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NIPAH PARAMYXOVIRUS AN EMERGING ZOONOSIS AND ITS SUPPORTIVE TREATMENT: A REVIEW

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Abstract:-
Nipah virus is a Paramyxo zoonotic virus, isolated during the Malaysian outbreak with severe and often lethal encephalitis. It is a RNA virus which belongs to the Paramyxoviridae family. Fruit bats are the natural hosts of Nipah virus and it can be transmitted to pigs and other animals including humans also. The route of infection of Nipah virus from bats to humans is by ingestion of NiV-contaminated raw date palm sap, consumption of partially eaten fruits by fruit bats or close contact with infected domestic animals (pigs, cats, goats, dogs). Nipah virus can infect a wide range of species and human-to-human transmission has been observed in Bangladesh outbreak. Ribavarin has the potential activity against the Nipah virus infection as it has anti-viral activity for RNA viruses. Indian Homeopathy claims Belladonna and some other natural drugs for prevention of infection and supportive care treatment for the symptoms of NiV infection.

Key words: - *Nipah virus (NiV), Ribavarin, Nyctanthus Arbortristis, Paramyxovirus, palm sap, Fruits Bat.*

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INTRODUCTION:

Nipah Virus (NiV) is a Paramyxo zoonosis that causes severe disease in both animals and humans. It gets its name from Sungai Nipah a Malaysian village [1], where pig farmers became ill with encephalitis. The natural hosts of the virus are fruit bats of the *Pteropodidae* family, *pteropus* genus [2] and contaminated date palm sap by Grey-headed flying foxes. It is a RNA virus of *Paramyxoviridae* family of order *Mononegavirales* and belongs to Genus-*Henipavirus* of species Nipah and virus name Nipah Virus [5, 22, 23]. The Mortality rate is very high in humans as per the reports of previous outbreaks and the average rate of Mortality is 80%. In 1998 the outbreak of Nipah virus infection in human was documented in Malaysia with approximately 100 deaths. At the time of Malaysian outbreak pigs were the intermediate hosts. In Bangladesh outbreak (2004) the Nosocomial transmission (human to human transmission) of NiV has been documented. And they are also became infected with NiV by consuming date palm sap, contaminated by infected fruits bats [3]. In India (May-June 2018) it claims 13 lives in Kozhikode district of Kerala state [29]. Previous outbreaks in India were reported at Siliguri (2001) and Nadia (2007) of West Bengal with 68% and 100% fatality rate respectively [30, 31].

Etiology:-

Nipah Virus (NiV) is a RNA virus belonging to the genus *Henipavirus* [5]. Family *Paramyxoviridae*, which was discovered in Malaysia (1998). It is closely related to Hendra Virus and Cedar Virus.

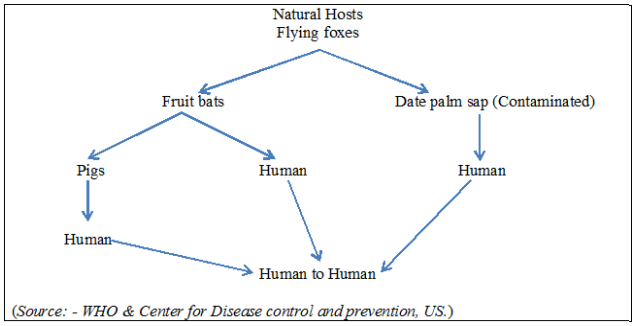
NiV has two Pedigrees [4]

I. A Malaysian strain (mNiV) and
II. A Bangladesh strain (bNiV)

A *Henipavirus* that recently caused an outbreak in the Philippines is also thought to be Nipah Virus.

Transmission:-

Fruit bats are the natural hosts of NiV. Flying foxes maraud on fruit trees near around the pig farms and the fruit bats dropped by them are responsible to get possessed of virus to pigs, were they are consider as the intermediate amplification hosts. The rate of pig to pig transmission is very high and rapid (NiV outbreak in Malaysia). Recent outbreak of NiV in Bangladesh have related with consumption of raw date palm sap, and it is believed to be, the sap collection jars were contaminated by NiV host's bat urine. NiV is transmitted to people who came in close contact with infected pigs [11] and their body secretions. According to recent outbreak of NiV in Bangladesh, it can be transfer human to human [17] by close contact with infected people and their body secretions and excretions (urine, saliva and lung secretion)[13, 14, 15]. It is well known as nosocomial transmission [16]. The chances of NiV transmission through sexual contact and breast feeding may occur.



Signs and Symptoms: -

- Most of the NiV symptoms in humans are common (Fever, Headache, Nausea, Vomiting, Drowsiness) and similar to Influenza-fever and muscle pain, which appears after 5 to 14 days of exposure to virus.
- Some patients show a respiratory illness during the early stage of their infections.
- This infection is associated with encephalitis with Migraine, Meningitis, Neurologic deficits, Emphysema, Mental confusion, Myalgia, Disorientation and Delirium [18].
- Encephalitis may present as acute or late onset.
- These signs and symptoms can progress to coma within 24 to 48 hrs.
- In some cases blurred vision and abdominal pain may occur.

How it spreads?

- Close contact with infected people's secretions and excretions
- Eating food which may have the droplets of saliva of infected bats
- Caretakers of Nipah infected patients without proper protective equipments
- Handling of dead bodies of Nipah patients; traditional cremation practices

Diagnosis and Tests: -

Nipah virus infection can be diagnosed by a number of different tests.

- Enzyme Linked Immunosorbent Assay (ELISA):

An indirect enzyme linked immunosorbent assay (ELISA) using recombinant NiV N protein as an antigen has been described for use as a diagnostic test [6]. Recombinant proteins allow use of the ELISA to test samples that have been treated to inactivate

the virus in biosafety level (BSL) diagnostic labs [6]. When compared to CDC inactivated-virus ELISA assays, the indirect ELISA for IgG detection had accordance of 98.6% sensitivity and 98.4% specificity using human serum samples, and 100% accordance (albeit only 16 samples) using swine serum samples [6]. In surveillance programs, a positive test would need to be followed with a positive virus neutralization result to confirm the diagnosis and prevent a costly and unnecessary response to a false positive result. In fatal cases, immunohistochemistry on tissues collected during autopsy may be the only way to confirm a diagnosis [9].

– Real time-Polymerase chain reaction (RT-PCR) assay and the method of virus isolation from cell culture:
Laboratory diagnosis of a patient with a clinical history of NiV can be made during the acute and convalescent phases of the disease by using a combination of tests. Virus isolation attempts and real time polymerase chain reaction (RT-PCR) from throat and nasal swabs, cerebrospinal fluid, urine, and blood should be performed in the early stages of disease.

Quantitative real-time PCR (qRT-PCR) primers and probes have been developed for the nucleocapsid (N) gene of NiV [9]. Primers for conventional PCR and sequencing of the matrix (M) gene have also been described [9]. Specific qRT-PCR primers and probes for the N gene of bNiV and mNiV have been described.

– Virus neutralization:
Virus neutralization tests (VNT) have been developed for high-throughput screening in BSL2 diagnostic laboratories [8] using recombinant vesicular stomatitis virus (rVSV) expressing NiV fusion (F) protein and glycoprotein (G). A VNT utilizing secreted alkaline phosphatase (SEAP) has been developed to detect antibodies to NiV. Using 75% reduction as the cut-off threshold, this VNT gave the same diagnostic results as a live NiV VNT performed in a BSL4 laboratory [8]. Another VNT with similar efficacy to a live NiV VNT test has been described using a luciferase reporter gene to detect neutralization of NiV proteins.

– Immunofluorescence:
Can rapidly detect NiV but cannot differentiate between henipaviruses, since mono-specific antisera to individual proteins of NiV will cross react with HeV [9]. Negative contrast electron microscopy can be used to identify viral particles [9]. Two monoclonal antibodies (MAb) with affinity for the N protein or P, V, and W protein of henipaviruses have been developed [7]. MAb 1A11 C1 can detect the N protein of both NiV and HeV, while MAb 2B10 p4 can detect HeV antigen better than NiV antigen, making it possible to use 2B10 p4 for differentiation between NiV and HeV [7]. To differentiate the two henipaviruses using immunofluorescence assays, reactivity to NiV or HeV specific antisera must be compared to positive controls of NiV or HeV[9]. Anti-HeV antiserum neutralizes HeV at a four-fold greater dilution than it neutralizes NiV, and anti-NiV antiserum neutralizes NiV four times more efficiently than it neutralizes HeV [9].

Treatment: -
There is no effective treatment for Nipah virus disease, but in the discovery of the etiologic agent of Nipah virus outbreak, ribavirin was used in an open-label trial. It was selected due to broad spectrum activity against both RNA and DNA viruses. It is also effective against viral hemorrhagic fever with renal syndrome and RSV (respiratory syncytial virus) infection [19, 20] because it is the only known treatment for a variety of viral hemorrhagic fevers [24]. Another study found that ribavirin potentiated the antiviral effect of acyclovir [25]. Furthermore, this drug has been demonstrated to cross the blood–brain barrier following oral (capsule or tablet) administration, making it useful for the treatment of viral encephalitis. The aerosol form has been used in the past to treat respiratory syncytial virus-related diseases in children. Ribavarin treatment in acute NiV encephalitis may alleviate the symptoms of nausea, vomiting, and convulsions which results to near about 36 to 40% reduction in mortality and more survivors without neurological deficits [21].

Ribavirin is a nucleoside inhibitor as it is ribonucleic guanosine analog use to stop viral RNA synthesis and mRNA capping. It is a pro drug, which when metabolized resembles purine RNA nucleotides and this form of ribavarin interferes with RNA metabolism required for viral replication [26].

Ribavirin's carboxamide group can make the native nucleoside drug resemble adenosine or guanosine, depending on its rotation. For this reason, when ribavirin is incorporated into RNA, as a base analog

of either adenine or guanine, it pairs equally well with either uracil or cytosine, inducing mutations in RNA-dependent replication in RNA viruses. Such hyper mutation can be lethal to RNA viruses [27, 28]. Primary intensive supportive treatment is mostly focused on managing fever and the neurological symptoms. Severely ill individuals need to be hospitalized and may require the use of a ventilator.

Indian Homeopathic medical association (IHMA) claims Belladonna and some other natural drugs for prevention and supportive care treatment for the symptoms of NiV infection. But up to today there is no any exact data found regarding to homeopathic medicine against the Nipah virus infection.

I. *Aconitum Napellus* or *Belladonna* is suitable in early stage from 12 to 24 hrs. of onset of first symptom when patient shows initial signs of illness that is fever and headache, this medicine can also be started in doubted cases to prevent infection without any side effect.
II. *Gelsemium sempervirens* is best indicated to the symptoms of central nervous system have developed like Dullness, Dizziness, Drowsiness, Disorientation, Tremors, Trembling and Blurring of vision.
III. *Nyctanthus Arbortristis* mother tincture is indicated in general (10 to 15 drops in half cup of water 3 to 4 times daily.)
IV. *Aspidosperma Quebracho* or *Blatta Orientalis* or *Arsenicum* Album is indicated homoeopathic remedies in patients showing symptoms of respiratory tract infection with breathlessness and choking sensation.
V. *Plumbum Metallicum* or *Ipecacuana* is indicated in patients who show symptoms like pain in abdomen, nausea and vomiting.
VI. *Stramonium* or *Baptisia* or *Zincum Metallicum* is best suited in later stages when patient is in delirium or comatose state.

Prevention:-

The ministry of health care and administration has issued guidelines of Do's and Don'ts for preventing the spread of Nipah virus infection.

Do's-

- Isolate infected livestock such as pigs, horses, dogs, cats as they acts as a intermediates host [10]; suspected human cases should be isolated
- Wear N95 mask at public places which prevents virus inhaling
- Stay away from Bat, pig and other animal droppings
- Wash, peel and/or cook well all fruits thoroughly before eating and make sure food and drinks might not have been contaminated by bats
- Maintain respiratory hygiene by avoiding spiting and coughing etiquettes, use clean handkerchief
- Maintain proper cleanliness and self-hygiene especially sanitary hygiene such as clothes, utensils of suspected cases and items typically used in the toilet or bathroom to be cleaned separately
- Health care workers are advised to use full barrier personal protective equipment such as mask and gloves before examination of patients
- Keep fruit bats away from pigs
- Visit the nearest health care center for any flu-like illness

Don'ts-

- Do not eat fruits that may have been bitten by birds and animals; avoid eating raw fruits and fruits damaged by fruit bats
- Do not drink unpasteurized fruit juices
- Avoid meat and animal products in the region of outbreaks
- Avoid travelling to affected regions and areas having fruit bats especially caves and under those trees where bats resides
- Avoid contact with pigs and pig holders
- Avoid hand shake and wash hands properly after contacting infected people
- Avoid contact with sick person's body secretions and excretions like saliva, sweat, urine etc.
- Don't use self-medication

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