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Nipah Virus and Its Implications in Pharmacy Practice: Prevention, Treatment and Patient Counselling – A Comprehensive Review.

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ABSTRACT:
The Nipah virus is a highly lethal RNA virus that belongs to the family of Henipavirus and which is commonly present in bats of fruits, though can infect humans and animals, especially pigs. Outbreaks have occurred in South and south east Asia with a high mortality rate in the form of severe respiratory diseases and encephalitis. No specific antiviral practice or approved vaccine exists and the primary mode of management is supportive care and containment of the infection. The reason is the potential pandemic, constant monitoring, and preparedness, which is indispensable, and pharmacists play an important role in the awareness of the community of health and responding to the outbreaks.

KEY WORDS : Henipavirus, Nipah Virus, Hendra virus, Pandemic, Encephalitis, Epidemiology, Pathogenesis, Zoonotic, Outbreak, Acute respiratory distress syndrome, Paramyxoviridae, Human to Human transmission, Respiratory system, Central nervous system, Pteropus bats, Genome, Symptoms, Reverse Transcription Polymerase Chain Reaction, Ribonucleic acid, Polymerase chain reaction, Enzyme-linked immunosorbent assay.

1. INTRODUCTION :

The Nipah virus, commonly referred to as NiV, is a RNA virus having single stranded nucleotides that belongs to the Henipavirus genus, which also includes the recently discovered Hendra virus, usually known as HeV, and Cedar virus. It is a member of the Paramyxoviridae family. Bats naturally contain henipaviruses. The World Health Organization (WHO) has made NiV one of its top priorities for research and development in order to be ready for any future pandemics or outbreaks. Malaysia published the first description of NiV in 1998. Since then there have been documented outbreaks in South and Southeast Asia. NiV is harmful to numerous animal species.. The virus may have pandemic potential because of its zoonotic and interhuman transmissibility [1]. This virus has a helical nucleocapsid and is encapsulated and single-stranded, that is 40–1900 nm long and a genome that is 18 knt long. It has frequent mutations like other RNA viruses. If the human-adapted strain spills over within South Asian communities, the high population density and international travel could make it spread fast from human to human. This spread could make a pandemic like COVID-19[2].NiV infections have a 4–14 day incubation period and range in severity from mild to severe. Fever, headaches, and respiratory distress are among the early symptoms. Sleepiness, confusion, a progressive

coma, and even death are possible outcomes of subsequent encephalitis. Survivors may experience long-term consequences like ongoing seizures or altered behavior. Vasculitis-associated thrombosis is the cause of the virus's multiorgan involvement. Neither specific antiviral medications nor targeted vaccines are currently on the market. Supportive care includes antipyretics, anti-convulsants, oxygen and fluid supplements, and nutritional assistance. Because NiV is transboundary and has no known cure, it poses a major health danger [3].

2. EPIDEMIOLOGY:

2.1. Malaysia & Singapore:

In Malaysia, human NiV infection was initially discovered between 1998 and 1999 [4]. Sungai Nipah (Nipah River village) is where the name "Nipah" originates. In September 1998, several cases from the Malaysian state of Perak were reported, exhibiting fever, headache, and decreased consciousness. IgM antibodies against Japanese encephalitis (JE) were found to be present in four instances, initially leading to the announcement of a JE outbreak [5]. An outbreak involving 11 cases and one fatality among slaughterhouse workers was reported from Singapore in March 1999 [6]. One risk factor for these outbreaks was determined to be close contact with pigs or pig waste[7].

2.2.India:

Two NiV outbreaks in humans were documented in West Bengal, India, in 2001 and 2007. Both outbreaks were marked by extremely high mortality rates: the first in the Siliguri district, where 45 out of 66 infected (68.18%) died, and the second in the Nadia district, where five out of five infected (100%) died. In May 2018, the districts of Kozhikode and Malappuram in the southern west coast state of Kerala, which is geographically distant from the previously affected areas, reported a NiV epidemic. Consuming date palm sap is unusual in this area. As of June 1, 2018, there were 17 fatalities and 18 confirmed cases [8].One person in the 2007 outbreak got the disease from drinking date palm-based alcohol, and everyone else, including a healthcare worker, got it from the first case [9].

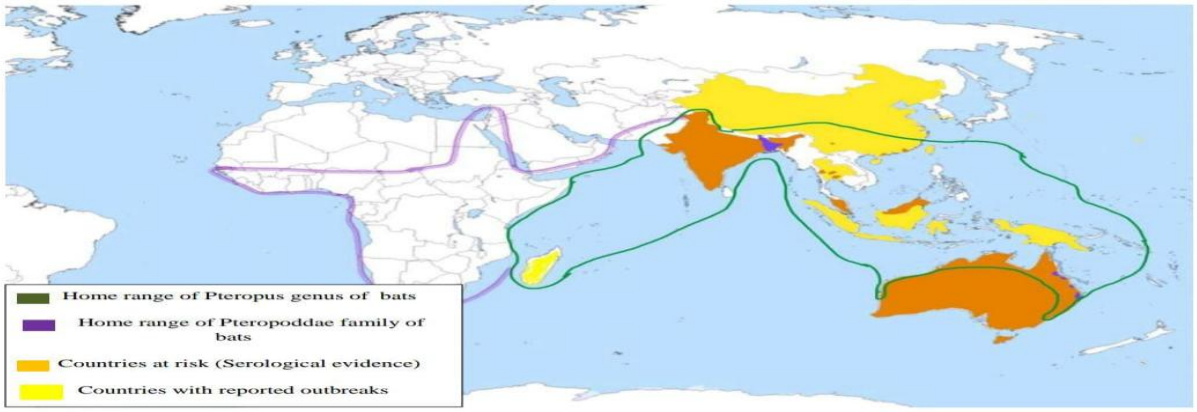

Fig 2.1 . Epidemological distribution of Nipah virus in India, Bangladesh, Malaysia and Philippines

2.3. Bangladesh ;

Bangladesh has experienced seasonal NiV outbreaks during the winter months since 2001, mostly in 20 districts. Pteropus has been found to be the NiV reservoir animal in these regions [10]. In Bangladesh, eating the raw sap of the date palm is the primary way that infections are spread, and this feeding habit gives scientists insight into how bats can infect humans [11]. Another significant pathway of transmission in Bangladesh is human-to-human contact, which has been linked to every outbreak; one of the most significant of these took place in Faridpur in 2004[12]. The disease may also be transferred through consuming fruits that has been eaten by a bat, according to some theories [13].

2.4. Philippines:

The Philippines experienced a NiV virus outbreak in 2014. With 17 confirmed cases82% of cases resulted in death. Ten people had previously interacted closely with horses or eaten horse flesh. Neurological signs were present in nine of the ten horses that died during that time. Horse samples, however, were not examined for NiV. The disease was spread from person to person among five patients, including two medical staff members. The Malaysian strain, which had not yet been demonstrated to have a distinct person-to-person dissemination, was closely related to this strain [14].

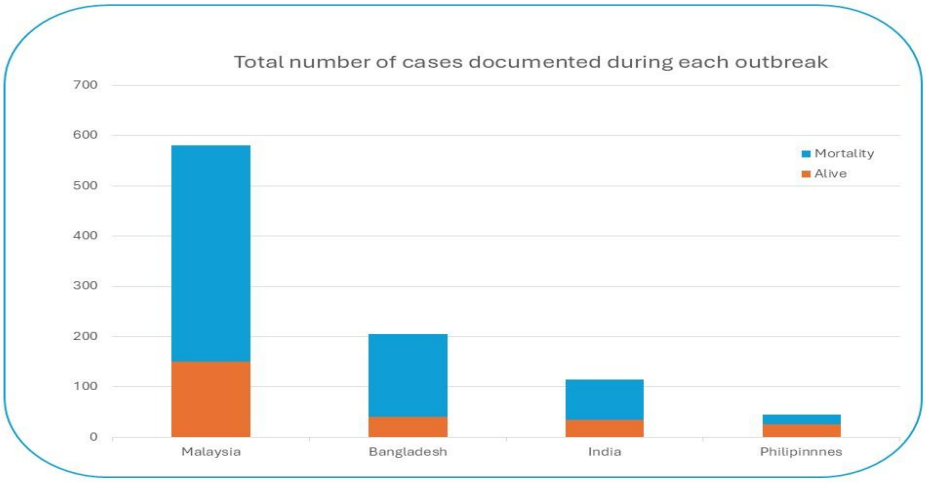

Fig 2.2 : The total number of cases reported for every outbreak.

3. PATHOGENESIS:

3.1. Cellular Mechanisms:

Henipaviruses are the only zoonotic paramyxoviruses. They are also remarkable due to their broad host range and high case fatality rates. Their negative-stranded RNA is not segmented. The genome encodes six structural proteins of the order 3′-N-P-M-F-G-L-5′: matrix protein (M), fusion protein (F), glycoprotein (G), phosphoprotein (P), large protein (L), sometimes called RNA polymerase, and nucleocapsid protein (N) [15]. The helical nucleocapsids that make up the genomes of C, V, and three additional anticipated non-structural proteins are encased to create pleomorphic, spherical to filamentous virus particles. Compared to other paramyxoviruses, HeV and NiV have significantly bigger genomes [16].

3.2. Virus entry:

Studies on infected pigs and hamsters have shown that the respiratory epithelium is the initial location of NiV infection and that the oronasopharyngeal pathway is the main method that NiV enters the host. NiV first multiplies in the respiratory system during viremia, infecting airway endothelial cells, before concentrating on bladder and kidney epithelial cells to propagate throughout the body. NiV enters the bloodstream and moves to the brain, stomach, and excretory systems as the disease progresses. NiV can enter the central nervous system (CNS) in a number of ways, such as through olfactory neurons in the nasal cavity, transmigration of NiV-bound uninfected leukocytes into the brain, and replication in endothelial cells that breaches the blood–brain barrier (BBB). NiV enters most animal models and then uses the effective mechanism of nucleoprotein aggregation in degenerating axons to disseminate throughout the central nervous system (CNS) [17].

3.3. Pathogen-host interaction:

The F and G proteins in the NiV virus's envelope control the virus's attachment and entrance into host cells . On neurons and epithelial cells, respectively, the G protein binds to host cell receptors known as ephrin-B2 (EFNB2) and ephrin-B3 (EFNB3). Seven successive residues on top of the globular head of the G protein mediate its interaction with the EFNB2 receptor [18].

A KKR motif in the cytoplasmic tail of the F protein facilitates viral penetration by promoting viral membrane fusion with host cells pH-independently [19][20]. The precursor F0, the first form of the F protein, is broken down by proteases. Cathepsin L in Vero cells and cathepsin B in MDCK cells are most likely responsible for this process, which produces disulfide-linked F1 and F2 subunits that form a full fusogenic F heterodimer. The main role of the F1 subunit is to facilitate the fusion of the viral membrane with the host cellular membrane [21].

3.4. Host Immune response:

When NiV attaches and unites with host cells, innate antiviral defense is affected because cytoplasmic RNA helicases identify viral RNA, which sets off a powerful IFN-I response that activates multiple IFN-induced genes, including OAS1, ISG56, and IP-10[22]. It has been demonstrated that the P gene products suppress interferon activity [23]. Another study has shown that NiV infection inhibits interferon production while having minimal impact on interferon signaling [24]. The lungs have been found to contain viral antigens, mostly in the bronchi and sometimes even in the alveoli. The expanded pulmonary tract epithelium brought on by the infection releases cytokines, which results in the development of a disease that resembles acute respiratory distress syndrome (ARDS) [25].The airway epithelium also releases inflammatory mediators such interleukin granulocyte-colony stimulating factor in the later stages of infection [26]. In addition to the IFN-I response, pro-inflammatory cytokines such TNF-α and IL-1 were also increased following Niv infection [27].

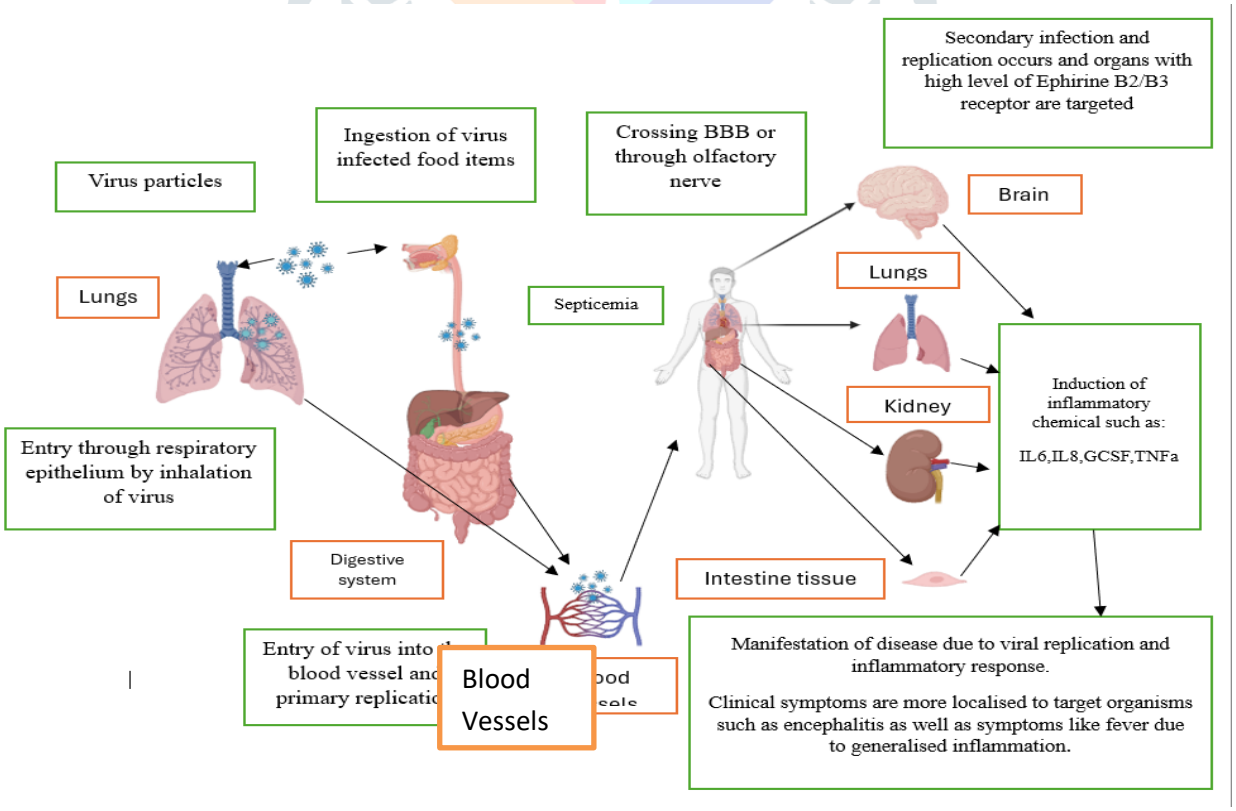

Fig 3.2: Pathogenesis of Nipah virus in humans.

4. PATHOPHYSIOLOGY OF NIPAH VIRUS:

A Nipah virus infection mostly affects the heart, brain, lungs, kidneys, and spleen. Primary signs can swiftly turn into an encephalitic syndrome, but they first resemble flu-like diseases, which includes fever, headache, and severe neurological symptoms[28].Research indicates that individuals who have physical contact with Nipah-positive individuals but are not exposed to bodily fluids are less likely to develop subclinical infections, even though latent infections may reoccur months or years after acute sickness [29].

4.1. In respiratory system: Acute respiratory distress syndrome (ARDS), coughing, pneumonia, and dyspnea are among the symptoms. The initial symptoms are similar to those of influenza and include muscle aches, headaches, sore throat, and fever.

4.2. In central nervous system: Within 24 to 48 hours, the Nipah virus causes encephalitis, or swelling of the brain, seizures, and coma. Neurological symptoms that frequently accompany flu-like symptoms include fever, headaches, tiredness, disorientation, convulsions, and coma.
When the virus replicates in the brain cells, inflammation takes place in the brain, which may cause nerve damage. Serious side effects include meningitis and meningoencephalitis, which include inflammation of the brain and spinal cord. Chronic neurological problems such as behavior disorders, motor impairments, and cognitive impairment may affect survivors [30].

5. NIPAH VIRUS GENOME:

Along with an unknown group of viruses and the five genera (Respiro-, Morbilli-, Rubella-, Avula-, and Henipavirus), the NiV belongs to the Paramyxovirinae subfamily of the Paramyxoviridae family [31]. Large RNA polymerase, matrix, fusion, phosphoprotein, nucleoprotein, and glycoprotein are all produced by the six genes that comprise the genome (N, P, M, F, G, and L) [32]. Compared to other paramyxovirus members, the Henipa group of viruses has a larger genome (roughly 18250 nucleotides) because the P gene's open reading frame is longer and all of the genes—aside from the L gene—have longer non-coding regions. The G and F proteins of NiV are essential for both facilitating the virus's entrance into the cell and initiating the generation of neutralizing antibodies [33]. The P gene of henipaviruses contains at least three non-structural proteins (C, V, and W), despite the fact that the P protein is the only gene product required for genome replication. The additional gene products are usually not required for virus replication in vitro, despite the fact that they frequently function as virulence factors in vivo.
Virus particles are between 120 and 500 nm in size. Thin-section electron imaging of infected cells revealed filamentous nucleocapsids within cytoplasmic inclusions incorporated into virions arising from the plasma membrane [34].

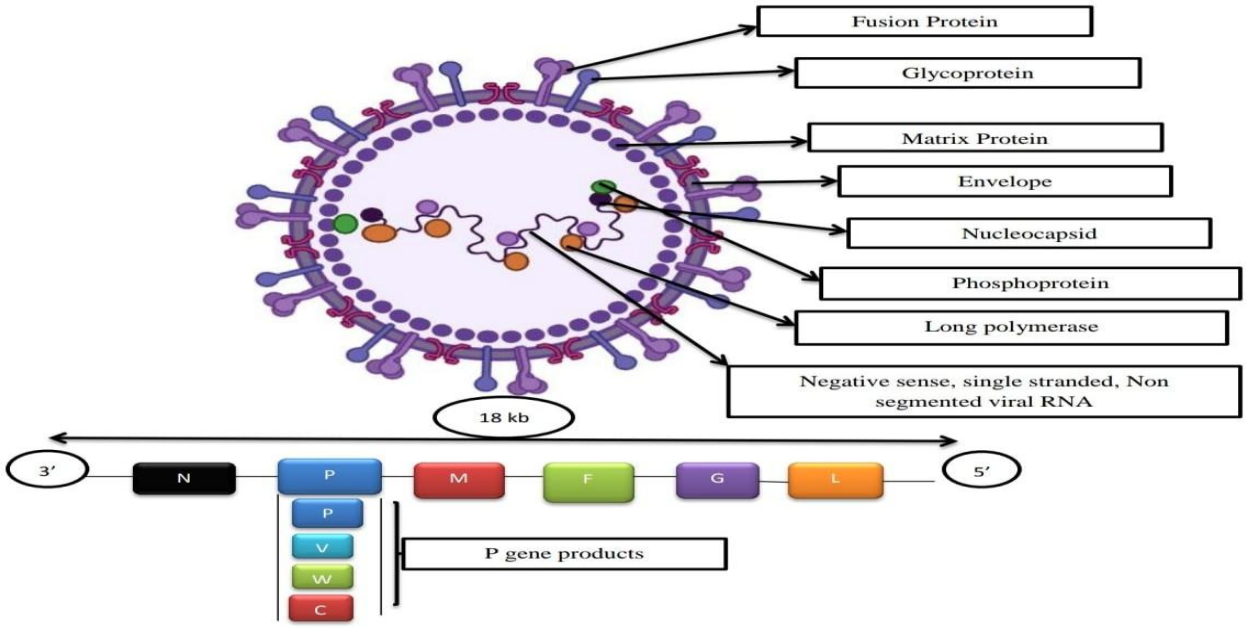

Fig 5: Structure of Nipah virus.

6. HOST RANGE:

6.1. Pteropus Bats:

The natural reservoir hosts of NiV are fruitbats, also referred to as flying foxes. They are P. vampyrus and P. hypomelanus, and they are found in Malaysia. The virus that infected the pig population is thought to have originated from Pteropus bat species. There are more than 60 insectivorous bat species, including two flying fox (Pteropid) bat species, and at least 13 fruit bat species in Southeast Asia [35]. Neutralizing antibodies were found in five bat species, four fruit bat species, and one insectivorous bat species during a serological survey conducted during the 1999 pandemic. This included 17% of Peninsular Malaysians with positive antibody status to Pteropus vampyrus (Malayan flying fox) and 31% of those with positive antibody status to Pteropus hypomelanus (island flying fox) [36].

Fig 6.1: Pteropus bats the main reservoir of spreading Nipah virus.

6.2. Pigs:

Pigs act as the amplifying host. Human outbreaks of encephalitis with a 40% case fatality rate in Malaysia and Singapore have been proven to be caused by exposure with diseased pigs. While the outbreak in Singapore stopped when pig imports from Malaysia were banned, the outbreak in Malaysia ended when almost 1 million pigs, or 45% of all pigs in Malaysia, were culled from the outbreak area and its immediate environs [37].

6.3. Cats:

Research has demonstrated that during the viremic phase, NiV is expelled by infected cats through their urine and nasopharynx [38]. High recoverable virus levels were found in the placenta and uterine fluid of a pregnant cat infected with experimental NiV. Given the elevation of viral replication and in embryonic tissues, spillover events—a critical element of the epidemiology of Henipa virus infection—may be caused by both vertical and horizontal transmission of NiV [39].

6.4. Dogs:

It has also been demonstrated that dogs in the outbreak area are infected with NiV [40] . Immunohistochemical analysis verified the NiV infection in one dead dog and one dying dog from the Malaysian epidemic area. Histologic evidence of severe disease was found in both [41].

7. ROUTE OF TRANSMISSION OF NIPAH VIRUS:

7.1. Through Pigs:

Humans contracted NiV through direct interaction with fresh pig products or pigs, supporting early results by medical professionals[42]. Direct contact with the pigs' respiratory, pharyngeal, and urinary secretions was the reason behind the disease's rapid spread among the pigs on the infected farm, as evidenced by the Malaysian experience. The findings regarding the respiratory system of pigs could support the notion that aerosol transfer from pigs to humans is the main mechanism of NiV infection and help to elucidate these animals' significant pulmonary symptoms [43].

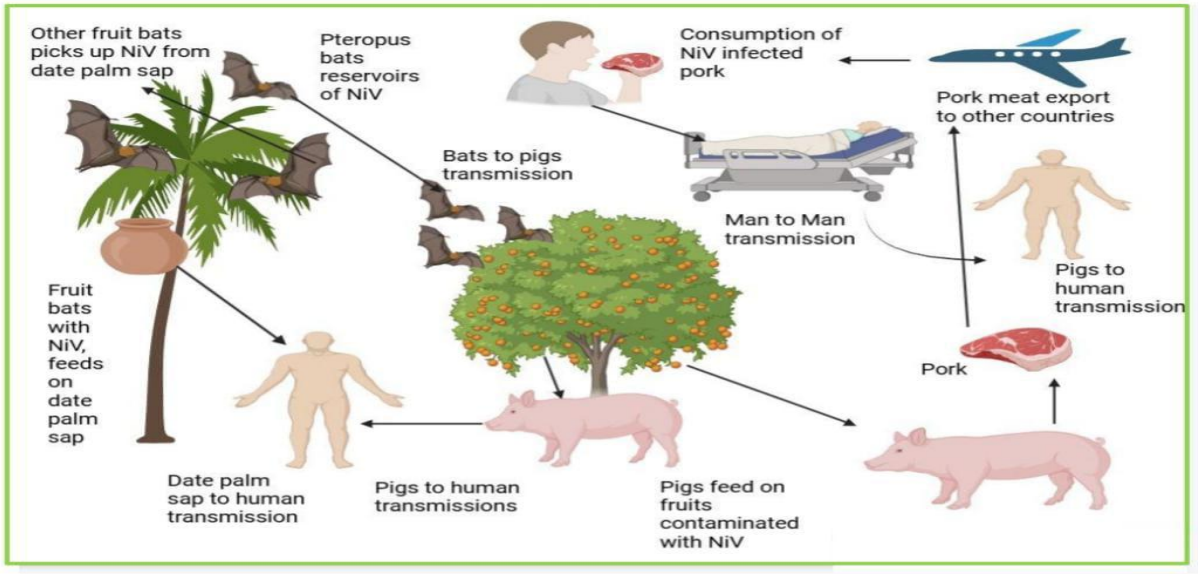

Fig 7 : Route of transmission of Nipah virus.

7.2. From dead bodies:

Funeral customs serve as a representation of additional potential risk factors for transmission. Exposure to NiV occurs during purification procedures after Because the virus can still be found in postmortem respiratory secretions, avoid making personal contact with the hands and face of the deceased. Use of gloves or masks during these ceremonies is not customary, which raises the risk of infection, particularly if the performer

comes into contact with the performance's face, eyes, or nose. Similarly, some religions allow for ceremonial baths in which water is poured directly onto the deceased's body[44].

7.3. Human to Human transmission:

Although 18% of cases in Bangladesh were solitary, Nipah illnesses typically occur in clusters or as an outbreak[45]. Human-to-human transfer is a major source of infection and a possible public health issue. Close touch with an infected person or their secretions may cause this. During required medical-nursing operations, direct contact might take the form of physical contact or interaction with the patient[46]. The most hazardous are respiratory secretions and saliva [47]. Sharing glasses and dishes with an ill person is another common way to spread the disease because it can be easier for saliva to spread the infection[48]. The sexual route is another method of human-to-human transmission that requires more research. Study says that semen from infected people contained the virus [49].

7.4. Through Bats

Villagers affected by NiV reported that bats were consuming fruit from trees like Litchi guava and mango. It is unknown if this tainted fruit acted as a vehicle of transmission, but it merits more research because it appears to be a likely route of transmission in theory.

The popular alcoholic beverage "toddy," which is made from coconut palms in places like Kerala, is thought to be a vehicle for the spread of NiV [50].

8. CLINICAL SIGNS:

8.1. In humans:

8.1.1. Stage I:

The majority of subjects (>90%) experience symptoms within two weeks of being exposed to NiV, with humans having an incubation period of four days to two months. Patients may experience headache, nausea, dizziness, and fever before developing severe encephalitis.

8.1.2. Stage II:

Many patients have significant signs of medulla oblongata dysfunction, such as aberrant pupillary reflexes, vasomotor abnormalities, seizures, and myoclonus, along with sensory blunting[51]. The medulla oblongata is focally involved in the multifarious neurological involvement, diffuse encephalitis, and meningitis. Cerebellar signs are relatively common [52].

8.1.3. Stage III:

Two features of NiV infection are recurrence and late onset of encephalitis in survivors, even months or years after the acute initiation [53]. Psychiatric symptoms may also include personality changes, sadness, difficulty focusing, and verbal and/or visual memory impairments [54]. The virus causes serious illness that can impact a person's respiratory and central nervous systems.

8.1.4. Stage IV:

There could be gastrointestinal bleeding, kidney damage, and the development of septicemia. In extreme cases, seizures and encephalitis may appear 24 to 48 hours apart, ultimately leading to coma [55]. In severe human outbreaks in Malaysia where 50–60% of patients develop ARDS, neurological manifestations are well-documented, particularly when the disease is in its advanced stages [56].

8.2. In animals:

8.2.1. Pigs:

The disease manifests in pigs as neurological and respiratory symptoms that vary in severity based on the age of the afflicted individual. The most obvious signs in suckling pigs (those younger than 4 weeks) are muscle tremors and dyspnea, and mortality rates can be as high as 40%. Fever (>39 ◦C), respiratory symptoms like dry, unproductive coughing, "open mouth" breathing, and epistaxis are the hallmarks of the sickness, which typically affects animals between the ages of one and six months [57].

8.2.2. Dogs & Cats:

NiV infection in dogs can cause lung inflammation, glomerular and tubular necrosis, and kidney syncytia. Endothelial syncytia and vasculopathy in several organs may develop in cats.

8.2.3. Other Terrestrial Animals:

Experimental NiV infection causes lesions in the CNS's parenchyma and vasculopathy in a variety of animals, including hamsters, guineapigs, chick embryos, and African green monkeys. However, for unclear reasons, mice and rats do not appear to exhibit clinical signs [58].

8.3. Findings during postmortems :

Research using human magnetic resonance imaging (MRI) has demonstrated that the brain's temporal lobes, pons, and cortex get involved. The white matter of the brain may exhibit bilateral abnormalities. The cerebral cortex may exhibit many hyperintensities (T1-weighted) that closely mimic laminar cortex necrosis. Additionally, lesions may manifest in the brain stem, cerebrum's cortex, and corpus callosum. It is crucial to keep in mind that these lesions are detected using diffusion weighted (DW)-MRI in this situation [59]. Vasculitis-induced thrombosis may result in a disseminated microinfarction in the brain. Direct involvement of the neurons is another possibility. The heart, kidneys, and respiratory system can all experience comparable vascular abnormalities. It's also noteworthy that when NiV infection occurs, the majority of blood vessels of medium and small size are affected, leading to the development of multinucleated syncytia and fibrinoid necrosis [60].

9. DIAGNOSIS:

Antigen detection, virus isolation, and serology can all be used to screen for this infection. Histopathology can be used to carry out detection. The Nipah virus in pigs has been found using respiratory secretions, blood, and various tissues. Additionally, cats' blood, urine, and respiratory secretions can contain the virus . However, the virus has also been found to infect the brain, spleen, kidney, adrenal gland, lungs, and liver in dogs. Respiratory secretions and tissue samples can be promptly diagnosed using the RT-PCR technique. A small number of labs work on virus isolation. Vero cells are used to isolate viruses, but other cell lines, like BHK, RK-13, and porcine spleen cells, can also be used for this purpose. Numerous techniques, including RT-PCR, immunostaining, and virus neutralization, can be used to identify an isolated virus. When it comes to virus detection, immuno-electron microscopy can yield useful results. RT-P C R and virus neutralization techniques can be used to distinguish between the Nipah and Hendra viruses[61].

10. DIAGNOSTIC TESTS FOR NIPAH VIRUS:

10.1. ELISA:

ELISA uses a diagnostic method based on monoclonal antibodies (mAb) to detect NiV [62]. Researchers cloned, synthesized, and purified the recombinant form of the NiV N protein—which is more commonly produced during the acute stage of NiV infection—in order to evaluate human sera using an IgM capture ELISA. IgM antibodies are usually detected within the first five days of symptoms and are among the first to appear after an infection. Over the course of two to three months, their levels progressively decline and eventually vanish [63].

10.2. PCR :

Because of its great specificity, PCR is a good method for detecting virus infections. NiV RNA can be detected in lungs secretions, urine, cerebrospinal fluid & serum using real-time PCR (qRT-PCR). Moreover, NiV can be found using RT-PCR, nested RT-PCR (nRT-PCR), and duplex, with additional confirmation obtained through amplicon nucleotide sequencing [64][65].

TaqMan-based qRT-PCR (Applied Biosystems, USA), by identifying unique sequences in the NiV N gene, it became possible to monitor newly developing Henipaviruses, including novel strains of NiV [66].RT-PCR investigations have also focused on the conserved N, M, or P sections of the NiV RNA genome. Because this PCR method does not require mRNA amplification, In comparison to traditional qRT-PCR, it might be more accurate. The Molbio Diagnostics Pvt. Ltd. and the National Institute of Virology (NIV). co-developed a portable, battery-operated PCR instrument that is now the only authorized fast diagnostic kit available on the market [67][68].

It allows the direct sequencing of the viral genome, which makes it possible to identify the virus and its lineage without disclosing details about the makeup of the virus. It enables one to ascertain the evolutionary evolution of viral organisms over time and space when applied retroactively [69][70].

10.3. Virus isolation:

When NiV is suspected in new outbreaks or in early cases, it is very helpful. Samples of the kidney, spleen, lung, and/or brain are available. On Vero cells, NiV may grow well. The cytopathic impact often manifests as distinctive syncytia and plaques in the cell monolayer after three days of growth [71]. Nucleus distributions on the syncytia of NiV and HeV are different, indicating that NiV creates larger syncytia than HeV [72].

10.4. Immunohistochemistry (IHC):

Formalin-fixed tissues of the heart, kidney, spleen, lung, and central nervous system have been stained with anti-NiV antibodies to detect viral antigens. NiV-associated lesions, including necrosis, flogosis, and vasculitis, are found in tissue sections [73].

10.5. Serum Neutralisation Test:

Despite requiring a BSL-4 facility, this test is regarded as the gold standard. After being treated with the virus, test sera are permitted to infect Vero cells. Three days later, tests can be read, and positive sera stop cytopathic effects from starting.. A 24-hour read of a modified neutralization test has been created [74]. A surrogate neutralization test can be carried out using pseudotyped viruses.

11. TREATMENT:

Nipah virus infection has been designated as a priority disease for the WHO Research and Development Blueprint, however there are presently no specific therapies or vaccinations available. Severe neurological and respiratory conditions should be treated with intensive supportive care. Monoclonal antibody therapy, an immunotherapeutic drug, is presently being researched and evaluated to treat NiV infections [75][76].

11.1. Drug therapies:

One crucial area of research is the creation of efficient therapies for NiV infection. Finding strategies to specifically target and eradicate the virus is crucial given its high mortality rate and propensity for outbreaks. This study examines a number of antiviral tactics, such as creating novel medications and repurposing already-approved ones. The ultimate objective is to improve patient outcomes and fight NiV infection by having safe and efficient treatments easily accessible [77]. Table 11.1 lists the therapeutic approaches that have been investigated thus far.

Strategy	Drug/therapeutic approach	Mechanism of action	Efficacy	Limitations	New or repurposed?	Development stage
Nucleoside analogues	Ribavirin	prevents the replication of viral RNA	36% fewer deaths from NiV encephalitis patients	Side effects; teratogenic; ineffective in in vivo models	Reused (used to different viral infections)	Suggested for use in an emergency
	4′-Azidocytidine (R1479)/Balapiravir	Inhibition of polymerase	Effective against HeV and NiV in vitro	More in vivo testing is necessary; harmful side effects	Utilized (created for HCV)	Prior to clinical
RNA polymerase inhibitors	Remdesivir	stops the viral RNA-dependent RNA polymerase (RdRp) from working. RdRp blocker	100% of non-human primates survive	Additional clinical testing is required for NiV.	Repurposed (created in response to Ebola)	Preclinical for NiV, often utilized for SARS-CoV-2.
	Favipiravir	RdRp inhibitor	Very effective in Syrian hamster models	NiV needs clinical studies.	Adapted (accepted for influenza in Japan)	Preclinical for NiV
Antimalarial drug	Chloroquine	hinders the entrance and replication of viruses	In vitro effective; in vivo unsuccessful	failed to keep hamsters from dying	Repurposed (antimalarial drug)	Preclinical
Monoclonal antibodies (mAbs)	m102.4	inhibits the binding of NiV-G to ephrin-B2/B3 receptors.	In India, it has been authorized for emergency usage and is effective in animal models.	Side effects and resistance in ferrets and AGMs have been recorded.	new	Phase I Clinical Trials
Immunomodulators	Poly (I)-poly (C12U)	Inducer of interferon	prevented hamsters from dying from NiV	Need to study in detail	-	Preclinical

Table 11.1 : Drug therapies for Nipah virus infection.

11.2. Vaccines:

Many NiV vaccination approaches have been developed and tested in animal models. A subunit vaccination based on HeV and NiV's G glycoprotein (sG) has been the most researched strategy. HeV-sG generates a cross-protective immune response against HeV and NiV [78].

There is also a vaccination made of virus-like particles derived from mammalian cells [79]. In a range of animal models, all of these techniques resulted in complete protection against oro-nasal NiV exposure after a single dosage. The efficacy of the sG vaccination in horses and the VSV vectored Ebola vaccine (rVSV-ZEBOV) make these two approaches intriguing for possible human usage.

Vector	Antigen used	Dose of immunization	Animal model	Route of vaccination	Administration Frequency	Challenge with virus titer	Route of challenge
Vesicular stomatitis virus (VSV)	rVSV expressing NiV G rVSV-ZEBOV-GP-NIVG Replication-defect-ive VSV	10^5 plaque forming units (PFU) 10^7 PFU 10^6 infectious particles	Hamsters African Green monkey Ferrets Female Syrian goldenhamsters	Intraperitoneal Intramuscular Intramuscular	Single Single Single	6.8×10^4 $TCID_{50}$(1000 LD_{50}) 10^5 $TCID_{50}$ (Malaysian strain) $\sim 5 \times 10^5$ PFU	Intraperitoneal Intratracheal Equally divided between intratracheal and intranasal routes.
Canarypox virus (ALVAC) vaccine vector	VCP2199, carrying the NiV-G and vCP2208, carrying the NiV F	10^8 PFU	Landrace female pigs	Intramuscular Intra muscular	Boosted 14 days postvaccination	$10^5$$TCID_{50}$ per hamster (>1000 times the LD_{50} Malaysian strain)	Intranasal challenge
Adeno-associated virus (AAV)	NiV G	2.1010/1.1010 gen-ome particles	Balb/c male mice	Intra muscular or	One Booster	10^4 PFU	Intraperitoneal
Vaccinia virus	NiV G and NIV F	6.1011 genome particles 107 PFU	Golden hamsters BALB/c female mice	intra-dermal Intra muscular Subcutaneously	Boosted with the same dose	1,000 PFU	Intraperitoneal
Measles virus based-vectors (HL strain or Edmonston B strain)	NiV G	1 x 105 TCID50 2 x 104 TCID50	African green monkeys Hamsters	Subcutaneously Intraperitoneal	One booster	1 x 105 TCID50 1 x 105 TCID50	Intraperitoneal Intranasal
Venezuelan equine encephalitis virus replicon particles	NiV G	3.1 x 105 IU	C3H/He mice	Foot pad inoculation	Single	PNL4-3.luc. E-R-reporter gene encoding retroviruses pseudo-typed with NiV F+NiV Gglycoproteins used in serum neutralization assay	_

Table 11.2 : Various vaccination techniques are available for Nipah virus infection.

12. PATIENT COUNSELING:

People in Bangladesh, Malaysia, India, and Singapore who have had Nipah virus (NiV) outbreaks should: Wash hands frequently with soap and water, Avoid sick pigs or bats, Avoid eating or drinking anything consumed by the bats, such as crushed fruit, uncooked fruit, and raw date palm sap, Avoid areas where bats commonly roost, Avoid contact with NiV-infected individuals and their bodily fluids. Standard infection control procedures and appropriate barrier nursing techniques are essential for preventing nosocomial transmission, or hospital-acquired infections, in patients with a confirmed or suspected NiV infection. This is due to the fact that NiV can transfer from one person to another.

13. CONTROL & PREVENTION:

In addition to the steps people can take to lower their chance of catching the virus, scientists and at-risk groups need to keep learning about NiV. in order to stop future epidemics.

13.1. More extensive preventative initiatives consist of:

- Increasing human and animal surveillance in regions known to harbor NiV.
- Studying fruit bat ecology to better understand their habitat and virus transmission to people and animals.
- Assessment on new techniques & approaches that reduce virus transmission in bat populations.
- Developing instruments for early virus detection in livestock and communities.
- Strengthening guidelines for standard in prevention of infection procedures in medical facility to stop the spread of infections from person to person.

13.2. Educating high-risk groups on NiV warning signs, symptoms, and risk factors:

- Geographic location
- Coming into contact with fruit bats and fruit bat-contaminated objects.
- Interaction with pigs or other creatures that fruit bats may encounter.
- Job in an medical facility & as an caretaker for NiV-infected individuals [80][81].

14. ROLE OF PHARMACIST IN PREVENTION OF NIV:

- Chemists are essential team members before, during, and after an outbreak.
- Chemists are the most approachable health care professionals, offering immunization recommendations, evidence-based information on disease transmission, and promoting disease prevention in communities and healthcare settings.
- During illness outbreaks, which can be upsetting for both patients and caregivers, chemists can alleviate public worry and carry out community-supporting activities by forming interdisciplinary teams[82] .

Fig 14: Role of Pharmacist in Prevention of NiV.

15. CONCLUSION:

The Nipah virus is one of the most concerning emerging infectious illnesses of our time. It is a serious issue for public health, particularly in areas where there are frequent interactions between humans and animals, due to its high mortality rate, zoonotic origin, and capacity to spread from animals to humans and then through human interactions. A thorough understanding of the Nipah virus's epidemiology, population spread, internal disease mechanism, and clinical manifestations in infected individuals is essential for prompt diagnosis and successful treatment. In current situation there is no approved vaccine or certain antiviral drugs for the Nipah virus, early detection and palliative care are even more crucial. The cornerstone of treatment is still supportive care, which can significantly impact survival rates and includes things like keeping patients hydrated, controlling fever, and managing complications. Pharmacists are becoming more and more important in this difficult environment. They do much more than just dispense medication. Pharmacists can be important educators and counselors for patients and the community, and they are frequently the most approachable medical professionals. They can assist people in comprehending the virus's mode of transmission, risk reduction strategies, and the importance of infection control procedures.

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