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THE LITERATURE REVIEW ON THE NIPAH VIRUS AND MONKEY POX

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ABSTRACT

Nipah virus, a paramyxovirus related to Hendra virus, first emerged in Malaysia in 1998. Clinical presentation ranges from asymptomatic infection to fatal encephalitis. Malaysia has had no more cases since 1999, but outbreaks continue to occur in Bangladesh and India. In the Malaysia-Singapore outbreak, transmission occurred primarily through contact with pigs, whereas in Bangladesh and India, it is associated with ingestion of contaminated date palm sap and human-to-human transmission. Bats are the main reservoir for this virus, which can cause disease in humans and animals. There are currently no effective therapeutics, and supportive care and prevention are the mainstays of management.

Key words : **:** Nipah virus, Outbreak, Zoonosis, Herbal Drugs, Treatment, Symptoms Petrous bat.

1. INTRODUCTION

Nipah virus (NIV) is a zoonotic virus, meaning that it can spread between animals and people. Human Nipah virus (NIV) infection is an emerging zoonotic disease which was first recognized ina large outbreak of 276 reported cases in Malaysia and Singapore from September 1998 to May1999. In India, during 2001 and 2007 two outbreaks in human were reported from West Bengal,neighboring Bangladesh. Large fruit bats of Pteropus genus are the natural reservoir of NiV. Recently outbreaks have been reported from Kerala in 2018, 2019 and 2021.

2. THE HISTORY OF NIPAH VIRUS

First identified

In 1998, the Nipah virus was first identified in Malaysia during an outbreak of neurological and respiratory disease in pigs. The virus was named after the Malaysian village of Sungai Nipah,where it was first identified.

2.1 Nipah virus Outbreaks

Malaysia-Singapore 1998–1999

NiV first emerged in Malaysia as a pig livestock disease transmitted to humans, causing a large encephalitic outbreak with an estimated mortality of 40%, which accounted for 276 cases and 106 deaths [4]. The epicenter was retrospectively located in a farm in the Ipoh village, where the first human case was reported in January 1997.

Afterwards, the virus disseminated throughout Peninsular Malaysia and Singapore through livestock sales during 1998/1999 [5,6].

The farm generated a key intersection between commercial fruit production, the livestock industry, and the local circulation of Pteropus bats (natural viral reservoir), establishing an ideal scenario for an outbreak origin. Fruit became an attraction for Pteropus, enabling the contact of livestock with chewed fruits and bat excreta spilled into pigsties, leading to bat–pig transmission and viralcirculation in a naïve pig population. Posterior pig-to-human transmission initiated the human outbreak.(3)

India

The territory reported outbreaks in 2001, 2007, and 2018, showing similar patterns ofinterhuman airway transmission as in Bangladesh

2.2 Transmission

Nipah virus is primarily transmitted through contact with infected animals or contaminated environments. The primary hosts are fruit bats (Pteropus species), which can spread the virus through their saliva, urine, and feces. Pigs are also susceptible and can act as intermediate hosts.Human-to-human transmission has been documented, particularly in healthcare settings and among close contacts of infected individual

2.3 Way of transmission

Fruit bat (Pteropus species) : when the infected bat transfer the virus (NV) to fruits of palm tree then it transfed to human beings who ate the plam fruits not only plam fruits and also remaining fruits.

Pigs : when the normal person direct contact with pigs or they(pigs) eaten by humans causetransmission of Nipah virus to humans

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Diagnosis

Nipah virus (NiV) infection can be diagnosed during illness or after recovery. Different tests are available to diagnose NiV infection. During early stages of the illness, laboratory testing can be conducted using real time polymerase chain reaction (RT-PCR) from throat and nasal swabs, cerebrospinal fluid, urine, and blood. Later in the course of illness and after recovery, testing forantibodies is conducted using an enzyme-linked immunosorbent assay (ELISA).(7)

Diagnosis of Niv is done by two methods:

1)RTPCR

2)ELISA

Sample collection and transport and testing guidelines

Laboratory confirmation of a suspect and also a symptomatic with definite history of contact casecan be made during the acute and convalescent phases of the disease by using a combination oftests. The samples have the be sent to designated laboratories identified as per protocols prepared.

Treatment of nipah virus

Currently there are no antidote for Nipah virus only treatment for minimizing the symptomsand boosting of our immune system available for Nipah virus (NIV) infection. Treatment is limited to supportive care, including rest, hydration, and treatment of symptoms as they occur.

Treatment of individuals infected with the NIV is currently limited to supportive care. Due to physical human to human contact being the highest risk factor for transmission of infection, extra caution is demonstrated during the management of these patients. There are no licensed therapeutic interventions for treating the NIV. While antiviral treatment seems to be the obviouschoice, current intervention strategies are remarkably few.

Treatment of Nipah virus in two methods they are

1. Anti viral drugs
2. Monoclonal antibodies

1. Anti-viral drugs: Antiviral drugs are the class of medication used fortreating of viral infections like Nipah virus. **e.**g. Remdesivir, Favipiravir, Ribavirin, Faldaprevir.

Remdesivir: Broad-spectrum RNA polymerase inhibitor antiviral prodrug. It has demonstrated potent replication-inhibitory activity in in vitro and in vivo experimentation. It constitutes a potential therapeutic candidate and a possible viral clearance adjuvant for survivors as a recurrence preventive measure. High seropositive maintained titers relate to incomplete viral clearance in patients and increased risk of infection recurrence; the intense viral clearance observed in experimental animals treated with remdesivir supports its use on selected patients

MONOCLONAL ANTIBODY (mAb): Normal B lymphocytes and plasma cells do not survive for long or secrete significant quantitiesof antibodies in tissue culture. However, there is a class of malignant B cell tumors called myelomas that can be propagated indefinitely in tissue culture and will proliferate rapidly, oftensecreting large quantities of immunoglobulins. Monoclonal antibodies are made by fusing antibody-secreting B cells with myeloma cells. These fused cells now become immortal (they willgrow and divide indefinitely) and are called hybridoma.

Eg : m102.u, n503.1, Nahi.3

Preparation of monoclonal antibodies

Preparation of monoclonal antibodies are prepared by using mice and myloma cells in six steps.

Step 1: Immunization of mice

Step 2: screening for antibodies production and removal of spleen at high level

Step 3: fusion of myloma cells with spleen cells by using polyethylene glycol

Step 4: selection of hybridoma cells culturing by using HAT Medium

Step 5: sub culturing of hybridoma cells

Step 6: collection of Hybridoma cells

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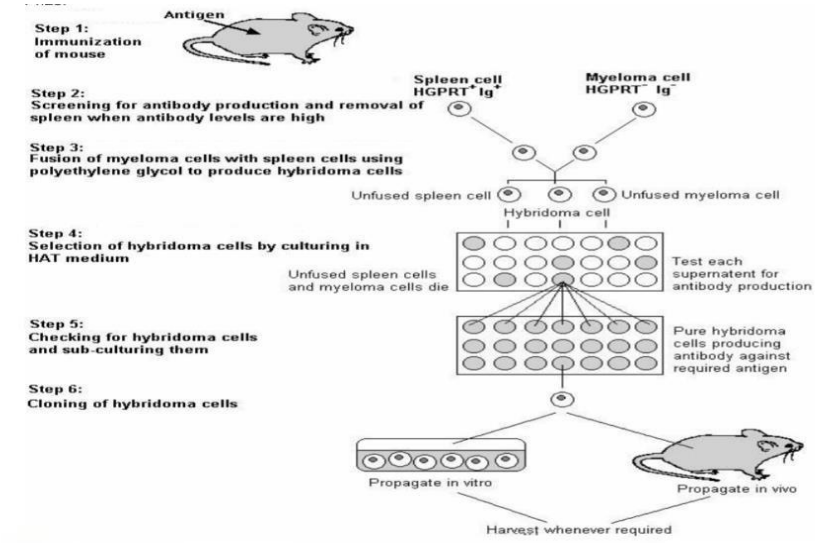

Fig 1: preparation of monoclonal antibodies in mice.

Herbal drugs used in nipah virus:

Herbal drugs are can't cure Nipah virus completely instead of that it boosting our immune system by producing new antibodies in our body. Many plants contain compounds that can support the immune system and help the body fight off infections. Some herbs also have antiviral properties—exactly what's needed against a virus like Nipah

The herbal medicine listed below can effectively cure Nipah virus infections without causingany negative side effects. This decoction, or kasha yam, can be made at home. Herbal stores willcarry all of the medicinal herbs listed below in powdered form.

Eg : Vishnukiranthai, Gudichi plant, pavalamalli plant, Vallarai plant,

vishnukiranthai : Also known as *morning glory , is* a medicinal herb with tinypurple blossoms

Synonym : slender dwarf morning-glory, dwarf morning-glory.

Biologicalsources : It is obtained from the flowers and leaves of Morning glory plant.

Family : flowering plant of Convolvulaceae.

Chemical constituents : The seeds of many species of morning glory contain ergoline alkaloidssuch as the psychedelic ergonovine and Ergine (LSA). Seeds of Ipomoea tricolor and Turbine corymbose (syn. R. corymbose) are used as psychedelics.

Uses

- It act as a Antiviral.
- It act as a anti - inflammatory.
- It has a immune-stimulating qualities.
- This demonstrates its ability to treat fevers.(19).

Fig 2 : Vishnukiranthai plant and powder

NiV emerged as a new virus exactly 20 years ago, causing severe morbidity and mortality in both humans and animals and destroyed the pig-farming industry in Malaysia, and it continues to cause outbreaks in Bangladesh and India. As the reservoir host Pteropus bat is widespread, and NiV has been found in bats in various countries, the potential for outbreaks to occur in new regions remains significant. In treatment of Nipah virus there is no specific antiviral agents but some agents are used and Herbal drugs shows better results then supportive care.

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Monkeypox is a zoonotic disease caused by the monkeypox virus (MPXV) and is transmitted through direct contact with infected animals or individuals exposed to infectious sores, scabs, or body fluids. The disease has been reported in Western and Central Africa since 1971 and has since spread internationally. Despite the use of anti-virals like cidofovir, Brincidofovir, and tecovirimat, there is still no definitive cure for monkeypox. Awareness about transmission and the development of appropriate diagnostic procedures and antiviral medication are needed.

Mpox is a disease caused by the mpox virus that has regularly been reported in some partsof the world. In May 2022, an international outbreak of mpox was identified in Western Europe,Canada, and the United States, where mpox does not typically occur. The mpox virus is closely related to the variola virus (the cause of smallpox) but is much less deadly. Initial symptoms of mpox disease include fever, headache and body aches, fatigue, and swollen lymph nodes, followed by a rash of lesions on the skin. Like smallpox and other pox viruses, mpox is classified as a high-risk pathogen because it can easily be transmitted from person-to-person, posing a danger to public health. Cases may be severe, especially in children, pregnant women, or peoplewith suppressed immune systems. As a result, on August 4, 2022, the U.S. Department of Healthand Human Services (HHS) declared a public health emergency (PHE) in response to the current outbreak

History :

It was in 1970 that the first patient of human monkeypox was diagnosed in the DRC. After that, more than 400 monkeypox patients were documented in Africa between 1970 and 1990. Of these,the vast majority were diagnosed at DRC monkeypox virus (MPXV), was recognized only in non- human hosts. Between 1970 and 1986, 10 cases of human monkey pox were reported from Western African countries (Sierra Leone, Nigeria, Liberia and Côte d'Ivoire) and 394 cases were reported from the Congo Basin countries of Cameroon, Central African Republic and Zaire (now Democratic Republic of the Congo).

India :

First case : The first case of mpox in India was reported in Kerala on July 14, 2022. It was suspected to be imported.

First locally transmitted case : The first locally transmitted case was reported in Delhi on July 24,2022. The patient was a middle-aged man who had not recently traveled abroad.

First case of Clade 1b strain : India reported its first case of the Clade 1b strain of mpox in September 2024. The patient was a 38-year-old man from Kerala who had recently returned fromDubai.

Transmission

Mpox spreads from person to person mainly through close contact with someone who has mpox, including members of a household. Close contact includes skin-to-skin (such as touching or sex) and mouth-to-mouth or mouth-to-skin contact (such as kissing), and it can also include being face-to-face with someone who has mpox (such as talking or breathing close to one another,which can generate infectious respiratory particles).

Mpox is caused by monkey pox (MPXV).

The virus that causes mpox can spread to humans from animals or from person to person. Thereare two types of virus: Clade 1 and clade 2. These clades also are called clade I and clade II. The term "clade" is the name for a group of related viruses.

The virus can spread from person to person through:

- Direct contact with the rashes, scabs or body fluids of a person with mpox. Close, face-to-face contact, intimate activities and sexual contact.
- Close, face-to-face contact, intimate activities and sexual contact.
- Contact with fabrics or objects that have touched the rashes or body fluids of a personwith mpox.
- A pregnant person who gets mpox can pass the virus to the unborn baby.

The virus also can spread to humans from direct contact with an infected animal, which includes:

- **Person-to-person:** Close contact with an infected person's skin, scabs, or bodily fluids cantransmit the virus. This includes:
- **Animal-to-human:** Physical contact with an infected animal, such as through bites or scratches, can transmit the virus. This can also happen during activities like hunting, skinning, trapping, cooking, or eating contaminated meat.
- **Pregnant women to fetus:** A pregnant woman can transmit the virus to her fetus throughthe placenta

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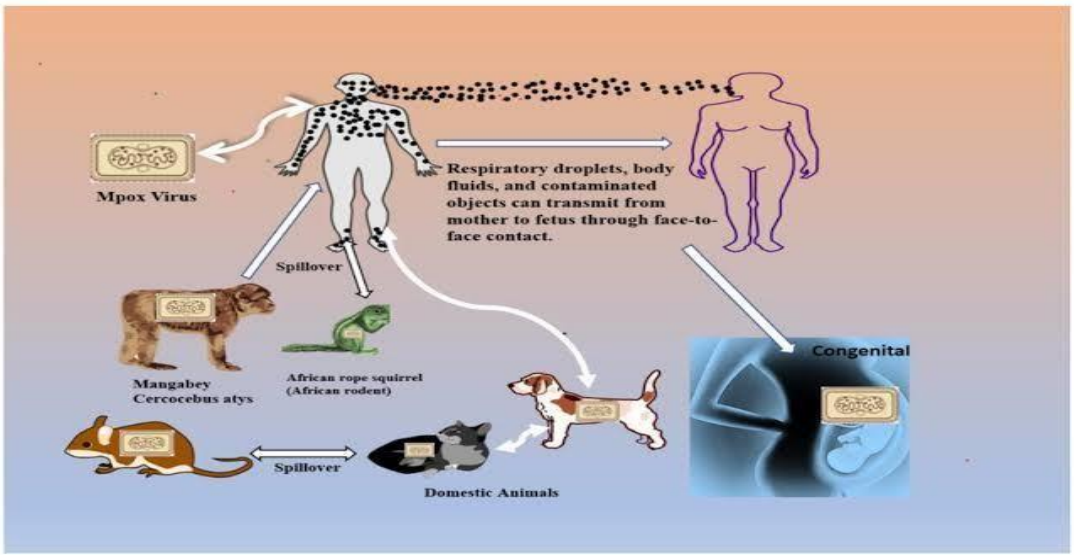

Fig 3 : Transmission of monkey pox

3. DIAGNOSIS OF MPOX VIRUS

3.1Mpox Laboratory-Based Testing Methods :

Identifying Mpox based on symptoms is challenging due to similar clinical manifestations from different OPVs. Early detection is crucial for isolation and treatment, and highly sensitive diagnostic techniques are needed. Common methods include PCR, immunological assays, and virus isolation. This article reviews current laboratory techniques and compares strengths and limitations of diagnostic tests.

3.2Nucleic acid amplification Testing *:*

Nucleic acid amplification testing (NAAT) confirms MPXV infections by identifying unique viral DNA sequences. It distinguishes Congo Basin and West African virus strains. Academic research validates PCR protocols for OPXV detection and MPXV clade identification, with commercial kits offering superior sensitivity and specificity.

3.3Serology

Serology for diagnosing MPXV should be avoided in isolation due to potential cross reactivity with other Ortho poxviruses and vaccinations. Testing should be limited to reference laboratories until further substantiation is provided for point-of-care tests. If validated, IgM or IgG detection in recently ill patients or paired serum specimens can enhance diagnostic accuracy.

4. TREATMENT OF MPOX VIRUS

While mild cases are managed with symptomatic treatment, in severe cases of mpox, supportive treatment and treatment of systemic complications and secondary bacterial infections continue to be the cornerstone. There are currently no approved treatments for mpox(formerly monkeypox), but some antiviral drugs may help in certain cases:

4.1 Antiviral Agents Anti viral agents completely cannot cure the mpox virus but they can boost uup our immune system.

Eg : Tecovirimat, Brancidiovir,

4.1 Tecoviremat

Tecovirimat is an antiviral drug that was identified via a high-throughput screen in 2002.2 It is effective against all Ortho poxviruses, including vaccinia, cowpox, ectromelia, rabbitpox, monkeypox, and Variola (smallpox) virus. Tecovirimat (ST-2462) is a derivative of 4- trifluoromethyl phenol, a low-molecular-weight compound. It inhibits the egress of the virus by

targeting the VP37 protein, which blocks the final steps in virus maturation, preventing it from leaving the infected cell.

Route of administration

Tecoviremat is available in oral and intravenous formulations

Mechanism of action :

The Ortho poxvirus P37 protein mediates the formation of enveloped virion forms, which are essential for cell-to-cell and long-range virus dissemination. It interacts with Rab9 GTPase and TIP47, components of late endosomal transport

vesicles, leading to the virus-specific wrapping complex for enveloped virions. Tecovirimat, an inhibitor of P37, blocks this interaction, preventing the formation of the wrapping complex.

Brincidofovir :

Brincidofovir is a oral antiviral agent act as a pro-drug. After enter into the cell it Cidofovirfurther get phosphorylation and become as a cidofovir diphosphate by intracellular kinases.

Mechanism of action :

Brincidofovir is delivered into target cells whereupon the lipid side chain is cleaved, releasing cidofovir to be further phosphorylated by intracellular kinases to cidofovir diphosphate. Cidofovir diphosphate acts as inhibitor of DNA Pol, resulting in decreased DNA synthesis and chain termination.

Route of Administrtion : It is Available in IV Route.

5. CONCLUSION

When some progress has been made in the development of drugs against Mpox, it is crucial to expedite the research progress. This will enable us to effectively combat potential long-term outbreaks and the emergence of drug-resistant Mpox virus strains.

In the development of drugs against Mpox, the following aspects should be given priority: Firstly, improving the specificity and delivery efficiency of drugs is essential to ensure accurate targeting of the Mpox and efficient transmission to the infection site. Secondly, development anti-Mpox drugs that are less prone to resistance is necessary to prevent the gradual emergence of drug-resistant strains and ensuring sustained efficacy of treatment. Additionally, exploring the development of sequential and combination drug therapies should enhance effectiveness against different stages of Mpox infections and their variants.

Lastly, attention should be paid to drug modifications to mitigate or eliminate toxicity, minimizing the adverse impact on patients during the treatment process. The early investment in drug development against Mpox is crucial in tackling the ongoing global Mpox outbreak.

Accelerating progress in the development of effective anti-Mpox drugs will help prepare for future challenges and provide more reliable protection for public health targeting the VP37 protein, which blocks the final steps in virus maturation, preventing it from leaving the infected cell.

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