, and 2 cases (2.6%) exhibited hyperpyrexia (temperature > 40°C). Fever was accompanied by headache, marked weakness, and malaise. A subacute onset with subfebrile temperature was observed in 22 patients (28.2%).

The primary clinical manifestation was central nervous system involvement presenting as meningitis (56%–71.8%)

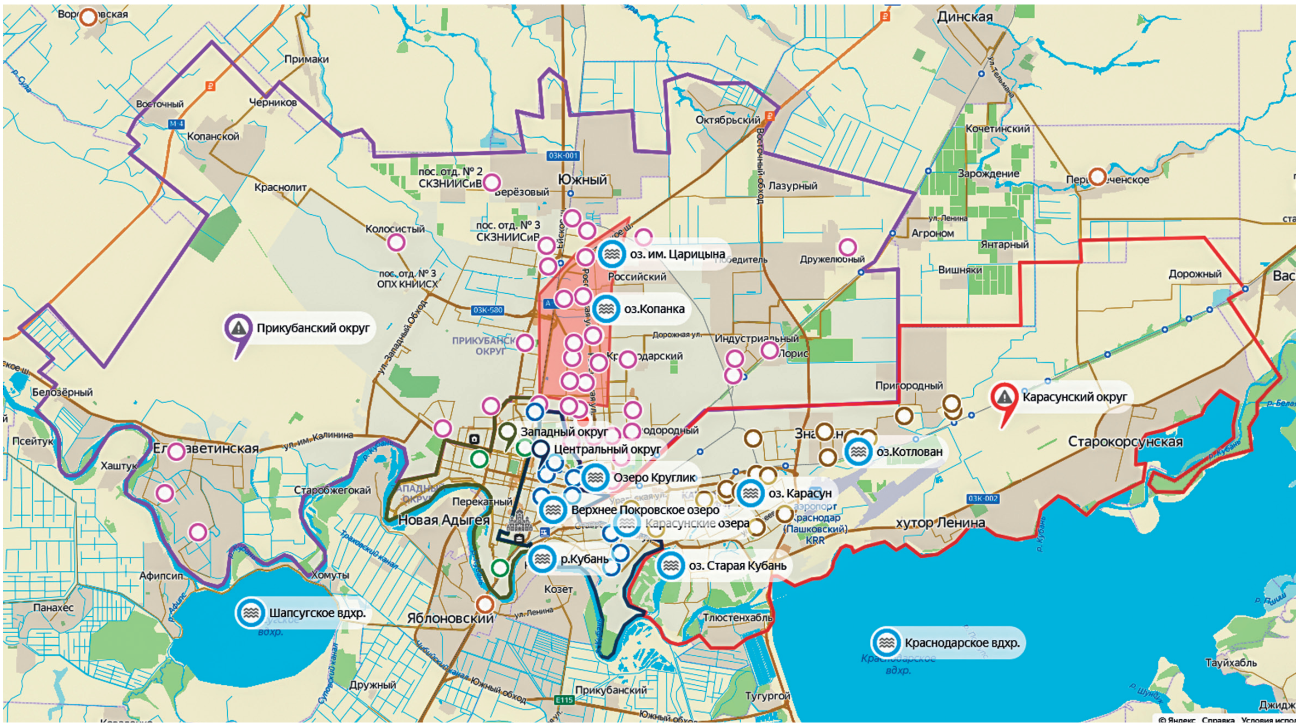

Fig. 6. Prevalence of West Nile fever in Krasnodar by patients' actual residence in 2019: Prikubansky District, Karasunsky District, Zapadny District, and Central District are highlighted in purple, red, green, and blue.

Table 1. Distribution of West Nile Fever cases by territorial districts of Krasnodar

Territorial districts of Krasnodar	West Nile Fever cases	
	absolute number	%
Prikubansky District	39	50.0
Central District	11	14.1
Karasunsky District	18	23.1
Zapadny District	3	3.8
Areas outside Krasnodar	7	9.0

and meningoencephalitis (2%–2.6%). These forms were observed in 58 patients (74.4%), constituting group 1. The disease onset with pyretic and hyperpyretic fever was observed only in this group. Fever and intoxication symptoms were accompanied by general cerebral symptoms, meningeal irritation signs, and loss of balance (ataxia). Hyperemia of the oropharyngeal mucosa was recorded in half of cases, while mucosal granularity, respiratory symptoms, and rash at disease onset were noted in only 10%–12% of cases (see Table 2).

Table 2. Frequency of clinical manifestations in patients with West Nile Fever by disease form

Clinical manifestation	Frequency of occurrence			
	Group 1 (*n* = 58)		Group 2 (*n* = 20)	
	absolute number	%	absolute number	%
Weakness	57	98.3	20	100.0
Headache	50	86.2	1	5.0
Dizziness	20	34.5	3	15.0
Malaise	56	96.5	19	95.0
Temperature: subfebrile	12	20.7	10	50.0
febrile	33	56.9	10	50.0
pyretic	11	19.0	-	-
hyperpyretic	2	3.4	-	-
Muscle pain	8	13.8	6	30.0
Nausea	37	63.8	6	30.0
Vomiting	24	41.4	4	20.0
Nasal congestion	2	3.4	1	5.0
Cough	6	10.3	6	30.0
Throat irritation	6	10.3	8	40.0
Sore throat	2	3.4	5	25.0
Sweating	8	13.8	1	5.0
Chills	8	13.8	5	25.0
Drowsiness	19	32.8	1	5.0
Ataxia	17	29.3	-	-
Exanthema	7	12.0	13	65.0
Cutaneous hyperesthesia	12	20.7	-	-
White coating on tongue	55	94.9	18	90.0
Lymphadenopathy	3	5.2	8	40.0
Pharyngeal hyperemia	28	48.3	15	75.0
Granularity of the pharynx	12	20.7	10	50.0
Harsh breathing	14	24.1	2	10.0
Positive Kernig sign	20	34.5	-	-
Positive occipital stiffness	39	67.2	-	-
Focal neurological symptoms	2	3.4	-	-
Hepatomegaly	3	5.2	-	-

Lumbar puncture was performed on admission in 59 patients (75.6%). It is noteworthy that in 15.4% (12 patients), despite intense headache, occipital stiffness and other meningeal signs were mild or absent, while cerebrospinal fluid showed pathological changes consistent with inflammation of the leptomeninges. Moderate lymphocytic pleocytosis was observed in most cases in cerebrospinal fluid, with an average of 81.3 ± 16.4 cells/μL, lymphocytes comprising 78.4% ± 3.02%, and protein concentration of 0.79 ± 0.082 g/L. Neutrophilic pleocytosis ranging from 31 to 633 cells/μL (mean 223.5 ± 88.07 cells/μL) was seen in 12 cases (15.4%), predominantly in older patients aged 48.1 ± 12.7 years ($p > 0.05$). Follow-up cerebrospinal fluid analysis after treatment showed improvement: cytosis decreased to 19.6 ± 0.86 cells/μL, lymphocytes increased to 88.1% ± 0.5%, and protein content decreased to 0.66 ± 0.113 g/L.

The influenza-like form was diagnosed in 20 patients (25.6%). The mean age in this group was 40.5 ± 3.71 years. Moderate intoxication syndrome with subfebrile (50%) or febrile (50%) temperatures was accompanied by myalgia (30%), dizziness (15%), and, in one third of cases, nausea and vomiting without positive Kernig or Brudzinski signs (see Table 2). Respiratory symptoms such as sore throat (65%) and cough (30%) predominated. Compared with group 1, rash (65%), lymphadenopathy (40%), and oropharyngeal mucosal hyperemia and granularity (75% and 50%, respectively) were significantly more frequent.

No statistically significant differences were found in age distribution between groups.

Complete blood count on admission showed no significant abnormalities (see Table 3). At discharge during early convalescence, elevated erythrocyte sedimentation rate of 20.1 ± 1.0 mm/h and lymphocytosis were recorded. Blood biochemistry revealed increased transaminase activity in some cases (11 patients, 14.1%) with normalization by convalescence, except 4 severe cases, where transaminases remained elevated. Severe cases were also characterized by marked elevation of CPK, LDH, and CRP, which significantly decreased by discharge.

Urinalysis on day 1 of hospitalization showed leukocyturia in 88.5% (69 patients), squamous epithelial cells in 83.3% (65 patients), microhematuria in 80.8% (63 patients), bacteria in 51.3% (40 patients), ketones in 47.4% (37 patients), and proteinuria in 37.2% (29 patients). By recovery, urinalysis normalized in almost all patients except one with acute kidney injury signs.

Additional investigations included electrocardiography in 88% (69 patients), chest X-ray in 68% (53 patients), and nasopharyngeal swab for meningococcus in 42% (33 patients). Neurologist, otolaryngologist and ophthalmologist consultations were performed in 70.5% (55), 51% (40), and 31% (24) of patients, respectively.

Due to lack of specific antiviral treatment, management of WNF was primarily focused on pathogenetic therapy and intensive rehabilitation. Considering the possibility of mixed viral-bacterial etiology in meningeal forms, empirical antibacterial therapy was initiated before laboratory confirmation. The majority of patients (92.5%) received antibiotics, either as monotherapy or in combination. After confirmation of WNF diagnosis, antibacterial therapy was discontinued unless other indications existed. The mean duration of therapy was 7.59 ± 3.91 days (see Table 4).

Table 3. Changes in laboratory parameters in patients with West Nile fever

Parameter	At admission	At discharge	***p*-value**
Leukocytes, 10^9/L	8.0 ± 0.43	6.7 ± 0.26	0.01
Erythrocytes, 10^{12}/L	4.6 ± 0.07	4.5 ± 0.07	0.31
Hemoglobin, g/L	134.4 ± 1.9	128.5 ± 2.85	0.08
Lymphocytes, 10^9/L	4.3 ± 0.97	6.3 ± 1.46	0.25
Platelets, 10^9/L	221.0 ± 9.96	256.9 ± 9.38	0.0097
Erythrocyte sedimentation rate, mm/h	12.6 ± 0.51	20.1 ± 1.22	< 0.001
Alanine aminotransferase, U/L	29.5 ± 3.91	68.4 ± 32.91	0.24
Aspartate aminotransferase, U/L	35.0 ± 5.06	40.2 ± 13.38	0.71
Creatine phosphokinase, U/L	234.0 ± 36.39	79.6 ± 34.33	0.0024
Lactate dehydrogenase, U/L	418.8 ± 17.50	338.4 ± 15.27	< 0.001
C-reactive protein, mg/L	11.1 ± 3.20	3.0 ± 0.95	0.0168
Creatinine, μmol/L	81.0 ± 5.06	79.4 ± 11.68	0.90
Urea, mmol/L	5.2 ± 0.29	4.5 ± 0.47	0.20
Total bilirubin, mmol/L	14.8 ± 2.08	10.7 ± 3.77	0.34

Table 4. Main types of therapy used in the treatment of patients with West Nile fever

Type of therapy	Patient category	Absolute number	%	95% confidence interval
Antibiotic therapy	Patients not receiving antibiotics	6	7.8	2.9–16.2
	Patients receiving III generation cephalosporins (ceftriaxone)	63	81.8	71.4–89.7
	Patients receiving fluoroquinolones (levofloxacin)	3	3.9	0.8–11.0
	Patients receiving combination therapy (ceftriaxone + levofloxacin)	5	6.5	2.1–14.5
Immunomodulatory therapy	Patients not receiving immunomodulatory therapy	63	81.8	71.4–89.7
	Patients receiving immunomodulatory therapy (meglumine acridone acetate)	14	18.2	10.3–28.6
Infusion therapy	Patients receiving infusion therapy in hospital	77	100.0	95.3–100.0
Glucocorticoid therapy	Patients without glucocorticoid therapy	60	77.9	67.0–86.6
	Patients receiving dexamethasone	15	19.5	11.3–30.1
	Patients receiving prednisolone	2	2.6	0.3–9.1

Pathogenetic treatment targeted correction of hemodynamic disturbances, hypoxemia, intracranial hypertension, seizure syndrome, electrolyte imbalance, and anemia. All patients received infusion therapy averaging 12.92 ± 7.19 days. Infusion regimens during the acute phase included 0.9% NaCl solution (250 mL) combined with 25% $MgSO_4$ solution (5–10 mL), or 0.9% NaCl (250 mL) with 2.4% aminophylline solution (5–10 mL). Glucocorticoids (GC) were indicated for severe disease with neurological symptoms (meningoencephalitis, encephalitis, cerebral edema and swelling, focal symptoms, suspected demyelination). GC therapy was administered to 22.1% of patients, with a mean duration of 4.35 ± 2.03 days.

All patients were discharged with clinical improvement.

Secondary Results

No secondary results were reported.

DISCUSSION

Since the 1990s, southern Russia has been considered a risk area for WNF transmission. In Krasnodar Territory, as in other southern regions, sporadic cases occur with periodic outbreaks. Outside epidemic peaks, diagnosis of sporadic WNF cases remains challenging. Due to the absence of pathognomonic symptoms and low clinical suspicion among physicians, cases without central nervous system involvement remain undiagnosed, preventing accurate assessment of the true disease burden in the region.

Environmental and socio-economic risk factors contributing to increased WNF incidence have been studied worldwide. Most researchers associate increases in incidence with weather conditions and the level of mosquito infection. Land use and socio-economic factors play a comparatively smaller role in predicting WNF cases, although occupational risk has been noted among agricultural and farm workers [16, 17]. When assessing the association between socioeconomic status and the risk of arboviral infection across different geographic regions, infection risk was shown to correlate with low levels of education and income, limited access to medical care, poor housing conditions, water supply disruptions, and migration status [18]. No such patterns were observed in our study; however, the highest incidence was recorded among unemployed individuals (44.9%) and retirees (17.9%).

Ambient temperature plays a significant role in the transmission of WNV, particularly in temperate climate regions [19]. Elevated temperatures in spring create favorable conditions for vector population growth, which can lead to an increase in human cases several weeks later. Awareness of such conditions early in spring can help public health authorities mitigate the risk before it becomes a tangible threat. An analysis of annual incidence trends in southern regions of Russia, correlated with detection of WNV in mosquitoes, has demonstrated the importance not only of ambient temperature, but also of road networks and proximity to water bodies [9]. In Krasnodar, average temperatures in the spring and summer of 2019 did not differ significantly from previous years, which precluded predicting the outbreak. Instead, an increase in monthly precipitation appeared to be more influential. July 2019 saw the highest rainfall in the past 20 years, coinciding with the onset of the WNV outbreak, which peaked in August.

Several studies have shown that urban environments significantly enhance the epidemic potential of a region and promote WNV circulation. Low-rise residential housing with private gardens located in suburban areas facilitates interaction between urban and rural transmission cycles [9]. Endemic transmission of WNV in urban settings has distinct features. WNV incidence within and around large cities is associated with the "urban heat island" effect, which results in additional warming of artificial and natural water bodies. Krasnodar is located in the Kuban River valley and contains several stagnant water bodies, including the Kuban Reservoir and the so-called Karasun Ponds—remnants of the 19th-century Karasun River—frequented by migratory birds. The city also has many small natural and artificial water bodies. As ambient temperatures rise, stagnant water bodies become enriched with organic material, facilitating mosquito breeding [19, 20]. Mapping of probable infection sites confirmed the epidemiologic importance of intra-urban aquatic habitats and served as the basis for identifying risk zones to guide targeted prevention efforts.

The broad clinical spectrum of WNV infection—ranging from asymptomatic or mild influenza-like illness to severe central nervous system involvement—necessitates identification of risk factors for disease severity. One avenue of investigation focuses on the roles of age and comorbidities. In several studies, age was the only consistent predictor of neuroinvasive disease and mortality [18]. High rates of chronic comorbidities have been reported in patients with severe flavivirus infections. The most common chronic diseases among patients with WNF were hypertension (mean 45.0%, 95% confidence interval 39.1% to 51.0%), diabetes mellitus (mean 24.7%, 95% confidence interval 20.2% to 29.8%), and cardiac disease (mean 25.6%, 95% confidence interval 19.5% to 32.7%). The odds ratio for severe flaviviral disease was 2 to 4 among infected individuals with diabetes mellitus, hypertension, or cardiac disease [21]. In another study, the risk factors for death from WNF included age, malignant neoplasms, coronary artery disease, quadriparesis, mechanical ventilation, and healthcare-associated infections [22]. In our cohort, cardiovascular disease (46.1%)—specifically, hypertension—was the most common comorbidity, recorded only in the group with meningeal forms. At the same time, a consistent association with patient age was observed: cardiovascular disorders were documented only in patients older than 48 years. The overall burden of comorbidity was higher in the group with meningeal forms of disease. Diabetes mellitus, hypertension, immunosuppression, chronic kidney disease, and liver disease in various combinations were noted in 84.5% of these patients.

During the 2019 outbreak, more than half of the affected individuals (57.7%) were under 50 years of age, and a new trend was noted: an increase in influenza-like cases and younger patients. Although older age is typically associated with more severe disease, we found no statistically significant difference in patient age between those with meningeal and influenza-like forms of disease.

A promising direction in the investigation of mechanisms underlying severe courses of infectious diseases is genetic research, which enables the identification of individual differences, including genetic predispositions and immune responses. Specific genetic mutations associated with WNV infection have been identified, including variations in *OAS1* (meta-OR = 0.83; 95% CI, 0.69–1.00) and *CCR5* (meta-OR = 1.29; 95% CI, 1.08–1.53) [5, 23]. These gene associations suggest that immune response mechanisms play a key role in susceptibility to severe disease. Another study of immune response profiles in patients with severe WNF during the acute phase showed elevated proinflammatory markers in innate immune cell types and reduced activity of regulatory T cells, whereas individuals with subclinical disease demonstrated increased expression of genes associated with anti-inflammatory $CD16^+$ monocytes [24].

The absence of typical clinical manifestations, predominance of symptoms related to intoxication syndrome, low public awareness of the risk of mosquito-borne infection, and infrequent reporting of WNF cases over the past 20 years have contributed to both delayed medical consultation and untimely diagnosis, thereby increasing the risk of complicated disease progression. Most patients were admitted to the hospital due to the appearance of generalized or meningeal neurologic symptoms. Meningitis was confirmed by characteristic changes in the cerebrospinal fluid. Routine laboratory tests were nonspecific and mostly reflected the severity of the intoxication syndrome; in some cases, elevated ALT, AST, CPK, LDH, and CRP were noted.

To date, no approved etiologic therapy or vaccine exists for the prevention of WNF. Experimental vaccines based on insect-specific classical flaviviruses are under development for human use [25]. The main preventive measures for WNF remain those aimed at controlling the vector [26].

CONCLUSION

WNF outbreak in Krasnodar, with a peak incidence in August 2019, occurred in the context of increased precipitation in midsummer (July). Reported cases were territorially linked to urban water bodies. Both large reservoirs, such as the Krasnodar and Shapsug Reservoirs, the Karasun Lakes network, and small unnamed water bodies within the city, as well as the growth of the mosquito population and lack of appropriate anti-epidemic measures, had epidemiological significance. The abundance of water bodies makes Krasnodar a favorable environment for WNV spread, whereas the warm mild climate and high humidity create conditions for the formation of an urban endemic focus. Prevention of WNV circulation requires an integrated application of ecological and entomological approaches. The role of the urban habitat of migratory birds and mosquitoes in forming conditions for WNV circulation should not be underestimated. Effective prevention of WNF in urban areas requires development of

DOI: https://doi.org/10.17816/EID636844

comprehensive measures for monitoring natural and artificial water bodies, mosquito control as the main vector, and epidemiological surveillance of areas where migratory and nomadic birds—sources of infection—concentrate.

For timely diagnosis of WNF, detection of WNV RNA in cerebrospinal fluid by polymerase chain reaction and blood testing for WNV-specific IgM antibodies using enzyme-linked immunosorbent assay are necessary. These methods should be included in the comprehensive laboratory examination of patients presenting with clinical signs of meningitis and meningoencephalitis, as well as fever of unknown origin accompanied by catarrhal syndrome, rash, and lymphadenopathy during the summer-autumn period in the southern regions of the Russian Federation.

ADDITIONAL INFORMATION

Funding source. This study was not supported by any external sources of funding.

Competing interests. The authors declare that they have no competing interests.

Authors' contribution. All authors made a substantial contribution to the conception of the work, acquisition, analysis, interpretation of data for the work, drafting and revising the work, final approval of the version to be published and agree to be accountable for all aspects of the work. M.G. Avdeeva, L.P. Blazhnaya: development of the concept and implementation of the study, preparation and editing of the text, approval of the final version of the article; M.I. Kulbuzheva: development of the concept and implementation of the study, preparation and editing of the text, conducting statistical analysis of data, approval of the final version of the article; V.A. Bakhtina, A.A. Vanyukov, A.V. Nezhurin: development of the concept and implementation of the study, preparation and editing of the text, approval of the final version of the article, resource support for the study; K.A. Arzumanyan, N.E. Mishchenko: development of the concept and implementation of the study, preparation and editing of the text, approval of the final version of the article, development of the methodology, preparation of graphic materials, conducting statistical analysis of the data.

REFERENCES

1. Chancey C, Grinev A, Volkova E, Rios M. The global ecology and epidemiology of West Nile virus. *Biomed Res Int.* 2015;2015:376230. doi:10.1155/2015/376230 EDN: UOOCNV

2. Ioannidi EA, Bozhko VG, Smelyansky VP, Bozhko ET. Clinical and epidemiological aspects and treatment of West Nile fever. *Lechebnyy Vestnik.* 2015;9(3):3–7. (In Russ.) EDN: VBNYMX

3. Durand B, Tran A, Balança G, Chevalier V. Geographic variations of the bird-borne structural risk of West Nile virus circulation in Europe. *PLoS One.* 2017;12(10):e0185962. doi: 10.1371/journal.pone.0185962 EDN: YHYLFQ

4. Correa-Morales F, González-Acosta C, Ibarra-Ojeda D, Moreno-García M. West Nile virus in Mexico: Why vectors matter for explaining the current absence of epidemics. *Acta Trop.* 2024;249:107065. doi: 10.1016/j.actatropica.2023.107065 EDN: ORMTUQ

5. Cahill ME, Conley S, DeWan AT, Montgomery RR. Identification of genetic variants associated with dengue or West Nile virus disease: a systematic review and meta-analysis. *BMC Infect Dis.* 2018;18(1):282. doi: 10.1186/s12879-018-3186-6

6. Putintseva EV, Lipnitsky AV, Alekseev VV, et al. Dissemination of the West Nile Fever in the Russian Federation and in the World in 2010. *Problems of Particularly Dangerous Infections*. 2011;(1): 38–41. doi: 10.21055/0370-1069-2011-1(107)-38-41 EDN: NQWIHD

7. Gorodin VN., Nezhurin AV., Zhukova LI. Current aspects of West Nile fever. *Infekc. bolezni (Infectious Diseases).* 2023; 21(1): 140–147. doi: 10.20953/1729-9225-2023-1-140-147 EDN: TXJOHI

8. *From the history of the sanitary-epidemiological service of Russia (briefly about various facts): West Nile fever (WNF) — a viral infection* [internet]. Available from: https://24.rospotrebnadzor.ru/press/100_let_SES/korotko_o_raznom/161013/ Accessed: 15 Jun 2024. (In Russ.)

9. Shartova N, Mironova V, Zelikhina S, et al. Spatial patterns of West Nile virus distribution in the Volgograd region of Russia, a territory with long-existing foci. *PLoS Negl Trop Dis.* 2022;16(1):e0010145. doi: 10.1371/journal.pntd.0010145 EDN: BKVFFY

10. Zhukova LI, Rafeenko GK, Gorodin VN, Vanyukov AA. Clinical and epidemiological characteristics of West Nile fever in the Krasnodar region. *Journal of microbiology, epidemiology and immunobiology.* 2016;93(2):74–80. doi: 10.36233/0372-9311-2016-2-74-80 EDN: ZRJCSN

11. *Annual report* [internet]. Available from: https://www.miackuban.ru/статистика/годовой-отчет Accessed: 15 Jun 2024. (In Russ.)

12. Baturin AA, Antonov VA, Smelyansky VP, et al. The Role of Birds as Potential Reservoirs of West Nile Virus in the Territory of the Russian Federation. *Problems of Particularly Dangerous Infections*. 2012;(4):18–21. doi: 10.21055/0370-1069-2012-4-18-21

13. Paz S, Malkinson D, Green MS, et al. Permissive summer temperatures of the 2010 European West Nile fever upsurge. *PLoS One.* 2013;8(2):e56398. doi: 10.1371/journal.pone.0056398 EDN: RJUNTL

14. Paz S, Semenza JC. Environmental drivers of West Nile fever epidemiology in Europe and Western Asia: a review. *Int J Environ Res Public Health.* 2013;10(8):3543–3562. doi: 10.3390/ijerph10083543 EDN: OJKZDK

15. Weather and climate [internet]. Available from: http://www.pogodaiklimat.ru Accessed: 15 Jun 2024. (In Russ.)

16. Wan G, Allen J, Ge W, et al. Two-step light gradient boosted model to identify human West Nile virus infection risk factor in Chicago. *PLoS One.* 2024;19(1):e0296283. doi: 10.1371/journal.pone.0296283 EDN: TFZUYC

17. Vonesch N, Binazzi A, Bonafede M, et al. Emerging zoonotic viral infections of occupational health importance. *Pathog Dis.* 2019;77(2):ftz018. doi: 10.1093/femspd/ftz018 EDN: SJXHYF

18. Power GM, Vaughan AM, Qiao L, et al. Socioeconomic risk markers of arthropod-borne virus (arbovirus) infections: a systematic literature review and meta-analysis. *BMJ Glob Health.* 2022;7(4):e007735. doi: 10.1136/bmjgh-2021-007735 EDN: HLMAQA

19. Yeung MW, Shing E, Nelder M, Sander B. Epidemiologic and clinical parameters of West Nile virus infections in humans: a scoping review. *BMC Infect Dis.* 2017;17(1):609. doi: 10.1186/s12879-017-2637-9 EDN: LHSYKF

20. David S, Abraham AM. Epidemiological and clinical aspects on West Nile virus, a globally emerging pathogen. *Infect Dis (Lond).* 2016;48(8): 571–586. doi: 10.3109/23744235.2016.1164890 EDN: YWDJXD

21. Badawi A, Velummailum R, Ryoo SG, et al. Prevalence of chronic comorbidities in dengue fever and West Nile virus: a systematic review and meta-analysis. *PLoS One.* 2018;13(7):e0200200. doi: 10.1371/journal.pone.0200200 EDN: YHJQQX

22. Nikolić N, Poluga J, Milošević I, et al. Neurological and neuromuscular manifestations in patients with West Nile neuroinvasive disease, Belgrade area, Serbia, season 2022. *Neurol Sci.* 2024;45(2): 719–726. doi: 10.1007/s10072-023-07025-y EDN: HXODRR

23. Kosch R, Delarocque J, Claus P, et al. Gene expression profiles in neurological tissues during West Nile virus infection: a critical meta-analysis. *BMC Genomics.* 2018;19(1):530. doi: 10.1186/s12864-018-4914-4 EDN: YIWKUX

24. Lee HJ, Zhao Y, Fleming I, et al. Early cellular and molecular signature correlate with severity of West Nile virus infection. *iScience.* 2023;26(12):108387. doi: 10.1016/j.isci.2023.108387

25. Zhang HQ, Li N, Zhang ZR, et al. A chimeric classical insect-specific flavivirus provides complete protection against West Nile virus lethal challenge in mice. *J Infect Dis.* 2024;229(1):43–53. doi: 10.1093/infdis/jiad238 EDN: KOJGIT

26. Cloherty ER, Mcallister JC, Ottea JA, et al. A survey on mosquito control knowledge and insecticide use in New Orleans, La, 2020–2021. *J Am Mosq Control Assoc.* 2023;39(4):243–250. doi: 10.2987/23-7123

СПИСОК ЛИТЕРАТУРЫ

1. Chancey C., Grinev A., Volkova E., Rios M. The global ecology and epidemiology of West Nile Virus // Biomed Res Int. 2015. Vol. 2015. P. 376230. doi: 10.1155/2015/376230 EDN: UOOCNV

2. Иоанниди Е.А., Божко В.Г., Смелянский В.П., Божко Е.Т. Клинико-эпидемиологические аспекты и вопросы лечения лихорадки Западного Нила // Лекарственный вестник. 2015. Т. 9, № 3. С. 3–7. EDN: VBNYMX

3. Durand B., Tran A., Balança G., Chevalier V. Geographic variations of the bird-borne structural risk of West Nile virus circulation in Europe // PLoS One. 2017. Vol. 12, N 10. P. e0185962. doi: 10.1371/journal.pone.0185962 EDN: YHYLFQ

4. Correa-Morales F., González-Acosta C., Ibarra-Ojeda D., Moreno-García M. West Nile virus in Mexico: Why vectors matter for explaining the current absence of epidemics // Acta Trop. 2024. Vol. 249. P. 107065. doi: 10.1016/j.actatropica.2023.107065 EDN: ORMTUQ

5. Cahill M.E., Conley S., DeWan A.T., Montgomery R.R. Identification of genetic variants associated with dengue or West Nile virus disease: a systematic review and meta-analysis // BMC Infect Dis. 2018. Vol. 18, N 1. P. 282. doi: 10.1186/s12879-018-3186-6

6. Путинцева Е.В., Липницкий А.В., Алексеев В.В., и др. Распространение лихорадки Западного Нила в мире и Российской Федерации в 2010 г. // Проблемы особо опасных инфекций. 2011. № 1. С. 38–41. doi: 10.21055/0370-1069-2011-1(107)-38-41 EDN: NQWIHD

7. Городин В.Н., Нежурин А.В., Жукова Л.И. Современные аспекты лихорадки Западного Нила // Инфекционные болезни. 2023. Т. 21, № 1. С. 140–147. doi: 10.20953/1729-9225-2023-1-140-147 EDN: TXJOHI

8. Из истории санитарно-эпидемиологической службы России (коротко о разных фактах): Лихорадка Западного Нила (ЛЗН) — вирусная инфекция [Интернет]. Режим доступа: https://24.rospotrebnadzor.ru/press/100_let_SES/korotko_o_raznom/161013/ Дата обращения: 15.06.2024.

9. Shartova N., Mironova V., Zelikhina S., et al. Spatial patterns of West Nile virus distribution in the Volgograd region of Russia, a territory with long-existing foci // PLoS Negl Trop Dis. 2022. Vol. 16, N 1. P. e0010145. doi: 10.1371/journal.pntd.0010145 EDN: BKVFFY

10. Жукова Л.И., Рафеенко Г.К., Городин В.Н., Ванюков А.А. Клинико-эпидемиологическая характеристика лихорадки Западного Нила в Краснодарском крае // Журнал микробиологии, эпидемиологии и иммунобиологии. 2016. Т. 93, № 2. С. 74–80. doi: 10.36233/0372-9311-2016-2-74-80 EDN: ZRJCSN

11. Годовой отчёт [Интернет]. Режим доступа: https://www.miackuban.ru/статистика/годовой-отчет Дата обращения: 15.06.2024.

12. Батурин А.А., Антонов В.А., Смелянский В.П., и др. Роль птиц как потенциальных резервуаров вируса Западного Нила на территории Российской Федерации // Проблемы особо опасных инфекций. 2012. № 4. С. 18–21. doi: 10.21055/0370-1069-2012-4-18-21

13. Paz S., Malkinson D., Green M.S., et al. Permissive summer temperatures of the 2010 European West Nile fever upsurge // PLoS One. 2013. Vol. 8, N 2. P. e56398. doi: 10.1371/journal.pone.0056398 EDN: RJUNTL

14. Paz S., Semenza J.C. Environmental drivers of West Nile fever epidemiology in Europe and Western Asia: a review // Int J Environ Res. Public Health. 2013. Vol. 10, N 8. P. 3543–3562. doi: 10.3390/ijerph10083543 EDN: OJKZDK

15. Погода и климат [Интернет]. Режим доступа: http://www.pogodaiklimat.ru Дата обращения: 15.06.2024.

16. Wan G., Allen J., Ge W., Rawlani S., et al. Two-step light gradient boosted model to identify human West Nile virus infection risk factor in Chicago // PLoS One. 2024. Vol. 19, N 1. P. e0296283. doi: 10.1371/journal.pone.0296283 EDN: TFZUYC

17. Vonesch N., Binazzi A., Bonafede M., et al. Emerging zoonotic viral infections of occupational health importance // Pathog Dis. 2019. Vol. 77, N 2. P. ftz018. doi: 10.1093/femspd/ftz018 EDN: SJXHYF

18. Power G.M., Vaughan A.M., Qiao L., et al. Socioeconomic risk markers of arthropod-borne virus (arbovirus) infections: a systematic literature review and meta-analysis // BMJ Glob Health. 2022. Vol. 7, N 4. P. e007735. doi: 10.1136/bmjgh-2021-007735 EDN: HLMAQA

19. Yeung M.W., Shing E., Nelder M., Sander B. Epidemiologic and clinical parameters of West Nile virus infections in humans:

a scoping review // BMC Infect Dis. 2017. Vol. 17, N 1. P. 609. doi: 10.1186/s12879-017-2637-9 EDN: LHSYKF

20. David S., Abraham A.M. Epidemiological and clinical aspects on West Nile virus, a globally emerging pathogen // Infect Dis (Lond). 2016. Vol. 48, N 8. P. 571–586. doi: 10.3109/23744235.2016.1164890 EDN: YWDJXD

21. Badawi A., Velummailum R., Ryoo S.G., et al. Prevalence of chronic comorbidities in dengue fever and West Nile virus: A systematic review and meta-analysis // PLoS One. 2018. Vol. 13, N 7. P. e0200200. doi: 10.1371/journal.pone.0200200 EDN: YHJQQX

22. Nikolić N., Poluga J., Milošević I., et al. Neurological and neuromuscular manifestations in patients with West Nile neuroinvasive disease, Belgrade area, Serbia, season 2022 // Neurol Sci. 2024. Vol. 45, N 2. P. 719–726. doi: 10.1007/s10072-023-07025-y EDN: HXODRR

23. Kosch R., Delarocque J., Claus P., et al. Gene expression profiles in neurological tissues during West Nile virus infection: a critical meta-analysis // BMC Genomics. 2018. Vol. 19, N 1. P. 530. doi: 10.1186/s12864-018-4914-4 EDN: YIWKUX

24. Lee H.J., Zhao Y., Fleming I., et al. Early cellular and molecular signature correlate with severity of West Nile virus infection // iScience. 2023. Vol. 26, N 12. P. 108387. doi: 10.1016/j.isci.2023.108387

25. Zhang H.Q., Li N., Zhang Z.R., et al. A Chimeric Classical Insect-Specific Flavivirus Provides Complete Protection Against West Nile Virus Lethal Challenge in Mice // J Infect Dis. 2024. Vol. 229, N 1. P. 43–53. doi: 10.1093/infdis/jiad238 EDN: KOJGIT

26. Cloherty E.R., Mcallister J.C., Ottea J.A., et al. A Survey on Mosquito Control Knowledge and Insecticide Use in New Orleans, La, 2020–2021 // J Am Mosq Control Assoc. 2023. Vol. 39, N 4. P. 243–250. doi: 10.2987/23-7123

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