Directorate of Health Services, Kerala

West Nile Virus infection- Guidelines

(adapted from relevant WHO and CDC documents and updated 18.3.2019)

Introduction

West Nile virus (WNV) infection is a mosquito-borne neuropathogenic zoonosis that is endemic in Europe, USA Africa, Middle East, and West Asia.etc. The virus is transmitted among birds via the bite of infected Culex mosquitoes, and incidentally humans and other mammals may become infected. About 80% of WNV infections in humans are asymptomatic. West Nile fever (WNF) is the most common clinical presentation. No specific prophylaxis or treatment exists against the disease in humans. West Nile Virus (WNV) was first isolated from the West Nile district of Uganda in 1937, since then many countries have been affected. During 1999-2010, 2.5million people were affected, 12000 severe cases of WNV related encephalitis/meningitis cases occurred and 1300 died in North America alone.

WN Virus

WNV is an enveloped positive-stranded ribonucleic acid (RNA) virus belonging to the Japanese encephalitis serocomplex (*Flavivirus* genus, *Flaviviridae* family). Eight phylogenetic lineages have been described, but only lineage 1 and 2 are associated with disease in humans.

Clinical features and sequelae

- Incubation period of WNV infection is usually 2 to 14 days, although incubation periods of up to 21 days have been reported in immunocompromised people. The viremia in humans is low, occurring 1 to 3 days after infection, can last up to 11 days and is not considered to be infectious to mosquitoes.
- Most WNV infections in humans are asymptomatic.
- About 20% of WNV infections in humans may cause WNF and less than one percent may cause West Nile Neuro Invasive disease (WNND).

- Very rarely, WNV infection leads to Guillain–Barré syndrome and other demyelinating neuropathies.

Symptoms

WNF is characterised by a sudden onset of symptoms that may include headache, malaise, fever, myalgia,vomiting, rash, fatigue and eye pain. Symptom severity ranges from a mild self-limiting illness from which patients recover within one week to a protracted debilitating disease that can last for months.

WNND involves symptoms that affect the central nervous system. These can manifest as

- meningitis,
- encephalitis
- acute flaccid paralysis
- or a combination of the above

High risk groups include -

- Advanced age, malignancies disrupting the blood–brain barrier, hypertension, hematologic disorders, diabetes mellitus, renal disease, alcohol abuse and genetic factors.

The case fatality ratio among patients with WNND can be up to 17%.

WNV infection in animals/birds-

- WNV infections among equines are usually asymptomatic. Approximately 10% may show neurological signs that can range from mild ataxia to total recumbence.
- Certain bird species, especially crows and sparrows, tend to be more sensitive to WNV infection and frequently develop clinical signs that lead to fatal outcomes. Avian mass mortality events are influenced by geographic and environmental factors, as well as by genetic differences of the WNV strains.
- In USA around 300 species of birds were detected to carry WNV.

Transmission

- Transmission of WNV is primarily vector borne spread by Culex mosquitoes and it occurs when mosquitoes are active.
- Mosquitoes become infected when they feed on infected birds, which circulate the virus in their blood for a few days. The virus eventually gets into the mosquito's salivary glands.
- During later blood meals (when mosquitoes bite), the virus may be injected into humans and animals
- WNV is transmitted in an enzootic cycle between Culex mosquitoes and birds with the respective hosts acting as vectors and amplifying hosts.
- Mammals can become infected from the bite of an infected mosquito, but are considered **dead-end hosts**.
- The virus may also be transmitted through contact with other infected animals, their blood, or other tissues.
- Birds when infected, dies due to the illness and hence bird deaths act as markers for the transmission. Such incidents need to be detected and investigated.

Human to Human transmission

- To date, no human-to-human transmission of WNV through casual contact has been documented, and no transmission of WNV to health care workers has been reported ***when standard infection control precautions have been put in place***.
- Human-to-human transmission may occur through substances of human origin (SoHO)(transfusion of blood and blood components or transplantation of tissues, cells or organs from an infected and viraemic donor)
- Mother to child transmission through breast feeding has also been reported very rarely.

Diagnosis

- Laboratory methods for the diagnosis of a WNV infection are most commonly indirect detection based on serology,
- The samples of choice are whole blood, plasma, serum, CSF (in case of neurological implications) and urine for genome detection and serum and CSF (in case of neurological implications) for serology.
- Lab diagnosis can also entail direct detection of the virus by specific methods
- Seroconversion for IgM typically occurs3 to 8 days post onset of WNF symptoms and IgM usually persists for 30–90 days.
- Caution:----A negative WNV IgM result in serum drawn less than eight days post-onset of symptoms does not exclude a WNV infection, while the presence of WNV-specific IgM does not always indicate a recent infection.
- WNV diagnosis based on serology is severely hampered by extensive cross-reactivity between antibodies triggered by related viruses of the genus *Flavivirus*, or by vaccination (e.g. yellow fever, tick-borne encephalitis, and JE vaccines).
- A WNV specific IgA antibody is observed to persist even up to 1 year after infection among high prevalence populations (refer Clinical Microbiology Review-American Society for Microbiology).

Case management and treatment

- No specific prophylaxis or treatment exists for WNV infections. The only available treatment is supportive care.
- Severe case requires intensive care in specialised tertiary care centres

Preventing infection in health-care settings

- Health-care workers caring for patients with suspected or confirmed WNV infection, or handling specimens from them, should implement standard infection control precautions. Samples taken from people and animals with suspected WNV infection should be handled by trained staff working in suitably equipped laboratories.

Public health control measures

Human

- Human transmission is very rare, but possible in special circumstances
- To prevent transfusion-transmitted WNV infections, hospitals should implement 28-day blood donor deferral or individual donation nucleic acid testing (ID-NAT) of prospective donors who have visited or live in an affected area.

Vector control

Culex mosquitoes viz. *Culex vishnui*, *Culex pseudo vishnui*, *Cx quinquefaciatus* are the mosquitoes that spreads the disease in India. Vector breeding sites include stagnant and often dirty water collections in dishes, buckets, barrels and cans, flowerpots, rain gutters, discarded tires and other containers that can collect water. In urban environments, infrastructure such as underground heating, sewage pipes and basements liable to flooding can act as breeding and resting sites for vectors.

Mosquito vectors may be controlled through larval source reduction and measures against adult mosquitoes. Integrated Vector Management is the strategy (IVM). Integrated mosquito surveillance and control in areas where the cases are being reported. IVM include source reduction, water management, chemical, biological control and personal protective methods.

Role of Veterinary/Animal Husbandry Department

Since WNV outbreaks in birds/animals precede human cases, the establishment of an active animal health surveillance system to detect new cases in birds and horses is essential in providing early warning for veterinary and human public health authorities.

Environmental studies to detect the reservoirs of infection are essential for a comprehensive disease control.

Events such as crow deaths can be investigated by multidisciplinary teams in line with One Health concept

Infection control, personal protection and prevention

Personal protection from mosquito bites is advisable for any person residing in or visiting affected areas, especially the elderly and immuno-compromised people

who are at higher risk of developing severe symptoms. Personal protective measures to reduce the risk of mosquito bites include the use of mosquito repellent in accordance with instructions indicated on the product label and wearing long-sleeved shirts and long trousers. In addition, window and screen doors can keep mosquitoes out.

Appendix

1. Serology details

Indirect detection of a WNV infection is based on detection of WNV-specific IgM and/or IgG. Multiple in-house and commercial serologic tests exist mainly based on enzyme-linked immunosorbent assay (ELISA) or indirect immunofluorescence (IIFA) principles.

WNV infection is mostly determined by detection of WNV-specific IgM in serum and/or CSF. Seroconversion for IgM typically occurs three to eight days post onset of WNF symptoms and IgM usually persists for 30–90 days. However, longer persistence has been described with the presence of IgM up to three years post-onset of symptoms. This implies that a negative WNV IgM result in serum drawn less than eight days post-onset of symptoms does not exclude a WNV infection, while the presence of WNV-specific IgM does not always indicate a recent infection. IgM detection in CSF of a patient with a functional blood–brain barrier points at an infection of the central nervous system. In patients with neuro-invasive disease, IgM can be detected in CSF usually one to eight days after onset of neurological symptoms.

WNV-specific IgG is typically detectable from eight days post onset of symptoms onwards and may persist for multiple years. Therefore, diagnosis based on IgG requires testing of an acute and convalescent serum to demonstrate seroconversion or a minimal four-fold increase in IgG titers.

WNV diagnosis based on serology is severely hampered by extensive cross-reactivity between antibodies triggered by related viruses of the genus *Flavivirus* (i.e. endemic flaviviruses such as tick-borne encephalitis and Usutu virus and exotic or travel-associated flavivirus infections such as dengue and Zika virus) or by vaccination (e.g. yellow fever, tick-borne encephalitis, dengue – very limited market – and Japanese encephalitis vaccines). In addition, an acute flavivirus infection may boost cross-reactive antibodies due to previous infection with or vaccination against another flavivirus, thereby obscuring antibody response to the present acute infection. ELISA and IIFA testing are only valuable as screening tests. Positive results obtained with these type of assays should be confirmed by virus neutralisation tests (VNT; plaque reduction neutralisation test – PRNT80 and PRNT90), preferably by parallel testing of acute and convalescent serum samples to distinguish recent infection from past infections. To exclude cross-reactions with other flaviviruses, PRNTs should be performed simultaneously against all potential flaviviruses. Such tests require biosafety level 3 facilities and appropriate reference viruses.

Direct detection

West Nile virus infection can be confirmed by virus genome detection or virus isolation. Viral genome is typically detectable in plasma from 2–18 days post-infection and up to five days post-onset of symptoms, although prolonged viremia (up to 35 days after symptom onset) has been reported. There is

evidence that whole blood is the best sample type, with 86.8% sensitivity, while sensitivity is lower in urine, plasma, serum and CSF [38]. Requirements for sensitivity of assays used depend on setting, e.g. SoHO screening of population samples versus identification of clinical cases.

Virus isolation is not considered as a test of choice for diagnosis, as it requires biosafety level 3 facilities and it takes up to five days to obtain a cytopathogenic effect. WNV antigen detection by immunohistochemistry is possible in post-mortem tissue of fatal encephalitis cases.

2. Blood and tissues transfusion safety-details

In affected areas, blood establishments should follow recommendations. Donors of organs, tissues and cells living in or returning from an affected area should be tested for WNV infection.

As part of a preparedness plan for WNV blood safety blood establishments in affected areas should:

- temporarily interrupt blood collection or implement NAT screening for blood donations from WNV affected areas
- quarantine, retest and discard positive blood components in storage at the time of implementation of measures and retrieve and quarantine blood components derived from whole blood donated 120 days prior the date of collection of the ID-NAT-positive donation
- enhance donor post-donation information, especially about fever, influenza-like illness or other acute symptoms within 15 days after donation
- strengthen post-transfusion haemovigilance and perform look-back analysis in any case of transfusion-transmitted WNV infection for a period dating 120 days prior to the donation of implicated blood components; and
- Consider the use of pathogen inactivation procedures.

3. Vector details

Ornithophilic (feeds on birds) mosquitoes belonging mainly to Culex species act as vectors for transmission of infection from infected birds to vertebrate hosts such as *Cx.modestus* (france),*Cx.Vishnui* complex(India and Pakistan), *Cx univittatus* complex(South Africa), *Cx. pipiens pipiens*(Romania, USA).

When Mosquitoes feed on an infected bird they become infected with the virus. The mosquitoes act as carriers (vectors) spreading the virus from an infected bird to other birds and to other animals. WNV is maintained in mosquito populations by transferring the infection through adults (mosquitoes) to eggs (vertical transmission).

Infection of other animals (e.g. horses, and also humans) is incidental to the cycle in birds since most mammals do not develop enough viruses in the bloodstream to spread the disease. They are "dead-end" hosts.

Culex vishnui, Culex pseudo vishnui, Cx quinquefaciatus are the mosquitoes responsible for spread in India.

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Any new version published later on by DHS Kerala will take precedence over all earlier versions of the same

- *As the situation is still evolving, the matter contained in this guideline is subject to modification at regular intervals*
- *Detailed reference documents to be read for additional information will be emailed to all DMOs and DSOs regularly*
- *All are advised to, regularly check DHS website or contact your DSO for updates*
- ***For assistance, or to speak to an appropriate health expert or official, please call 24 x7 Health Dept NHM help line DISHA on 0471 255 2056 , or 1056 toll free at any time***