

**NIPAH –A NARRATIVE REVIEW OF RARE INTRACTABLE KILLER DISEASE****Reshma B. V.\***

Assistant Professor, Department of Pharmacology, SKCPRC, Trivandrum, Kerala. India.

**\*Corresponding Author: Reshma B. V.**

Assistant Professor, Department of Pharmacology, SKCPRC, Trivandrum, Kerala. India.

Article Received on 28/07/2019

Article Revised on 18/08/2019

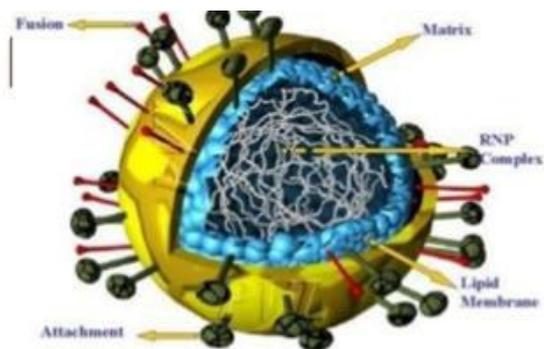
Article Accepted on 08/09/2019

**ABSTRACT**

NiV infection is an emerging zoonotic infectious disease causing sporadic outbursts in many developing countries within Asia, Africa, and South America. Pteroid bats are the natural reservoirs, but human-to-human transmission is possible. Clinical course ranges from non-specific influenza-like symptoms to rapidly progressive respiratory and neurologic complications. Vector control has been challenging because of its widely distributed ecological niche. Currently, no definitive treatment protocols are available in humans, but profound breakthrough in vaccine technology and successful equine vaccines has shown the way for the development of NiV vaccine and immunization in the near future.<sup>[1]</sup> A review of the current literature is performed going through online search engines: PubMed and Google Scholar. The search strategy was focused on two main components, first on the NiV ('Nipah' OR 'Nipah Virus') and subsequently on its epidemiology, including determinants and preventive measures ('Epidemiology/determinants' OR 'Epidemiology/prevention')

**KEYWORDS:** Nipah virus, epidemiology, viral characteristics, killer virus, vaccines.**INTRODUCTION**

Nipah virus, an enveloped ribonucleic acid virus, has been a major cause of encephalitis out-breaks with high mortality, primarily in the Indo-Bangladesh regions. Except for the first outbreak in Malaysia-Singapore, which was related to contact with pigs and the outbreak in Philippines associated with horse slaughter, most other outbreaks have affected the Indo- Bangladesh regions. The Indo-Bangladesh outbreaks were associated with consumption of raw date palm sap contaminated by fruit bats and had a very high secondary attack rate. The patient usually presents with fever, encephalitis and/or respiratory involvement with or without thrombocytopenia, leukopenia and transaminitis. Diagnosis can be confirmed by isolation and nucleic acid amplification in the acute phase or antibody detection during the convalescent phase. Treatment is mostly limited to supportive care and syndromic management of acute encephalitis syndrome. Ribavirin, m102.4 monoclonal antibody and favipiravir are the only anti-virals with some activity against Nipah virus. Standard precautions, hand hygiene and personal protective equipments are the cornerstone of comprehensive infection prevention and control strategy. With the recent outbreaks affecting newer geographical areas, there is a need for physicians to be aware of this disease and keep abreast of its current detection and management strategies.<sup>[2]</sup>

**Viral Characteristics and Epidemiological Determinants**

NiV infection is an emerging zoonotic infectious disease causing sporadic outbursts in many developing countries within Asia, Africa, and South America. Pteroid bats are the natural reservoirs, but human-to-human transmission is possible. Clinical course ranges from non-specific influenza-like symptoms to rapidly progressive respiratory and neurologic complications. Vector control has been challenging because of its widely distributed ecological niche. Currently, no definitive treatment protocols are available in humans, but profound breakthrough in vaccine technology and successful equine vaccines has shown the way for the development of NiV vaccine and immunization in the near future.

### Case Fatality Rate and Risk Factors for Nipah Virus

A wide range of Nipah virus (NiV) encephalitis case fatality rates (CFR) have been reported. Data on the involvement of several potential risk factors in Nipah virus transmission remain controversial. We performed a systematic review and meta-analysis to estimate the pooled CFR of NiV encephalitis and to assess the risk factors for NiV infection.

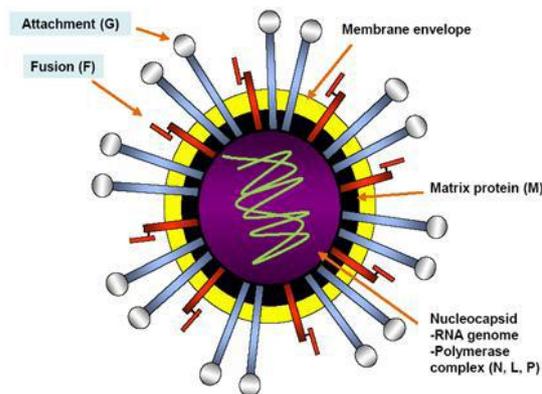
Articles published up to the 27th of November 2018 in MedLine, Embase and Web of knowledge databases were considered for this study. We included cross-sectional, cohort, and case-control studies that have reported NiV CFR and/or risk factors. Data were pooled with random-effects model. This review was registered in the PROSPERO, CRD42018116242.

This global review included 22 citations (25 studies) including 2156, 1682, and 474 suspected, probable, and confirmed cases of NiV encephalitis, respectively. We determined a pooled CFR for NiV encephalitis at 61.0% (95% CI, 45.7-75.4;  $I^2 = 96.8\%$ ). Climbing trees (OR = 1.4; 95% CI; 1.0-1.9), male gender (OR = 1.5; 95% CI; 1.1-2.0), travel outside their own sub-district (OR = 2.0; 95% CI; 1.4-2.9), and exposure to date palm sap (DPS) (OR = 5.7; 95% CI; 3.8-8.6) or pigs (OR = 7.6; 95% CI; 1.2-45.4) were significantly associated with NiV infection.

Findings from this study suggest that NiV Encephalitis is associated with a high CFR and that male gender, travel outside their sub-district, climbing trees, and exposure to pigs and DPS are associated with an increased risk of NiV encephalitis.<sup>[7]</sup>

### Henipavirus Infection of The Central Nervous System.

Nipah virus (NiV) and Hendra virus are highly pathogenic zoonotic viruses of the genus Henipavirus, family Paramyxoviridae. These viruses were first identified as the causative agents of severe respiratory and encephalitic disease in the 1990s across Australia and Southern Asia with mortality rates reaching up to 75%. While outbreaks of Nipah and Hendra virus infections remain rare and sporadic, there is concern that NiV has pandemic potential. Despite increased attention, little is understood about the neuropathogenesis of henipavirus infection. Neuropathogenesis appears to arise from dual mechanisms of vascular disease and direct parenchymal brain infection, but the relative contributions remain unknown while respiratory disease arises from vasculitis and respiratory epithelial cell infection. This review will address NiV basic clinical disease, pathology and pathogenesis with a particular focus on central nervous system (CNS) infection and address the necessity of a model of relapsed CNS infection. Additionally, the innate immune responses to NiV infection in vitro and in the CNS are reviewed as it is likely linked to any persistent CNS infection.<sup>[3]</sup>



### Nipha- Rare and Intractable Disease

Nipah virus, an enveloped ribonucleic acid virus, has been a major cause of encephalitis out-breaks with high mortality, primarily in the Indo-Bangladesh regions. Except for the first outbreak in Malaysia-Singapore, which was related to contact with pigs and the outbreak in Philippines associated with horse slaughter, most other outbreaks have affected the Indo- Bangladesh regions. The Indo-Bangladesh outbreaks were associated with consumption of raw date palm sap contaminated by fruit bats and had a very high secondary attack rate. The patient usually presents with fever, encephalitis and/or respiratory involvement with or without thrombocytopenia, leukopenia and transaminitis. Diagnosis can be confirmed by isolation and nucleic acid amplification in the acute phase or antibody detection during the convalescent phase. Treatment is mostly limited to supportive care and syndromic management of acute encephalitis syndrome. Ribavirin, m102.4 monoclonal antibody and favipiravir are the only anti-virals with some activity against Nipah virus. Standard precautions, hand hygiene and personal protective equipments are the cornerstone of comprehensive infection prevention and control strategy. With the recent outbreaks affecting newer geographical areas, there is a need for physicians to be aware of this disease and keep abreast of its current detection and management strategies.<sup>[4]</sup>

### Vaccine Development for Nipah Virus Infection In Pigs

Nipah virus (NiV) causes a severe and often fatal neurological disease in humans. Whilst fruit bats are considered the natural reservoir, NiV also infects pigs and may cause an unapparent or mild disease. Direct pig-to-human transmission was responsible for the first and still most devastating NiV outbreaks in Malaysia and Singapore in 1998-99, with nearly 300 human cases and over 100 fatalities. Pigs can therefore play a key role in the epidemiology of NiV by acting as an "amplifying" host. The outbreak in Singapore ended with the prohibition of pig imports from Malaysia and the Malaysian outbreak was ended by culling 45% of the country's pig population with costs exceeding US\$500 million. Despite the importance of NiV as an emerging

disease with the potential for pandemic, no vaccines, or therapeutics are currently approved for human or livestock use. In this mini-review, we will discuss current knowledge of NiV infection in pigs; our ongoing work to develop a NiV vaccine for use in pigs; and the pig as a model to support human vaccine development.<sup>[6]</sup>

### **Killer Virus Called Nipah**

Nipah virus (NiV) is a deadly virus with a high mortality rate that has affected many developing countries in the past. According to the Centers for Disease Control and Prevention (CDC), many economically deprived countries such as Madagascar, Cambodia, and Thailand are also at high risk for future outbreaks. The first case of NiV was reported in 1998 and almost two decades later, little scientific progress has been made in finding a proper treatment and prevention vaccine. As many developing countries are not properly equipped to fight the infection, it is vital to properly educate the health systems. The aim of this review is to provide an epidemiological background as well as to understand the transmission routes, presentation, and the diagnosis and prevention of this deadly virus.<sup>[5]</sup>

### **CONCLUSIONS**

The NiV poses a significant public health risk because of its intricate transmission cycle, unpredictable viral course, murky management protocol, and unavailability of vaccine. Complicated by emergence and subsequent reemergence, prevention and containment are the two most important public health promotion strategies. Early anticipation, intergovernmental preparedness and cooperation, and surveillance of zoonotic infections still remain the key to mitigate the risk. NiV infection is an emerging zoonotic infectious disease causing sporadic outbreaks in many developing countries within Asia, Africa, and South America. Pteroid bats are the natural reservoirs, but human-to-human transmission is possible. Clinical course ranges from non-specific influenza-like symptoms to rapidly progressive respiratory and neurologic complications. Vector control has been challenging because of its widely distributed ecological niche.

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