

Research Article

Addressing West Nile Virus Threats in the Middle East: A Multidisciplinary Approach to Epidemiology, Biosafety, and Biosecurity

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Abstract

West Nile Virus is a rising public health concern in the Middle East, transmitted by the *Culex* mosquito among various hosts including humans, birds, and horses. This complex transmission cycle demonstrates the urgent need for a One Health approach that integrates human, animal, and environmental health for effective surveillance and risk management. However, current surveillance and response systems across the region remain fragmented and inconsistently integrated across these sectors. This review critically examines the current epidemiological landscape, identifies major gaps in surveillance and biosafety, and argues that establishing a regionally coordinated One Health framework is essential to strengthen early detection, improve outbreak response, and enhance biosecurity. By emphasizing the need for further research into the virus's epidemiology and transmission patterns, this paper aims to inform the formulation of prevention strategies that will significantly enhance public health preparedness for West Nile Virus and other emerging zoonotic arboviruses in the Middle East.

Keywords: West Nile Virus; Middle East; Biosecurity; One Health; Epidemiology

1. Introduction

West Nile Virus (WNV) is transmitted by mosquitoes as it infects animals as well as humans. Hence, it is dangerous as it belongs to the Flaviviridae family which comprises 75 different viruses' species. The West Nile Virus is divided into the Japanese Sero-complex, which comprises other viruses like the St. Louis encephalitis virus (SLEV). The West Nile Virus infects birds, horses, as well as humans. However, it originally started in regions like Europe, Africa, the Middle East, and Asia. It causes mild fever in humans. Yet, in rare cases, it causes severe conditions such as encephalitis or paralysis [1-3]. WNV is one of the most widespread arboviruses, found extensively across Africa, the Middle East, parts of Europe, the former Soviet Union, South Asia, and Australia. Before the 1999 outbreak in New York City, it had not been detected in the Americas, but the exact means of its introduction to the United States remains unclear. Early genetic studies pointed to a Middle Eastern origin for the virus in North America; still, later research

suggests that current strains in Europe and Israel may have originated from a common source, which is presumed to be North Africa [4]. This study is considered as an examination of the West Nile virus issue in the Middle East through providing and integrating biological, epidemiological, clinical, and biosafety data through a One Health lens. This review also reports on the non-vector routes of transmission, evaluates the geographic distribution of the virus and its clinical manifestations in humans and animals, and looks for gaps in the current biosafety and control measures. For the purposes of encouraging early detection, halt epidemics, and enhance overall biosecurity readiness, a regionally coordinated single health surveillance and response architecture that integrates environmental, veterinary, and human monitoring systems is severely required. The assessment revealed that the current response to WNV is insufficient and too fragmented.

2. Methodological Framework

To guarantee openness and scientific integrity throughout this review process, a structured narrative review was prepared utilizing a methodical approach. The major scientific databases, such as PubMed, Scopus, Web of Science, and Google Scholar, were used in a formal literature search to find all published studies from 2000 to 2024 that either laid the groundwork for the field or were the most recent to be published on the subject.

Using Boolean operators (AND, OR), the search method narrowed the results by combining relevant terms and phrases such as "biosafety," "biosecurity," "biological risk management," "laboratory containment," "BSL requirements," "pathogen handling," and "regulatory frameworks."

Peer-reviewed publications, official guidelines (e.g., WHO, FAO, EU, CDC), systematic reviews, and English-language regulatory documents that specifically addressed biosafety and biosecurity principles, laboratory standards, or biological risk management systems were all included in the inclusion criteria. The exclusion criteria included research unrelated to laboratory biosafety or biosecurity governance, non-peer-reviewed sources, opinion articles with no scientific basis, and duplicate publications.

A full-text examination of a few selected papers was carried out after titles and abstracts were initially screened for relevance. Definitions, legal frameworks, implementation tactics, and risk management concepts were the main topics of the thematic synthesis of the gathered material. After that, the results were arranged to give a logical summary of the standards, difficulties, and potential future paths in biosafety and biosecurity.

3. Biological and Structural Aspect

Like other Flaviviruses, WNV has a positive single-stranded RNA genome [5, 6]. The C protein is important for viral replication due to interaction with E3 ligases such as HDM2 [7, 8]. The prM protein has been thought to play a vital role in preventing the premature fusion of E-proteins with the host cell membrane [5]. As a transmembrane protein, the E protein plays a key role in maintaining the structural integrity of the viral envelope [9].

At the same time, non-structural protein 1 (NS1) has a significant role to play in the replication and evasion of the immune system [10]. As for the other non-structural protein 2A (NS2A), it's an important factor in the replication process and modulation of host immune response [11, 12]. NS2B and NS3 proteins perform a critical step in the viral replication by cutting or cleaving the flavivirus polyprotein in the onset of clinical infections [13]. NS3 also interacts with NTPase (an RNA helicase) which is critical for RNA replication and viral production; as a result, it has become a target for antiviral drugs because of its critical function in the life cycle of the virus [14, 15]. Differently, the NS4A plays a vital role in the membrane remodeling induced by flavivirus infection supporting the viral replication, this occurs due to the reorganizing the ER membrane and interacting with other protein parts (i.e., NS1, NS4A, NS4B), disrupting the host immune response and enhancing the viral replication and immune suppression [16, 17]. The NS5 is considered the most significant protein in flaviviruses [18], NS5 methyltransferase (MTase) allows the virus to escape the host's innate immune defenses, it also inhibits the translation of interferon-stimulated genes (ISGs) therefore enhancing the virus's ability to evade immune detection [1]. A summary of the virus parts in could be checked in **Figure 1**.

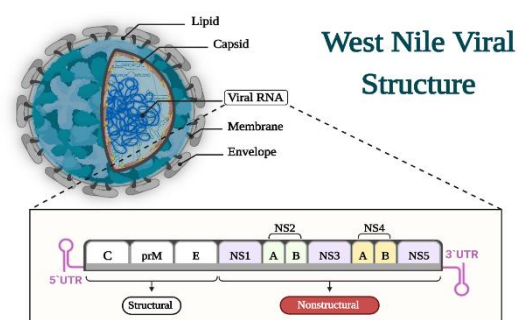


Figure (1). represents the structure and genome of the West Nile Virus (WNV), which consists of a lipid membrane embedded with envelope proteins and enclosing a capsid that protects the viral RNA. It includes structural proteins (C, prM, E) and nonstructural proteins (NS1, NS2A, NS2B, NS3, NS4A, NS4B, NS5), with the 5' and

3' untranslated regions (UTRs) at the end of the RNA [1].

4. Pathological and Transmission Dynamics

WNV begins with a mosquito bite, entering the skin and infecting local cells [19]. First, it binds to specific receptors on host cells and enters via clathrin-mediated endocytosis [20]. Just like other Flaviviridae family viruses such as Zika or dengue, the fusion with the endosome releases viral RNA into the cytoplasm, which moves to the ER for translation within replication complexes that support viral assembly. After forming, immature virions bud into the ER and travel via

the trans-Golgi network, where they are matured by furin cleavage and acidic conditions. Infectious virions are then released when vesicles merge with the plasma membrane [21-23]. It's vital to mention that the Mosquitoes are the primary vectors and also act as intermediate hosts [24]. Refer to **Figure 2** for an overview of the transmission cycle. Non-vector transmission occurs through organ transplants, needlestick injuries, hemodialysis, and blood transfusions from infected donors [25, 26]. Transmission has also been observed in goose farms via contact with infected blood or tissues [27]. Although less common, these routes emphasize the importance of preventive measures.

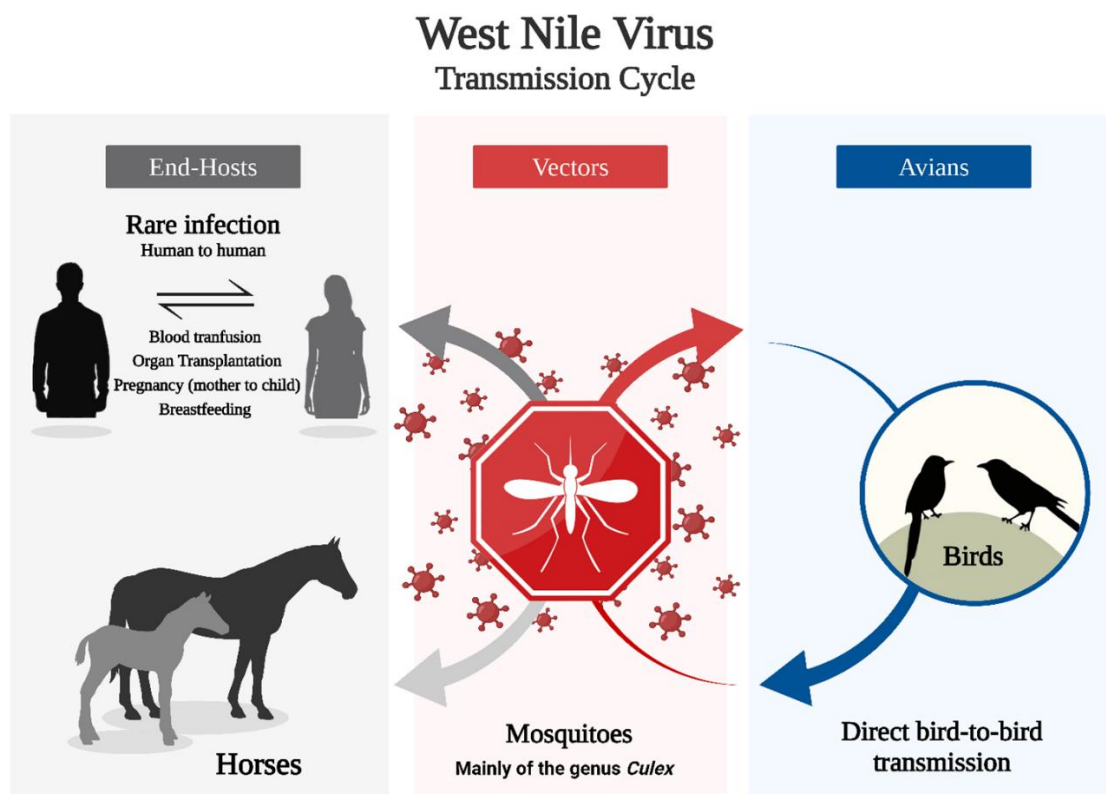


Figure 2. The WNV transmission cycle shows that avian species in the right panel serve as hosts capable of transmitting the virus. In contrast, the left panel shows end-hosts (including humans and horses) that typically do not contribute to further viral transmission. In rare cases, human-to-human transmission can occur through blood transfusion, organ transplantation, pregnancy, and breastfeeding [28].

5. Main Vectors and Hosts

WNV is primarily transmitted by *Culex* mosquitoes, which maintain the virus in bird populations. While other animals (e.g., elephants,

rhinoceroses, lemurs) can be infected, only birds develop sufficient viral levels, making them key reservoirs and amplifiers that infect mosquitoes and indirectly humans and other mammals, which are dead-end hosts [1, 29]. In addition to *Culex*

mosquitoes, other species may act as WNV vectors, but their transmission efficiency is lower and typically limited to localized spread [30]. WNV is present in the Middle Eastern countries, where transmission occurs through mosquito species such as *Culex pipiens*, *Culex perexiguus*, and *Aedes caspius*, which play key roles in spreading the virus among birds, humans, and other animals [31]. The four stages of development for *Culex* mosquitoes start with egg,

larva, pupa, and adults. The first three develop in water, and depending on the circumstances, it takes about 7–10 days to reach adulthood. In order to spread WNV, females lay 100–300 eggs on water. The larvae feed and molt, pupae grow, and adults emerge to seek out blood meals, frequently from birds. As dead-end hosts, humans do not spread the virus to mosquitoes. [32, 33]. Check the details in **Figure 3** about the *Culex* mosquito lifecycle.

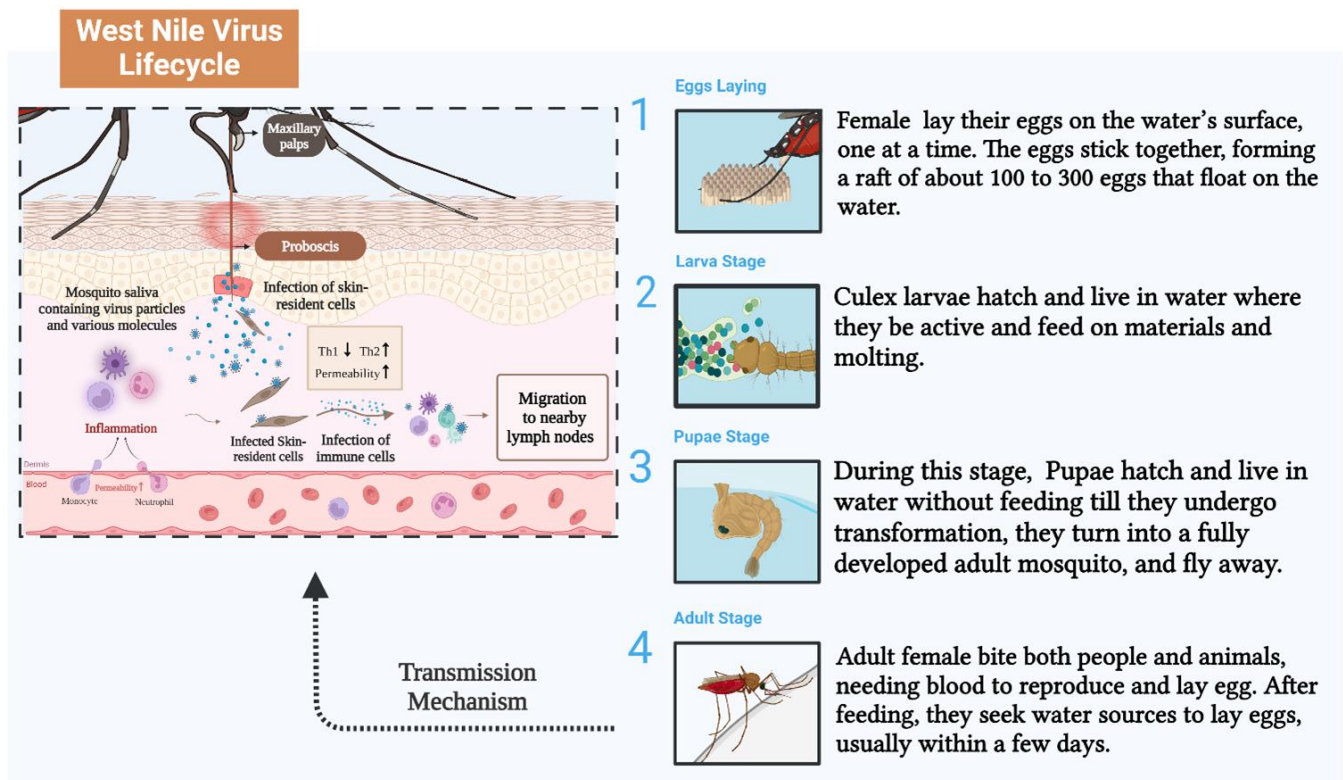


Figure 3. This figure summarizes the four stages of the *Culex* mosquito's lifecycle and their anatomical features. The cycle includes egg-laying on water surfaces; larval development, where they actively feed; a pupal stage characterized by transformation without feeding; and adulthood, where females seek blood meals for reproduction [33]

Infected mosquitoes transmit WNV through saliva (by biting) into the skin, where it infects cells and spreads via lymph nodes. It can cause a variety of diseases in humans, with erythematous macules being the most common skin sign, or more rarely, acute paralysis [34, 35]. Clinical manifestations of WNV vary with host species, age, health, viral strain, and host–virus interactions [1]. In humans, early symptoms include fever ($>38^{\circ}\text{C}$), headache, depression, altered mental state, and personality changes, sometimes with rashes, swollen lymph nodes, or

enlarged liver/spleen. Children, the elderly, and those with chronic conditions are at higher risk. Meningoencephalitis may cause neck stiffness, photophobia, muscle weakness, or paralysis, while gastrointestinal involvement can lead to nausea, vomiting, and loss of appetite [36–38]. However, in susceptible avian species, signs include ruffled feathers, lethargy, ataxia, abnormal posture, flight difficulty, head tremors, seizures, paralysis, and nystagmus [39, 40]. **Table 1** shows further epidemiological details of West Nile virus integration in each host and the clinical manifestation that accompanies it.

Table 1: West Nile Virus Epidemiology and Clinical Presentation

WNV Host	Main vector	Symptoms (May Vary)	Drugs /Vaccine names	References
Human	<i>Culex. tarsalis</i> <i>Culex. pipiens</i> <i>Culex perexiguus</i> <i>Culex quinquefasciatus</i>	Myalgia, malaise, fever, headache, eye pain, vomiting, anorexia, rash, encephalitis, meningitis	Cilnidipine Mycophenolate mofetil Nitazoxanide Teriflunomide	[28, 41, 42]
Avian	<i>Culex. tarsalis</i> <i>Culex thriambus</i> <i>Culex perexiguus</i> <i>Culex nigripalpus</i> <i>Culex quinquefasciatus</i>	Ruffled feathers, lethargy, ataxia, abnormal posture, difficulty flying, seizures, leg paralysis, nystagmus	WNV RSP ChimeriVax-WN WNV-DNA-1/2 pVWN	[28, 39, 40, 43]
Equid	<i>Culex. pipiens</i> <i>Culex perexiguus</i> <i>Culex quinquefasciatus</i> <i>Aedes albopictus</i>	Ataxia, circling, hind limb weakness, limb paralysis, muscle fasciculation, proprioceptive deficits, blindness, fever, acute death, and neurological disease	West Nile-Innovator (Killed virus vaccine) Prestige WNV (Recombitek WNV) PreveNile (Inactivated flavivirus chimera vaccine)	[28, 43-45]

6. Geographical Distribution in The Middle East

West Nile virus (WNV) was first identified in Uganda's West Nile district in 1937 and was isolated from a febrile woman from which the virus derives its name [46]; it had been present in Africa, the Middle East, and South Asia for over 60 years before it reached the Americas. Initially isolated from a person with mild illness, WNV was not linked to deaths in early outbreaks. Although its introduction to the Americas allowed researchers to track its spread, epidemics in Africa and surrounding regions were thought to have occurred before the recognition of clinical cases. A serosurvey in 1939-1940 revealed widespread human exposure to WNV in Uganda, Sudan, the Democratic Republic of Congo, and Kenya, with over 50% seropositivity in some areas. Additional seropositivity was later found in Nigeria, South Africa, and among various animals, indicating the virus had been circulating across much of Africa long before clinical cases were documented [47]. **Table 2** displays cases from Middle Eastern countries with WNV-reported cases using clinical and experimental data.

6.1 Iraq

In the city of Nasiriyah in Iraq, scientists sought to understand the arbovirus infections by examining approximately 399 serum samples collected in the country in 2012–2013. The researchers established the high seroprevalence of mosquito-borne flaviviruses, such as the West Nile virus (WNV), in the southern regions of Iraq at approximately 11.6%. These statistics are similar to those reported in neighboring countries such as Turkey, Jordan, and Iran. The identification of the key mosquito vectors for the WNV, which are the *Culex pipiens* and *Culex quinquefasciatus*; indicates the high seroprevalence of the virus in the region. The virus could be the reason for the feverish illnesses and the neurodegenerative conditions reported in the region. The environmental conditions in Iraq are also conducive to the transmission of the virus. The identification of the two mosquito species in the city indicates the potential for the transmission of the virus in the region. The virus could be transmitted in areas with standing water where mosquito populations are high. However, because the country has limited diagnostic services, the region is likely to have a high

seroprevalence of the virus, which needs to be addressed [48]. The frequency of illnesses like dengue fever and malaria in Iraq is a major factor in vector control initiatives, with government-run public health and sanitation initiatives being crucial. The primary strategies include the use of chemicals like insecticides and larvicides, physical and mechanical tactics, and some biological controls. However, the market is challenged by a lack of resources and an inadequate infrastructure for waste management, which makes it easier for pests like rodents and mosquitoes to breed [49].

6.2 Qatar

A research investigation of blood donors conducted in Qatar determined the WNV antibody levels were as follows: 10.4% (IgG) and 3.3% (IgM). Sudanese (37%) and Egyptian (33%) blood donors had the highest number of WNV antibodies, while blood donors from Qatar and Lebanon had the least. Some of the variables contributing to WNV transmission are as follows: international travel, migratory birds, and mosquito populations, specifically *Culex* species mosquitoes [50]. Camels in the area may play a role as hosts for the virus, according to another study that examined them for WNV antibodies and found a 10% seropositivity rate, indicating that camels there could be susceptible to the infection—though at a lower rate than other species studied [51]. 23.5% of the 260 horses in another research had WNV-pE antibodies, indicating prior exposure, but no new WNV infections were discovered (all tested negative for IgM). Thoroughbreds were twice as likely to exhibit seroconversion as mixed breeds, indicating a connection between horse type and WNV exposure. Seroprevalence varied across six locales (10–35%) [52]. In order to combat the West Nile virus, Qatar has implemented a proactive approach that prioritizes early detection, coordinated vector surveillance, and preventive control measures. In addition to strengthening laboratory diagnostic capabilities and raising public awareness of environmental sanitation and personal safety, health and veterinary authorities regularly monitor mosquito populations and possible animal hosts. These efforts are led by the Ministry of Public Health in

collaboration with relevant municipal and animal health sectors to reduce transmission risk and respond promptly to any suspected cases[53].

6.3 Jordan

About 8% of participants in Jordan showed evidence of past West Nile virus (WNV) infection, with no cases of active infection. Some studies though have found that the infection rates were slightly higher in females and seemed linked to factors like age, income, domestic animals and mosquito bites, though none were statistically significant. The only markable risk factor was living within 2 km of a wastewater treatment plant, where participants were four times more likely to have been infected [54]. Meanwhile, other studies revealed that males were 1.73 times more prone to be infected than females, and older adults had significantly higher odds of infection than younger individuals, as WNV seroprevalence of 8.61% indicating its circulation in the region. Factors influencing seropositivity included gender, age, geographical location, household income, and drinking water sources, those living in the Jordan Valley and Badia regions showed dramatically increased odds of infection, as did individuals with lower household incomes and those using spring lakes for drinking water [55]. Additionally, a study reported clinical cases of WNV infection in horses in Jordan, and in late 2012, two mares displaying neurological symptoms tested positive for WNV IgM antibodies and recovered after symptomatic treatment. Following these cases, 253 healthy horses were surveyed across five regions. Although none had an active WNV infection, the seroprevalence was 24.9%. The Jordan Valley and Balqa region had the highest prevalence of horses, and the region's hot, humid climate encouraged mosquito activity and participation in polo were risk factors [56]. Monitoring, early detection, vector management, and cross-sector collaboration are the pillars of the Ministry of Health's (MoH) all-encompassing strategy to battle the West Nile virus. It involves increasing lab testing, providing free diagnoses, and keeping an eye out for suspicious cases at strategic areas. Prevention efforts target mosquito mapping and control in high-risk areas, coordination with the Ministries of Agriculture, Environment, and

Local Administration, public awareness campaigns, healthcare staff training, and monitoring migratory and wild birds to reduce transmission and prevent outbreaks [57]. The Jordan Center for Disease Control (JCDC) has strengthened national preparedness by assessing public health risks, establishing rapid response teams, providing specialized training, and advancing ongoing studies and evaluations on vector control and mosquito-borne diseases in collaboration with international partners [58].

6.4 Lebanon

A study conducted in Lebanon investigated the occurrence of WNV among blood donors at Hôtel Dieu de France University Hospital in Beirut. The study had approximately 640 participants, mostly from Central Lebanon, with some participants also coming from Beirut. The study participants were mostly people who spent a lot of time outdoors, such as those involved in fishing, hunting, and camping. From the study, six participants were found to be positive for WNV IgG antibodies, with the positive participants being confirmed through a seroneutralization test. The study participants were all males, with ages ranging from 22 to 43 years. The study participants were also all involved in outdoor activities such as hunting and camping. The study found a low WNV incidence rate of around 1 out of 200, in contrast to other neighboring nations like Israel, where WNV has been rising. [59]. Later, in 2021, serological screening was done on human, horse and chicken sera collected from the Bekaa and North districts to investigate the potential circulation of WNV around, the screening revealed a seroprevalence of 1.86% among humans and 2.47% among horses; however, cross-reactivity suggests the presence of other flaviviruses in the region, highlighting a complex viral landscape. The study was also the first to document WNV occurrence in horses in Lebanon and the need to be on the lookout for emerging zoonotic diseases in both animals and humans [60].

6.5 Saudi Arabia

A research that was conducted in Saudi Arabia between 2013 and 2015 found that 200 horse serum samples were positive for WNV

circulation. Al-Qateef (55.6%) and Al-Jubail (60%) had the greatest seroprevalence, whereas Riyadh had 17.3%, perhaps due to environmental variables [61]. Saudi Arabia has implemented a coordinated national plan to prevent and control West Nile virus, centered on active surveillance of horses and mosquito vectors, routine laboratory testing, strict quarantine and import regulations for equines, vector control measures in high-risk areas, and public awareness campaigns [62]. The Weqaa Center in Saudi Arabia monitors and controls disease vectors in order to protect animal and public health under a One Health framework. The National Center for the Prevention and Control of Plant Pests and Animal Diseases play a central role through continuous surveillance, integrated prevention programs, research on vector biology, farmer education, coordination with organizations such as the World Organization for Animal Health, and rapid outbreak response measures [63].

6.6 Palestine

Equids (horses and donkeys) had the highest rates (~73%) of WNV seroprevalence in 717 household animals, according to a recent survey conducted in Israel and Palestine. Israel had a significantly greater seroprevalence (84.6%) than Palestine (48.6%), perhaps as a result of vegetation and rainfall. The results demonstrate that geography, climate, species, and age all influence WNV infection rates in domestic animals and suggest possible cross-species transmission [64]. The World Health Organization supported the Ministry of Health in launching a two-phase response plan. The early steps focused on vector control using spraying in and around Jenin camp, together with awareness campaigns and guidance to the medical community. The effort subsequently expanded with an emphasis on enhancing public health education and surveillance systems to provide for early detection and response. In addition to helping expedite the distribution of diagnostic kits and providing nutritional education materials, in order to improve health workers' preparedness and capacity to handle mosquito-borne infections, WHO has also arranged seminars. This emphasizes the necessity of constant observation

and cooperative initiatives to lessen the impacts of diseases spread by mosquitoes [65].

6.7 Egypt

Research conducted in Egypt examined donors' levels of WNV antibodies and RNA in order to determine the risk of WNV transmission through blood donations. Among 160 blood donors tested, (~ 55%) were found to have anti-WNV IgG antibodies. A higher prevalence of WNV seropositivity was observed in donors from rural areas and the Nile Delta region compared to other regions, suggesting that individuals in these areas may face a greater risk of WNV exposure, highlighting the importance of monitoring WNV in blood donations to prevent transmission through transfusions [66]. A prospective cohort study in Egypt further investigated the prevalence and incidence of WNV across various regions, including upper, middle and lower areas, as well as North and South Sinai. Human seroprevalence rates vary by region, with the highest in Upper Egypt (35%) and the lowest in North Sinai (1%). Seroconversion rates in upper, middle and lower Egypt ranged from 7% to 18%, with nearly half of seroconverts reporting undiagnosed febrile illnesses. The virus was also detected in sentinel chickens and mosquitoes, confirming its active circulation during the study period. All this evidence highlights the widespread presence of WNV in Egypt and its contribution to febrile illness [67]. Egypt was reported that it has strengthened its prevention strategy by tightening health screening at airports, seaports, and land borders, activating quarantine monitoring, referring suspected cases to hospitals, and requiring aircraft arriving from affected areas to conduct insect control measures to prevent the introduction of the virus [68]. Although specific surveillance and response techniques conducted by Egypt were not previously stated regarding the control of WNV, Egyptian authorities implemented a range of coordinated measures to eliminate malaria (which is a mosquito-borne virus), including early environmental interventions such as restricting rice cultivation and other crops near residential areas to reduce mosquito breeding sites. The government strengthened national surveillance by officially classifying malaria as a notifiable disease and

establishing specialized research and control centers to support monitoring and scientific investigation. Large-scale epidemiological surveys were conducted to map disease prevalence and guide control strategies. Authorities have put in place rapid response strategies for epidemics that help to quickly identify and diagnose cases, ensure that patients receive immediate treatment, create an awareness of the disease within the public, and implement targeted mosquito control measures to reduce the spread of the disease to the communities that have been infected. [69]. Despite existing policies addressing vector-borne diseases and climate-related risks, Egypt still needs stronger surveillance, improved identification of high-risk populations, better international coordination, enhanced pathogen detection, expanded environmental control measures, and greater health system capacity supported by multidisciplinary training and public awareness programs [70].

6.8 Iran

Finally in Iran, a study focused on the risk of WNV transmission via blood transfusions and was assessed in a retrospective study investigating the virus infection in 540 blood donors from Chabahar. The IgG antibodies of the virus were detected using ELISA, and 17.96% (97 donors) tested positive but only 1.48% (8 donors) remained positive after further confirmation using immunofluorescence assay (IFA); this means that only 8.24% of the initial ELISA results were confirmed. These results highlight the importance of refining the criteria used for selecting blood donors, as a positive test for IgM antibodies found in blood donors can sometimes reflect prior infection instead of exposing the donor to subsequent risk of infection [71]. A study conducted in Mashhad in 2015 used ELISA testing methods to look at WNV seroprevalence from blood donor donations. The study included 182 individuals, and the findings indicate that 11% of the samples tested had IgG antibody levels consistent with exposure history. Since none of the samples contained measurable IgM levels, the authors concluded that none of the individuals had a new infection. All this accentuating the need for healthcare professionals to be vigilant about the

virus in this region [72]. Iran's approach to managing West Nile Virus involves a surveillance system that tests for the virus in encephalitis cases, which has revealed a "silent circulation" of WNV, especially in southern provinces where many people have been exposed without showing

severe symptoms. To control its spread, the country's primary defense is not based on treatment but on prevention, focusing on vector control and public education to raise awareness on avoiding mosquito bites [73].

Table 2: Geographical Distribution of WNV In the Middle East with Clinical Data of Reported Cases

Country	Seroprevalence Rate	Detection Tool	Host	Vector	# of Cases	Reference
Jordan	8.61% - Humans 24.9% Horses	• ELISA	Humans Horses	<i>C. pipiens</i> <i>C. quinquefasciatus</i>	801/Human 253/Horses	[55, 56]
Palestine-Israel	Israel (84.6%) and Palestine (48.6%).	• ELISA	Equids	N/A	717/Equids	[64]
Iraq	11.6%.	• ELISA	Humans	<i>C. pipiens</i> <i>C. quinquefasciatus</i>	400/Human	[48]
Lebanon	1.86% (Humans) 2.47% (Horses)	• ELISA • PRNT	Humans Horses	<i>C. pipiens</i>	202/Horse 1091/Human	[60]
Iran	8.24% in Chabahar 11% in Mashhad	• ELISA • IFA	Humans	N/A	540/Human 182/Human	[71, 72]
Egypt	35%, UE 27%, ME 14% LE 1% NS 7% UE	• ELISA • PRNT • IFA	Humans	<i>C. Antennatus</i> <i>C. Perexiguus</i> <i>C. Papiens</i>	160/Human ~6000/Human	[66, 67]
Qatar	10.4% specific IgG 3.3% IgM antibodies Total: (1-26)%	• ELISA	Camels Humans Horses	<i>C. Papiens</i>	29/Camel 1,948/Human 260/Horse	[50-52]
Saudi Arabia	17.3% in Riyadh 55.6% in Al-Qateef	ELISA	Horses	N/A	200/Horses	[61]

7. Biosafety and Biosecurity Strategies Against West Nile Virus

Although Biosafety and biosecurity are connected, they operate separately under legal and regulatory frameworks as both are designed to ensure dangerous pathogens remain within designated areas but address different concerns. Biosafety is the collection of guidelines, procedures, and protective measures used in laboratory settings to minimize the risk of exposure to infectious agents and to prevent their

accidental release, thereby safeguarding personnel and the community [74]. On the other hand, Biosecurity is an integrated framework of policies and regulations aimed at managing risks to food safety, public health, animal and plant health, and the environment [75]. Furthermore, surveillance programs of WNV are designed to monitor the spread of the virus from one vector to another, it involves testing the mosquito population for any WNV, monitoring dead birds, testing other animals like horses, and keeping track of human infections. The data is then

analyzed to identify the areas where the virus is more prominent, as well as the success of control measures in them. All these activities are to ensure early detection and response to any possible outbreak, hence promoting public health [76]. Laboratories that study emerging pathogens are a growing global health concern, because even with risk awareness the workers there are still at high risk of infection if not being careful and strict. Their increasing number is critical evidence for the need of strict adherence to biosafety measures to prevent and protect any lab-acquired infections or mistakes. Therefore, ensuring that only well-trained workers could deal with these pathogens and to recognize the risk of transmission is important, as well as having adequate facilities, procedures, and of course, waste management in labs to ensure the safety of both the workers and the public from any possible exposure [77, 78].

It's important to understand the biosafety levels as they rank from 1 to 4, corresponding to the increasing level of danger posed by the biological agents being handled. First, the BSL-1 as an elementary, posing little risk and it does not require specialized containment equipment but must implement basic safety measures; BSL-2 requires personal protective equipment and restricted access due to potential risks; BSL-3 involves high-risk agents, necessitating controlled environments and stringent safety procedures; and finally BSL-4, for the most hazardous agents which imposes strict safety protocols like the use of full-body protective suits and highly secure facilities [79, 80]. The West Nile virus can cause severe and fatal diseases, and there are no treatments for such severe cases yet, most of the work with this virus was done in a biosafety level 3 environment. Its first recording dates to 1999 in the USA; recently, however, there has been a shift in the USA and the virus is now able to be handled at a lower biosafety level as it has become widespread and generally causes only mild symptoms [81]. Part of the safety measures for laboratory personnel working with WNV involve them wearing protective clothing, gloves, face shields, and gowns so as not to be exposed directly to infected samples. It is recommended to avoid contact between their skin or mucous membranes and any WNV, contaminated tissues

or fluids, follow good sharps management procedures and dispose of biohazardous materials properly. It is also crucial that they wash their hands very well after taking off their protective gear and if possible, limit the production of aerosols during work; employers have to provide sufficient training and keep an eye on their employees for any signs of WNV exposure or symptoms of illness [82]. Some prevention paths focus on avoiding mosquito bites through repellents, protective clothing and/or reducing mosquito habitats. No specific antiviral treatments or vaccine are available in humans against WNV yet as most people recover without medical intervention, but those with severe symptoms (e.g., encephalitis or meningitis) often require hospitalization [76]. In some laboratories settings, a high-dose Ribavirin and interferon- α 2b have shown effectiveness against West Nile Virus (WNV) but no clinical trial evidence confirms their efficacy in humans. Most treatment is supportive, focusing on fluids, pain relief, and breathing support in severe cases. Complications and subsequent infections are additional potential healthcare needs for hospitalized patients. To reduce transmission, public health efforts target mosquito control through monitoring, insecticides, and eliminating standing water where they breed [83]. Recent research of four FDA-approved drugs: cilnidipine, mycophenolate mofetil, nitazoxanide, and teriflunomide, were effective against WNV infection in human cells significantly reduced the infection in Vero and human neuroblastoma SH-SY5Y cells; thus, nitazoxanide and teriflunomide demonstrated the highest potential, showing antiviral effects in both cell lines and protecting some mice from lethal infection challenges [42]. These findings mainly suggest their promise as treatments for WNV in humans although further clinical studies are required to confirm their safety, efficacy, and optimal therapeutic use.

Managing the virus effectively requires collaboration across all levels of government, including structured programs to monitor mosquito populations, track wildlife, and raise public awareness about disease risks. There are challenges to be addressed, including how to adapt to the endemic presence of the virus while

adhering to international regulations. Although maintaining an updated surveillance system and implementing proper control measures is an ongoing need for the protection of public health against disease-causing agents [84], the implementation of biosafety and biosecurity is being hampered in the Middle East by limited infrastructure, political instability, and limited resources. Additionally, many countries do not have complete regulatory systems in place to adequately enforce safety measures and there are insufficient training or qualified personnel available for effectively managing biological risk, making certification of laboratory equipment difficult. These issues are further compounded by the presence of high-threat pathogens coupled with a need for improved control mechanisms [50, 85].

8. One Health Approach and WNV

The One Health concept highlights the mutual dependence of environmental, animal, and human health, particularly with regard to zoonotic illnesses like WNV. It involves coordinated surveillance systems that track the virus by testing mosquitoes, monitoring bird populations (the main reservoirs), and observing human cases to better understand its spread. Since WNV mainly circulates between birds and mosquitoes, with humans and other animals as incidental hosts, this approach emphasizes collaboration in surveillance, vector control, and vaccination efforts [76]. Please refer to Figure 4 for a visual summary of One Health Approach.

Monitoring is essential for the early identification and management of WNV epidemics. By integrating data from humans, mosquitoes, birds, and other animals, reactions may be made more quickly, protecting people by

seeing threats before the virus spreads [76, 84]. For example, countries can implement bird and mosquito testing alongside human clinical monitoring and weather change through the One Health approach since it can favor the mosquito vector population, providing comprehensive insight into WNV transmission dynamics [86]. There is no available WNV vaccine for humans, but developing an effective vaccine remains a high priority. Under a One Health framework, the strategy for vaccine deployment could initially focus on equine populations and other susceptible species to WNV and serve as sentinels in some cases [34]. Vaccinating horses could reduce the incidence of disease in animals and potentially lower the overall viral burden in areas where both human and animal transmission risks are high, as evidenced in studies conducted in the United States of America (USA) [87]. Also, effective mosquito control measures, including habitat management, insecticide application, and community engagement, reduce WNV vectors' prevalence in urban and rural areas [88]. Finally, collaborative research and policies across countries could enhance preparedness and response to WNV, cross-border data sharing and collaborative policymaking, which is essential in regions where migratory bird patterns can spread WNV across national borders, as suggested in Europe [34]. In Middle Eastern cases, many countries have plans to go against WNV. For example, Egypt plans to improve its communication locally and globally to identify pathogens and infections around the country; Turkey focused on the vulnerable target group of agriculture workers when no other country-specific risk group for the virus, and occupied Palestine aims to improve vector management regulations regarding environmental changes [89].

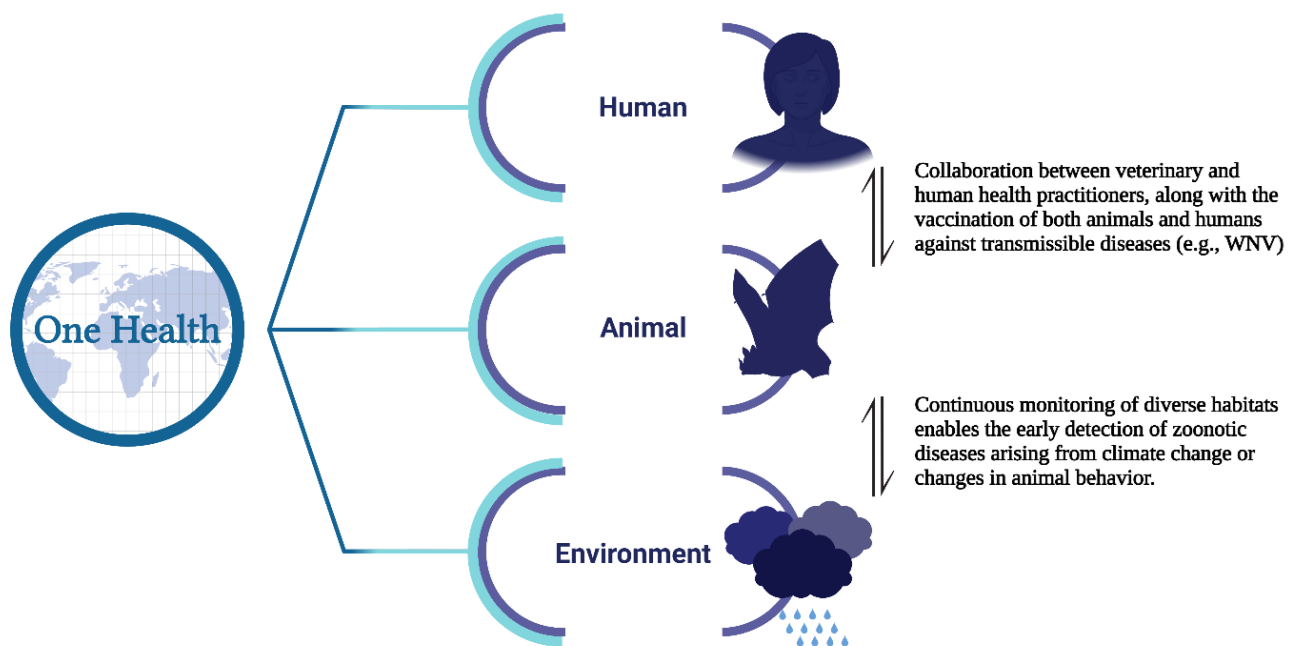


Figure 4. This graph explains the interconnectedness between humans, animals, and the environment in the One Health Approach, which helps detect earlier zoonotic diseases and promotes collaboration between practitioners and scientists [1].

9. Recommendations for Regional One Health Framework and Surveillance

There are many interventions that could enhance WNV management and control in the Middle East. To strengthen the One Health approach, it is crucial to advance beyond informal agreements by establishing formal governance architecture with a supporting legal framework that institutionalizes collaboration between human, animal, and environmental sectors. To guarantee a truly coordinated response, this structure should be backed by a specialized regional workforce or technical body in charge of managing shared data platforms, standardizing standards, and increasing capacity. Proactive risk communication and community involvement should also be part of the strategy for the purpose of making the public active participants in surveillance and prevention. This strategy creates a more robust and long-lasting defense against zoonotic diseases like the West Nile Virus [90]. Implementing a One Health framework in the Middle East based on the Italian model that was proposed to evaluate the extent of the One Health

implementation in Italy, the region should first establish a cross-border committee with representatives from public health, veterinary, and environmental sectors to define unified surveillance goals for West Nile Virus. Addressing the communication and learning gaps that the Italian research highlighted as problems quickly, it must next establish a centralized data-sharing platform and standardized training programs. To ensure continuous improvement, this new framework should be periodically evaluated using the same quantitative "One Health-ness" scoring method, allowing leaders to systematically identify and strengthen the weakest parts of their integrated strategy [91]. As the Centers for Disease Control and Prevention (CDC) advises, the construction of an integrated strategy for West Nile Virus based on a staged response plan should incorporate the appropriate actions to be taken depending on the level of risk. Initially, complete and integrated surveillance systems should actively monitor mosquito populations, as well as wildlife populations, (species of birds in particular via carcass reporting) and horses, thereby providing information on the presence of the virus before

humans become infected. As the likelihood of an epidemic rises, changes in environmental surveillance should lead to additional vector control activities such as controlling the habitats of vector developing (e.g., controlling larval habitats) and applying larvicides/adulticides as appropriate. Crucially, this tiered response must be supported by a strong public communication and community engagement program that educates on personal protection, encourages residential source reduction, and clearly communicates the reasons behind any emergency control operations.

10. Conclusion

In the Middle East, the West Nile virus (WNV) is a chronic but little-known public health threat. It is produced by complex interactions between mosquito vectors, bird reservoirs, environmental variables, and human populations. Despite increasing evidence of ongoing viral circulation and variable seroprevalence rates in both humans and animals, regional preparedness remains fragmented. This is largely due to significant gaps in diagnostic capacity, vector surveillance, and biosafety infrastructure, which weaken early detection and response efforts.

This review argues that the absence of a coordinated One Health framework is a critical vulnerability. Therefore, establishing a regionally integrated strategy is essential for strengthening preparedness. A central priority should be integrated surveillance systems that simultaneously monitor human infections, animal hosts, and mosquito populations to enable early detection. This must be coupled with an expansion of laboratory capacity and biosafety governance, including improved BSL-2/BSL-3 infrastructure and harmonized regulatory standards. At the policy level, sustainable vector control programs and enhanced regional cooperation—through joint surveillance platforms and coordinated response mechanisms among Ministries of Health, Agriculture, and Environment—are critical to addressing the transboundary nature of WNV and transforming fragmented national responses into a unified, effective regional strategy.

Author Contribution

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