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West Nile Virus- A Neuroinvasive Disease

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INTRODUCTION

The world's population is growing at an alarming rate, posing the greatest threat to animals and their environments. Rapid urbanization is a major contributor to global warming and irreversible factors such as increased human-animal interactions, deforestation, and increased resistance to antimicrobials (Mwangi et al. 2016). These factors lead to the transmission and emergence of infectious diseases that primarily affect humans, animals and the environment (Thompson and Polley 2014). About 60% of the emerging humans' diseases are zoonotic in nature, and more than 70% are patented by wildlife species (WHO 2010).

West Nile virus (WNV) is a mosquito-borne neurotropic disease transmitted to humans via infected mosquito bite (Kramer et al. 2007). It is a significant disease that has a major public health concern worldwide (Granwehr et al. 2004; McVey et al. 2015). Firstly, it was reported in 1937 in Uganda. It has been transmitted in the outskirts of the Middle East, Africa, Russia, and Europe for more than 60 years (May et al. 2011). West Nile virus (WNV) belongs to the family Flaviviridae, which includes three genera. It incorporated 3 important viruses including Dengue virus (DENV), yellow fever virus (YFV) and West Nile virus (WNV). Flaviviruses that are transmitted by mosquitoes are largely habitat dependent. The most common is *Culex pipiens*. (Bredenbeek et al. 2003).

Furthermore, the WNV virion is approximately 50 nm in diameter and its single copy is embedded within multiple copies of the capsid protein. Its genome consists of 11,000 nucleotides (Klema et al. 2015). WNV consists of the enveloped single-stranded positive-sense RNA genome of the virion. The genome is a single 11 kb open reading frame and lacks a polyadenylation tail at the 3′ ends of the genome. The genome has noncoding regions at both the 3' and 5' ends that form perfect loop structures for replication processes including transcription, translation, and packaging. The virus tends to occupy a membrane envelope and the nucleocapsid contains the viral genome (Khromykh et al. 2001). Moreover, WNV infection has been reported in over 150 species of birds and animals, such as dogs, wolves, horses, goats and squirrels (Nosal and Pellizzari 2003).

Historical Significance

West Nile virus (WNV) was first identified in febrile patients in the West Nile region of northern Uganda in 1937. This patient was seen as part of a pivotal epidemiological study of the yellow fever virus. However, when mice were injected with the patient's serum, viruses with similar characteristics to her two flaviviruses, St. Louis encephalitis virus, and Japanese encephalitis virus, were isolated and shared immunological links with these viruses. These initial experiments with the newly found virus showed that the disease largely impacted the central nervous system (CNS), indicating its neurotropic nature, even though the index patient initially appeared with fever (Smithburn et al. 1940).

In-depth descriptions of the epidemiology and ecology of WNV were initially made during several outbreaks in the Mediterranean basin in the early 1950s and 1960s. In 1951, a little village in south of Haifa in Israel had the first known outbreak of WNV. There were 303 residents over there, and disease was confirmed in 123 patients with no fatalities. The bulk of the cases was in children under the age of five. The different clinical characteristics of the illness during this epidemic curve were first thoroughly characterized with the primary symptoms of fever, headache, myalgias, anorexia, stomach discomfort, exanthems and vomiting. Symptoms like lymphadenopathy, angina, and diarrhea were less frequently observed (Murgue et al. 2001).

Between 1951 and 1954, several significant outbreaks in Egypt enhanced the knowledge of ecology, epidemiology, and clinical features of WNV (Taylor et al. 1956). In 1950, WNV was found in the blood of many adolescents, and because of the high seroprevalence, it was detected among

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residents of villages in north of Cairo (Taylor et al., 1956). Extensive studies on WNV have been conducted yet. The research began in 1950 in the Upper Nile Delta region. Investigations included human and animal serosurveys, isolation and characterization of viral vectors, experimental infections of birds, horses, arthropods and humans and ecological evaluations. The study results have greatly improved the understanding of many clinical and epidemiological aspects of the virus. Results of serosurveys showed that WNV was endemic along the Nile, with seroprevalence approaching 60%. Younger children reported more symptomatic disease, but older children and adults appeared to have higher seroprevalence, indicating that WNV was primarily an early childhood infection. Infections were often febrile and self-limited with a low risk of meningitis or encephalitis (Philip and Smadel 1943; Sejvar 2003).

Transmission

Culex mosquitoes act as the main vectors of WNV. However, other mosquito species may also be involved. Mosquito bites are the main cause of WNV infection in vertebrate hosts. More than 300 bird species serve as natural breeding hosts for approximately 100 species of mosquitoes that are the main carriers of WNV. Other animals, including horses and humans, are casual hosts with low viremia and are not involved in the infectious cycle (Fig. 1).

The natural reservoir hosts for WNV include house finches, grackles, sparrows, and corvid species (crows, jays, and magpies). They get WNV from mosquitoes, and birds that eat insects infected with the virus (Davis et al. 2006). Mosquito species differ in their ability to act as disease vectors, feeding on diseased hosts and spreading illness to susceptible hosts (Reisen et al. 2005; Turell et al. 2005). Additionally, the specific mosquito species' host preferences significantly affect the transmission patterns. As an illustration, Culex species often prey on birds, but Aedes and Ochlerotatus species prefer to prey on mammals (Bohart and Wishino 1978; CDC 2003). Some infected mosquitoes don't like to bite birds; this increases the risk of infection in people and other animals. Most mammals do not seem to be involved in the enzootic spread of the virus because when an infection occurs, viremia develops, but it is insufficient for further distribution. Subsequently, these types of hosts may or may not develop the clinical symptoms of the disease, and these hosts are referred as dead-end hosts (Bohart and Wishino 1978).

WNV can potentially spread to humans and animals through non-mosquito-borne routes. Mice exposed to WNV in an investigation transmit the virus through the placenta (Julander et al. 2006). The possibility of WNV spreading directly to the host has been shown by various investigations using experimentally infected animals (Klenk et al. 2004; Although the risk is still incredibly low, the infection has also occurred following the transfusion of blood products contaminated with WNV (Pealer et al. 2003: Stramer et al. 2005). It has also been shown that contact transmission occurs in commercial geese farming. It was believed to be linked to cannibalism and picking at afflicted birds' feathers (Banet-Noach et al. 2003). According to a study, alcoholism was identified as a significant potential cause of WNV infection (Lindsey et al. 2012). WNV infection can also be spread through organ transplants and a blood transfusion from people who have already contracted the virus (Yango et al. 2014). Additionally, the transmission via faeco-oral mode has also been verified (Klenk et al. 2004).

Pathogenesis

While the majority of WNV infections are asymptomatic, seroprevalence studies suggest that 20 to 30 percent of infected individuals have WNV fever and a flu-like disease (Petersen and Marfin 2002; Watson et al. 2004). Nearly, 1 in 150 individuals in a subgroup gets a neuroinvasive condition (Petersen and Roehrig 2001; Weaver and Barrett 2004). Only a few clinical signs of a severe WNV infection include a severe headache, visual abnormalities, muscular weakness, cognitive impairment, tremors, and flaccid paralysis resembling poliomyelitis (Bakri and Kaiser 2004). According to O'Leary et al. (2004), 50% of patients who experience neurologic long-term consequences and 10% of patients who develop neuroinvasive illnesses die (Klee et al. 2004). Elderly people infected with WNV become immunocompromised and are at risk of developing fatal encephalitis (Lim et al. 2011). Understanding the etiology and dissemination mechanisms of WNV has been made possible by rodent models. Initial WNV replication is assumed to happen in Langerhans dendritic skin cells after peripheral injection (Byrne et al. 2001). It causes primary viremia and infection of peripheral organs like the kidney and spleen. The infected cells then travel to lymph nodes. By the end of the first week, WNV has mostly been eliminated from serum and peripheral organs, and only a small percentage of immunocompetent animals have developed CNS infections. A CNS disease comparable to that seen in human WNV cases develops in the infected and damaged brain stem, hippocampus, and spinal cord neurons in infected rodents that die of the infection (Diamond et al. 2003; Arya et al. 2004). In populations of non-neuronal CNS cells in people or animals, WNV infection is not substantially detectable. WNV is eradicated from every tissue compartment in living wild-type mice within two to three weeks of infection. Furthermore, it has been researched that the brains and kidneys of infected hamsters and brains of perforin deficient mice results in chronic viral infection (Shrestha and Diamond 2004; Shrestha et al. 2006; Tesh et al. 2005). A WNV-infected immunosuppressed patient whose viremia was identified for more than 60 days also had a persistent infection (Brenner et al. 2005). Although known about WNV pathogenesis in avian hosts, the virus has been identified in the brains, lungs, livers, hearts, spleens, and kidneys of spontaneously infected crow’s and blue jays using histology,

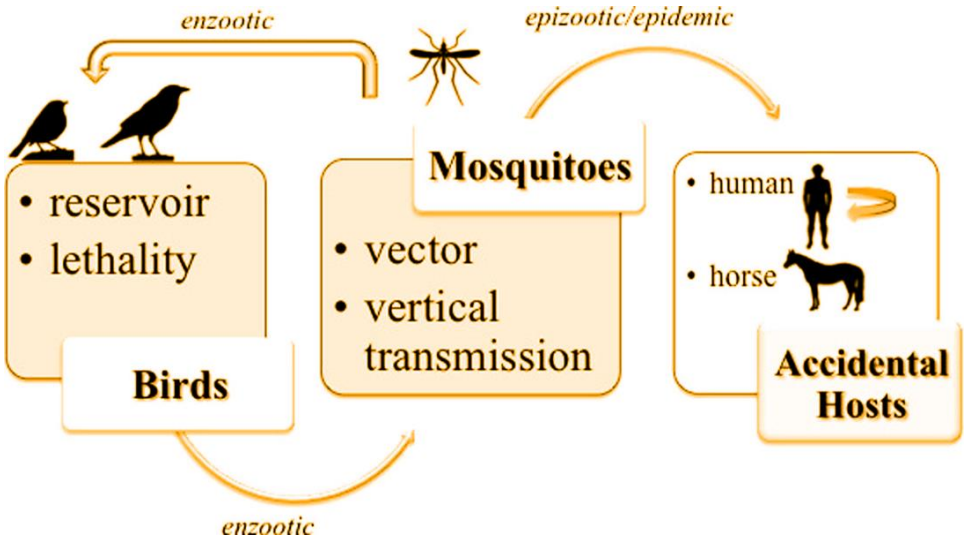

Fig. 1: Infectious cycle of West Nile Virus

reverse transcription-PCR and virologic tests (Panella et al. 2001; Gibbs et al. 2005). Although alterations in endothelial cell permeability caused by tumor necrosis factor-alpha (TNF-α) may make it easier for WNV and other neurotropic flaviviruses to enter the central nervous system (CNS), the exact processes by which they do so remain largely unclear (Wang et al. 2004).

Sometimes, the earlier viral entrance into the brain coincides with greater viral load in serum, so it is probable that WNV infects the CNS at least in parts via hematogenous spread. Additional pathways, such as (i) passive transport or infection across the choroid plexus epithelial cells or endothelium, may contribute to WNV CNS infection (Kramer Hämmerle et al. 2005), which is direct axonal retrograde transport from infected peripheral neurons; (ii) infection of olfactory neurons and spread to the olfactory bulb; (iii) a "Trojan horse" method in which the virus is delivered by infected immune cells that go to the CNS; and (iv). Changes in cytokine levels that may regulate blood brain barrier permeability and infection of blood monocytes and choroid plexus cells have been shown in animal models, even though further research is needed to determine the specific mechanisms of WNV CNS penetration in humans (Samuel and Diamond 2005; Garcia Tapia et al. 2006). Within 24 hours of infection, WNV exhibited large viral yields and progressed cytopathic effects in human brain glioma cells. It is proved that human glioma cells from the CNS might become infected with WNV and are useful for researching the pathophysiology of viruses (Samuel and Diamond 2006). Activation of the innate antiviral immune response pathways is typically the basic cause of pathogenic effects. Double-stranded RNA with viral replication complexes causes transcriptional activation of the interferon-/ (IFN-/) or type-I IFN pathways (Samuel 2001). This work shows that a number of interferon-induced proteins, including IFIT1, IFIT2, IFI27, IFITM1, IFITM2, and G1P2, are activated in glioma cells, validating this pathogenicity mechanism. Glial cells are useful in our inquiry since they are immune cells with CNS origins. Glial cells have the potency to activate the macrophagic potential and immune mediated neuropathologic changes that reflects conditions in the normal CNS host cells. Glial cells can also change the immune response by activating the type-II (IFN-) pathway. Additionally, it was shown that indoleamine 2,3 dioxygenase (INDO) was increased in WNV-infected A172 cells (Koh and Ng 2005).

In neuroinflammatory illnesses, glial cells produce more INDO (Indoleamine), which damages the neurons (Grant and Kapoor 2003). The amplified inflammatory response caused by the overexpression of the pentaxin-related gene (PTX3) is also connected to local tissue damage (Bottazzi et al. 1997). It was also discovered that a collection of apoptosis-causing genes was activated, illuminating the pathways connecting viral replication and apoptosis. These genes include spermidine/spermine N1-acetyltransferase, nuclear factor of kappa light chain gene, tumor necrosis factor superfamily (TNFSF14) and TNF receptor-associated factor (TRAF1) (SAT). WNV propagation is controlled by this highly conserved cellular self-destruction pathway (Chu and Ng 2003).

Life Cycle

The four main stages of the life cycle are attachment/entry, translation, replication and assembly/egress. After attaching to the surface of cells, WNV enters with the help of receptor-mediated endocytosis. Several molecules, including DC-SIGN, e.g., mannose receptors and glycosaminoglycans, have been suggested as West Nile virus receptors (Davis et al. 2006). Endosomal compartment acidification induces a conformational shift in the E protein, fusing the endosomal and viral membranes and releasing the virus nucleocapsid

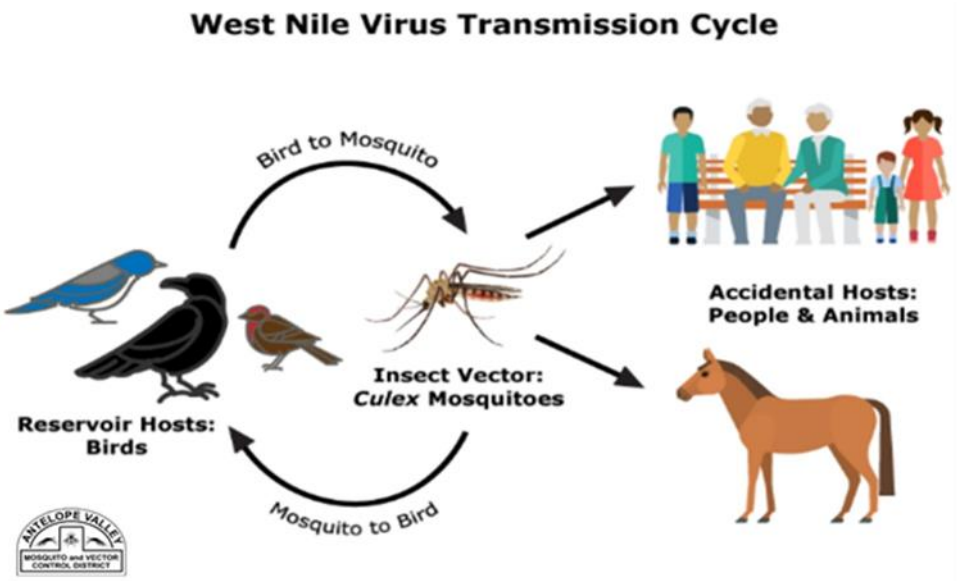

Fig. 2: Transmission cycle of West Nile Virus

into the cytoplasm. After the capsid dissociates, the genome of RNA is copied, and the well-established procedure for viral assembly is started. The ten viral proteins are expressed as a consequence of the translation and processing of the viral polyprotein on intracellular membranes. Cellular and viral proteins duplicate the viral RNA to create numerous copies that may be utilized to create new virions (Rossi et al. 2010). The Golgi network allows the structural proteins to blossom into the cytoplasm once assembled in the endoplasmic reticulum on membranes and joined to the nucleocapsid. Exocytic vesicles carry the virus to the cell surface, where it develops when cellular enzymes break the prM, releasing the mature virus from the cell surface. The function of partly or completely immature flavivirus particles during infection has recently attracted much attention (Colpitts et al. 2012). During maturation, budding and the ineffective cleavage of the prM protein from the virion surface result in the formation of these immature flavivirus particles. According to research, DENV and WNV flavivirus particles, either immature or partly mature, may make up to 40% of the overall virus population in a particular disease (Moesker et al. 2010). When bound by antibodies against the M or E protein, immature WNV particles may be highly infectious and immunogenic in vivo and in vitro. However, these were previously believed to be non-infectious. The Fc receptor on these immature viruses (antibody-bound particles) allows them to infiltrate immune cells and cause productive infection (Colpitts et al. 2012). The transmission cycle of WNV has been illustrated in Fig. 2.

Clinical Signs

The mosquito-borne West Nile virus (WNV), which has the potential to cause catastrophic neurological illness and has achieved worldwide significance, can infect the CNS of a variety of host animals (Hayes et al. 2005). Eighty percent of WNV infections result in asymptomatic patients. The majority of individuals who have symptoms experience an acute, generalized fever known as "West Nile fever" after an incubation period of approximately two to fourteen (2-14) days. Nearly 20% of patients eventually develop WNV fever. In 25 to 30 percent of instances, this self-limiting flu-like virus results in fever, muscular pains, headaches, and digestive problems. There is 25 to 50 percent probability that the body's limbs and trunk will have maculopapular skin irritation (Anderson et al. 2004; Watson et al. 2004; Sejvar 2014).

Regarding neurological symptoms, due to which it is known as "West Nile neuroinvasive illness", there is the presence of encephalitis with the signs of paralysis (Chung et al. 2013). Patients typically experience altered mental conditions, as well as generalized weakness and anomalies of the cranial nerves. In addition to mental disability, encephalitis patients exhibit various extra clinical findings consistent with WNV's ability to affect various brain regions, including the spinal cord. Human infections include the symptoms of everything from fever and muscle aches to infection of the meninges and brain and even death (Petersen et al. 2002). Meningitis caused by the WNV is similar to other viruses' meningitis in clinical indications (Sejvar et al. 2008).

Symptomatic infections can range in severity from mild illnesses resembling the flu to severe brain disorders for which there is no known cure. Many individuals completely recover from fever and viral meningitis. The prognosis is typically benign, and in rare instances, lethargy, headaches, muscle aches, and pain may linger for weeks, months, or even years (Sejvar et al. 2008; Anastasiadou et al. 2011; Murray et al. 2014). More than 1% of infections in human's result in serious illness, and the most common risk factors

include advancing age, immunological suppression, and long-term medical problems, including an increase in blood pressure, diabetes and kidney failure, among others (Bode et al. 2006; Patnaik et al. 2006). Children and people under 30 years are rarely reported to have West Nile neuroinvasive disease (Yim et al. 2004). Older people (over 55 years) and those with weak immune systems due to HIV infection, organ transplants, or recent medication may be more susceptible to the severe signs of WNV infection (Kumar et al. 2004; Pattan et al. 2009). The case-fatality rate varies from 15% to 29% in people over 70 years (Petersen et al. 2002). Homelessness, previous history of cardiovascular illness or kidney diseases, hepatitis C virus and immunosuppression, are all potential causes of brain inflammation and mortality (Murray et al. 2006; Sejvar et al. 2011). The neurological syndrome experiences long-lasting disability. Some patients experience acute muscle weakness and loss of muscle tone (Pealer et al. 2003).

Diagnosis

The diagnosis of WNV depends on the clinical findings and different assays for antibody response (Busch et al. 2008). The European Union case definition states that a person is considered to have a case of human WNV infection if there is the presence of fever, inflammation of the brain along with the inflammation of the meninges, and, according to laboratory standards, a minimum of one requirement must be met to verify the case, such as virus separation or detection of nucleic acid of virus in the cerebrospinal fluid or any other source such as blood. Furthermore, the presence of WNV IgG and a high titer of IgM antibody against WNV are included in the laboratory standards, which are later validated by a neutralization assay (Fox et al. 2006).

Like other viruses, the viral RNA is also detected using several molecular techniques. WNV RNA is found in clinical samples using molecular diagnostic techniques such as amplification techniques, which form the basis for directly detecting acute WNV infection. When symptoms eventually manifest, viral ribonucleic acid is no longer detectable in the blood in about 70–80 percent of infections. According to Chung et al. (2013) and Barzon et al. (2012, 2013), the viral RNA can be detected in urine for a longer time and at a greater titer than in CSF and blood between 2-3 and 14-18 days after infection. WNV antibody detection in serum and CSF is done using immunofluorescence and enzyme immunoassays. It is one of the most popular techniques for determining whether a person has a WNV infection. Because the IgM antibody cannot cross the blood-brain barrier, its existence in the CSF shows an infection in the central nervous system. When symptoms first appear, roughly 80% of patients have shown no longer viremic due to the brief viremic phase's length and the blood's low viral load. Antibodies, specifically IgM, can be found approximately 4 days post-infection, and a few days later, IgG molecules commonly come next (Prince et al. 2005; Tilley et al. 2006; Busch et al. 2008; Prince et al. 2009). A neutralization experiment must follow an enzyme immunoassay or immunofluorescence test to confirm a positive result since flavivirus antibodies might react with one another (cross-reactivity) (Chabierski et al. 2013). There is a specific interaction in the neutralization assay between a laboratory strain of WNV and neutralizing antibodies obtained from patient sera infected with this virus. The virus is bound by neutralizing antibodies, which prevent the virus from attaching to cells and spreading. The serodiagnosis to differentiate different flaviviruses, the plaque-reduction neutralizing test (PRNT) by using live viral particles, is regarded as the "gold standard" (Niedrig et al. 2007; Sanchini et al. 2013).

Diagnosis can also be made using conventional PCR methods. Broad-range PCR-based testing and sequence-independent metagenomic approaches are used to detect the presence of viruses in persons who may be ill when findings from conventional PCR techniques are negative. These methods have made it possible to discover new pathogens in clinical samples and even to recognize infections that were previously unidentified but were crucial to public health (Svraka et al. 2010) Recently, many serological and genetic methods have been utilized to identify WNV infection. These assays must take into account the WNV genome's diversity to distinguish the WNV from other flaviviruses. It is anticipated that new methods will be used for WNV diagnosis as laboratory technology advances and aids in understanding the pathophysiology and diversity of WNV. WNV infection diagnosis is based on various variables, including environmental circumstances, behavioral patterns, and clinical signs. The patient's medical history will provide vital diagnostic hints. For instance, if a patient exhibits clinical signs like fever and headache, one must consider the spread of WNV and its mosquito vector. WNV infection must be considered in endemic locations, particularly during the summer. The patient's medical history should also include exposure to mosquitoes from outside activities. A first physical examination will establish the presence of meningitis, flaccid paralysis, or more serious clinical symptoms such as fever, headache, and myalgia (Sejvar 2014).

Moreover, mosquito bites on the skin will also aid in diagnosis (Rossi et al. 2010). Brain tissue taken during surgery or an autopsy may be used to make the diagnosis. Pathological analysis of mortality revealed widespread neuronal degeneration, perivascular cuffing, and pervasive brain and spinal cord inflammation. These findings result from WNV replication leading to damage, a cytotoxic reaction, and inflammation (Kemmerly 2003).

A- Serological Diagnosis

Checking for WNV-specific IgM antibodies in cerebrospinal fluid or blood typically results in a laboratory diagnosis. A strong indication of the illness is the presence of WNV-

specific IgM in the blood and cerebrospinal fluid. The mostly used diagnostic method for identifying WNV is the enzyme-linked immunosorbent test (ELISA). In serum and spinal fluid, the test's sensitivity ranges from 95% to 100%. (Kemmerly 2003). This test is economically feasible and easily accessible in the market. Additionally, serology can be utilized to study immune responses. In CSF samples, reactive lymphocytes or monocytes indicate WNV neurologic infection. More strikingly, a massive influx of polymorphonuclear cells occurs. Neutrophils make up more than 40% of the CSF cells in people with WNV neuroinvasion. testing for plaque neutralization and reduction. IgM antibodies specific to WNV are typically detected 4 to 8 days after the occurrence of the disease and may last for 30 to 90 days. The lack of virus-specific IgM does not necessarily describe the detection of WNV infection if the serum is taken within eight days of disease onset, and tests may be performed on subsequent samples (Lustig et al. 2018). WNV-specific IgM antibodies are not detectable until the end of viremia. Encephalitis and meningitis are shown to occur when a high level of WNV-specific IgM antibodies is present in a person. It may persist for a longer period, from several months to more than one year. It represents the central nervous system infection because Humoral IgM cannot cross the blood-brain barrier. A virus neutralization antibody test should confirm all positive samples. The flaviviruses are antigenically closely related with each other. Recent vaccination against yellow fever or the Japanese encephalitis virus may result in false-positive results on WNV IgM antibody testing. Testing for WNV may cross-react with tests for other infectious diseases, including dengue, St. Louis encephalitis, and other arboviruses. It is still necessary to look for a four-fold increase in neutralizing antibody titer to diagnose WNV infection. It is preferred to employ CDC-defined IgM and IgG ELISA. Plaque-reduction neutralization tests that compare the titers to cross-reacting chemicals may help to identify IgM antibody capture test results that are mistakenly positive. ELISA is more sensitive in case of WNV infections as compared to virus isolation and polymerase chain reaction (PCR) (Kemmerly 2003; De Filette et al. 2012).

B- Nucleic Acid-based Diagnosis

Blood, CSF, and tissue samples may be used for viral cultures and tests to identify viral RNA using reverse transcriptase-polymerase chain reaction (RT-PCR) in the early stages of the disease (Kemmerly 2003). Numerous studies have shown that RT-PCR-based detection is an efficient technique for identifying WNV in clinical samples. Single-tube, real-time PCR is superior to endpoint RT-PCR in a number of ways, including speed, often greater sensitivity, and specificity, and decreased contamination (Lustig et al. 2018). Real-time PCR can also be standardized and allows for the measurement of nucleic acids (De Filette et al. 2012).

C- Miscellaneous Diagnostic Techniques

The WNV antigen may also be recognized by immunohistochemistry (IHC). The lack of WNV infection is not ruled out by negative test results (Kemmerly 2003). In this method, fluorescent protein was used to monitor and detect flavivirus RNA in patients' infected samples using CRISPR-cas13 technology, establishing a viral diagnostic platform with excellent performance and minimal equipment or sample processing requirements (Lustig et al. 2018).

Public Health Importance

WNV is a transboundary disease of One Health concern due to its complex life cycle, which encompasses humans, animals, and the environment (Parkash et al. 2019). Its interactions with reservoir hosts and vectors are necessary for its life cycle. In the end, factors like ambient outside temperature and rainy weather are crucial contributors to the growth of the mosquito population and the strengthening of WNV in susceptible hosts (Baba et al. 2006). In 1998, WNV isolates were found in Israel, demonstrating the virus' propensity for spreading internationally (Banet-Noach et al. 2003). Extreme urbanization, agriculture, and land usage are examples of factors that have diverted from the natural environment and increased the prevalence and incidence of WNV in humans (Kilpatrick 2011). Furthermore, growing crops such as rice need abundant water and a good irrigation system. It causes the mosquito population to increase in the field's stagnant water, resulting in WNV outbreaks (Pradier et al. 2008). Most researchers hypothesized extreme summer temperature was the main culprit in the mosquito population during a heat wave in the U.S. in 1999 (Esser et al. 2019). Moreover, WNV outbreaks are not only associated with mosquito bites but also through organ or blood donation, during lactation, pregnancy, and exposure to infected laboratory instruments (CDC 2002).

WNV incubation periods vary from 3 to 14 days in humans. Febrile illness was reported in 20% of infected people in data reported from New York City (Petersen and Marfin 2002). The signs and symptoms reported in infected individuals include; anorexia, pyrexia, rash, eye swelling, vomiting, myalgia, rash on the body that lasts approximately 3 to 6 days and meningoencephalitis in severe cases. Infected individuals with a previous history of the neurological syndrome have experienced long-lasting disabilities. Some patients may also experience acute muscle weakness and loss of muscle tone (Petersen and Marfin 2002; Pealer et al. 2003).

Conclusion

West Nile virus (WNV) is a neurotropic human pathogen. Its importance as zoonotic disease cannot be neglected due to complex life cycle and global persistence of the mechanical vectors. The fatality rate depends upon the level of infection

prevailing in an individual. The lethal disease is very important regarding public health significance and needs appropriate measures for its control.

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