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Review Article

NIPAH VIRUS INFECTION-A REVIEW

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ABSTRACT

Nipah viral disease is a zoonotic infection caused by Nipah virus (NiV), a paramyxovirus belonging to the genus Henipavirus of the family Paramyxoviridae. First emerged in Malaysia in 1998 and has sinces caused outbreaks in other parts of south and south east Asia. It is an emerging bat-borne pathogen. It causes severe neurological and respiratory disease which is highly lethal. Nipah virus 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. Rapid diagnosis and implementation of infection control measures are essential to contain outbreaks. Different types of enzyme-linked immunosorbent assays along with molecular methods based on polymerase chain reaction (PCR) have been developed for diagnostic purposes. A number of serological and molecular diagnostic techniques have been developed for diagnosis and management arise when a new area is affected. However, no effective treatment or prophylaxis is readily available, though several approaches show promise.

Keywords: Nipah virus, Bats, Outbreak, Diagnosis, Treatment

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INTRODUCTION

Nipah virus (NiV) is an RNA virus belonging to family paramyxoviridae. It belongs to the genus Henipavirus which also contains Hendra Virus (HeV) and the recently described Cedar Virus. Bats are the natural reservoir of Henipavirus [1]. While cedar virus has not been found to be pathogenic to any animal, NiV and HeV cause lethal neurologic and respiratory disease [2]. NiV is one of the pathogens on the WHO priority list of pathogens likely to cause outbreaks needing urgent research and development action [3]. It first emerged in Malaysia in 1998 and has since caused several outbreaks in South and Southeast Asia. NiV is highly pathogenic to as well as person to person transmission [4]. A high proportion of victims had physical contact with pigs, unlike in the case of a mosquito-borne disease. Group of symptomatic cases among members of the same household was as high as 33% [5]. More than 500 stockyard workers were screened at the communicable diseases centre (Singapore) in the following week, and those with fever and synptoms and signs of respiratory or neurological diseases were admitted to hospital for investigation and management. An additional 7 identical patients, as well as the 4 index cases, were confirmed to have acute Nipah virus infection, based on raised IgM in serum. Nipah virus was also identified by reverese transcriptase PCR in the cerebrospinal fluid and tissue of a patient who died [6].

Pigs from Nipah affected areas of Malaysia were imported and slaughtered 2 to 3 w before the development of disease in patients, which would be consistent with the expected incubation period of a paramyxovirus. This, together with the nucleotide sequences of reverse transcript in–PCR (RT-PCR) products isolated from the Singaporean cases being identical to Nipah virus sequences from Malaysian cases and pigs [7]. Fruits eaten by bats may have been dropped or thrown into dump areas and subsequently infected the pigs that consumed the contaminated fruit [8].

Discovery of Nipah virus

In early March 1999, virologists from the University of Malaya had isolated a virus from cerebrospinal fluid of an encephalitis patient. Vero cells inoculated with cerebrospinal fluid specimens from the three fatal cases of encephalitis developed syncytia. Electron microscopic studies of the virus demonstrated features characteristic of a virus belonging to the family Paramyxoviridae. The name Nipah virus, was proposed because the first isolated was made from clinical material from a fatal human case from kampong sungai Nipah, a village in Negeri Sembilan [9].

Classification

NiV is the second member of the genus Henipavirus is the family paramyxoviridae. The prototype virus of the genus is the closely related Hendra virus (HeV), discovered during an investigation of the 1994 lethal disease outbreak in horses and humans in Australia [10]. In 2002 the International committee for Virus Taxonomy (ICTV) approved the establishment of the new genus Henipavirus [11].

Morphology

Similar to other paramyxoviruses, NiV particles are pleomorphic, spherical to filamentous, and range in size from 40 to 1900 nm. They contain a single layer of surface projections with an average length of 17 [12].

Genetic diversity

Among the Niv known to cause disease in humans, there are two genetic lineages i.e., NiV Malaysia (NiV-MY) and NiV Bangladesh (NiV-BD).

Genome size and structure

The genome of the Malaysia NiV is 18,246 nucleotides (nt) in length, whereas that of the Bangladesh NiV is 18,252 nucleotides. The potential role of this genome size increases in virus pathogenesis and interhost transmission is yet to be determined [12].

Nipah virus

Niv infects its host cells via two glycoproteins, i.e. G and F proteins. The glycoprotein mediates attachment to host cell surface receptors and the fusion (F) proteins makes fusion of virus–cell membranes for cellular entry. The G protein of NiV binds to host ephrin B2/3 receptors and induces conformational changes in G protein that trigger the F protein refolding have demonstrated the monomeric ephrin B2 binding that pave the way to its full activation and receptor-activated virus entry into the host cells [13, 14]. The diagrammatic structure of Nipah virus is depicted in fig. 1.

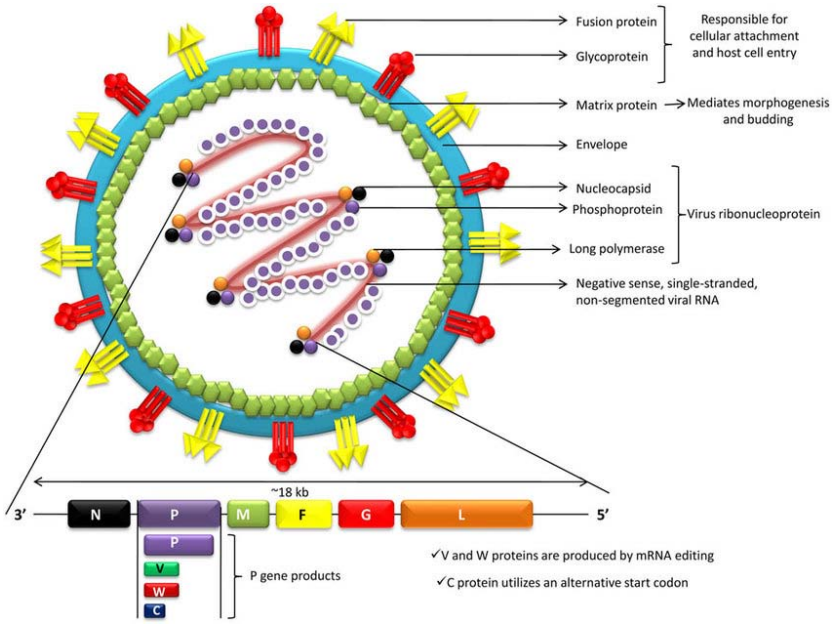

Fig. 1: Structure of nipah virus

Transmission of the Nipah virus

In the Malaysian outbreaks, there were reports of person-to-person transmission, especially in families of affected index case [4]. In a study of>300 health care workers in the 3 hospital that had looked after 80% of encephalitis patients [15], there were no reports of any serious illness, encephalitis or hospital admissions among any health care workers or pathology workers. However, 3 nurses who had cared for outbreak-related encephalitis patients had second serum samples that were positive for nipah virus IgG antibodies. Although the authors concluded that these were false positives because they had no symptoms of encephalitis and blood samples showed no IgM response and were negative for anti-Nipah virus neutralizing antibodies, one was a staff nurse who also had magnetic resonance imaging changes similar to those seen in acute NiV. Since she had cared for the infected patients but had no previous contact with pigs, it is likely that she had an asymptomatic or mild NiV infection.

The situation was very different in Bangladesh and India, where several outbreaks have resulted from person-to-person transmission. About half of the cases identified in Bangladesh between 2001 and 2007 involved human-to-human transmission [16]. The clearest illustration of person-to-person transmission occurred during the Faridpur outbreak in 2004, where the chain of transmission eventually involved 5 generations and affected 34 peoples [17].

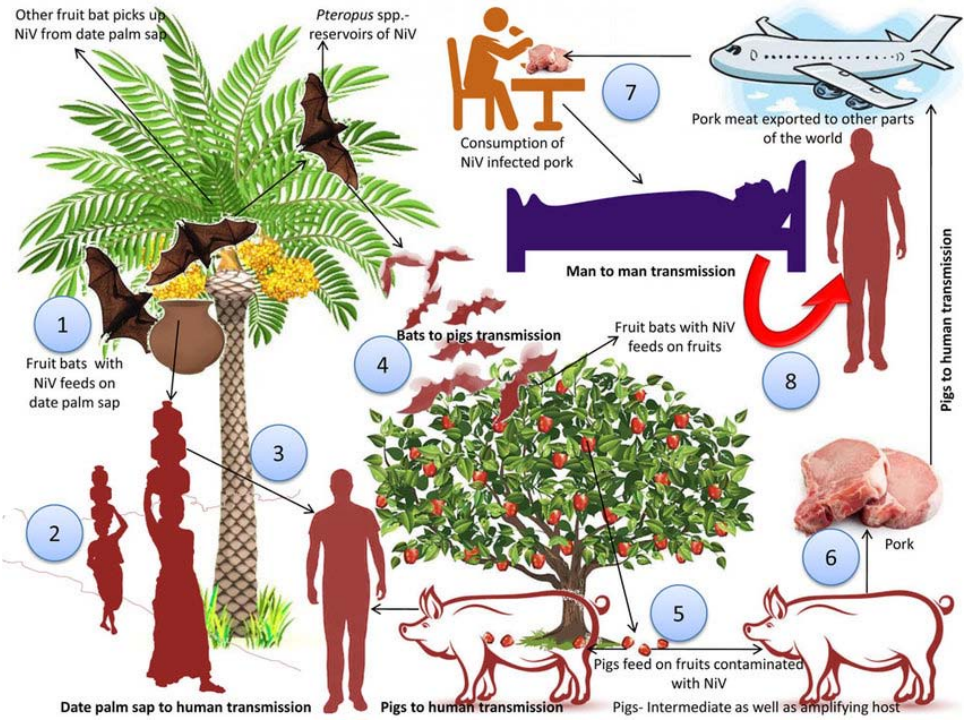

Fig. 2: Transmission of Nipah virus

Epidemiology and disease outbreaks

Malaysia/Singapore

In 1998, NiV disease was recognized for the first time in Malaysia in persons who were in contact with swine population. In march 1999, one outbreak of acute Nipah virus infection was recorded in 11 male abattoir workers (average age of 44 y) in Singapore where pig meat was imported from Malaysia, with one dead. Patients showed higher level of IgM in serum and some unusual symptoms of atypical pneumonia and encephalitis with characteristic focal areas of increased signal intensity in the cortical white matter in MRI. The patients were treated by intravenous acyclovir and eight were cured [18, 19]. From September 1998 to june 1999, 94 patients (both males and females), with an average age of 37 y, reporting close contact with swine population and diagnosed with severe viral encephalitis were investigated. Results shoed a direct transmission of Nipah virus from pigs to human beings. The illness showed a very short incubation period and the symptoms include headache, dizziness, fever, vomiting, doll's-eye reflex, hyptonia, tachycardia, lowering of consciousness, areflexia (loss of spinal reflex) hypertension and high mortality [20].

Bangladesh

The epidermiology of NiV is significantly different in Bangladesh. Since 2001, seasonal outbreaks of NiV have occurred in Bangladesh in the winter months, primarily in 20 districts [21] in central and north-western Bangladesh, where the majority of spillover events occurs. Pteropus bats have been identified as the reservoir [22]. Pterocarpus bats have been found to visit date palm sap is the most common form of transmission of infection from bats to humans [23]. The largest person to person outbreak occurred in Faridpur in 2004. NiV is transmitted via droplets infection and NiV RNA has been detected in the saliva of patients [24]. Consumption of bat bitten fruit has also been suspected of being a potential mode of transmission, though definitive evidence has so far been exclusive [25]. The primary modes of transmission in Bangladesh have been found to be date palm sap consumption and person-to-person transmission [26].

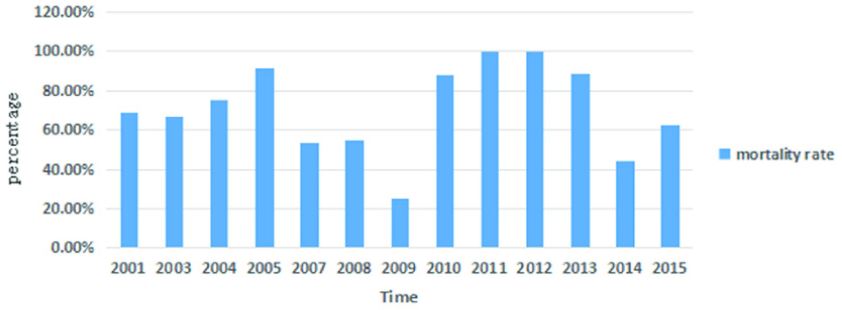

Fig. 3: Mortality rate of Bangladesh

India

In India, there was a large outbreak (66 probable cases and 45 deaths) in siliguri, West Bengal in 2001 and another smaller outbreak (5 cases, 100% fatality) in 2007 in Nadia district, West Bengal. These outbreaks were across the border from the Nipah belt in Bangladesh. In May 2018, an outbreak of NiV was declared in Kozhikode and Malappuram districts of Kerela, a southern state in the west coast, which is geographically disconnected from previously affected areas. Date palm sap consumption is not a common practice in this area. There were 18 confirmed cases and 17 deaths as of 1 June 2018. All cases belonged to the economically productive age group, with no sex differential [28]. All cases belonged to the economically productive age group, with no sex differential. In 2001 in siliguri, the index case remained unidentified but was admitted to siliguri District Hospital and infected 11 secondary cases, all patients at the hospital. These patients were transferred to others hospitals and further transmission infected 25 staff and eight visitors. The 2007 outbreak consisted of one person who contracted the disease due to consumption of alcohol made from date palm and all the others, includind one healthcare worker, acquired the disease from the first case. At least one healthcare professional also contracted the disease in a healthcare setting in the recent outbreak in 2018 [29].

Table 1: Morbidity and mortality of NiV in different regions

S. No.	Year/Month	Country	location	No. of cases	No. of deaths	Case fatality rate%
1	SEP1998	Malaysia	Perak, Selanger, Neegeri sembilan states	265	105	39.6
2	Mar1999	singapore	singapore	11	1	9
3	Jan 2001	india	siliguri	66	45	68.2
4	Jan 2001	Bangladesh	Meherpur	13	9	69.2
5.	Jan 2003	Bangladesh	Naogaon	12	8	66.7
6.	Jan 2004	Bangladesh	Rajbari, Faridur	67	50	74.6
7.	Jan 2005	Bangladesh	Tangail	12	11	91.7
8.	Jan 2007	Bangladesh	Kushtia,Naogaon, Natore.	18	9	50
9.	Apr 2007	India	Nadia	5	5	100
10.	Feb 2008	Bangladesh	Manikgarij,rajbari	11	9	81.5
11.	Jan 2009	Bangladesh	Gaibandha,rangpur	4	1	25
12	Feb 2008	Bangladesh	Faridpur, Rajbari	17	15	88.2
13	Jan 2011	Bangladesh	Comilla, Faridpur	44	40	90.9
14	Jan 2012	Bangladesh	Joypurhat	12	10	83.3
15	Jan 2013	Bangladesh	Gaibandha, Natore.	24	21	87.5
16	Jan 2014	Bangladesh	13 districts	18	9	50
17	Mar 2014	Philippines	Phillippines	17	9	52.9
18	Jan 2015	Bangladesh	Faridpur,Magura	9	6	66.7
19	May 2018	India	Kozhikode, Mlappuram	18	17	94.4
Total				643	380	59

Philippines

An outbreak of NiV infection occurred in the Philippines in 2014. 17 cases were confirmed, the case fatality rate was 82%. 10 patients had a history of close contavt with horses or of horse meat consumption. Deaths of 10 horses were reported in the same time period, of which 9 showed neurologicalsymtoms. However, samples from horses were not tested for NiV.5 patients, including 2 healthcare personnel, acquired the disease through person-to-person transmission. This strain was closely related to the Malaysian strain where definite person to person spread had not been previously identified. This suggests the possibility of co-evolution of different strains of NiV in bats or of strain mutation as the likelihood of mutation increases with each spillover event [27].

Pathogenesis

The Henipaviruses are the only zoonotic paramyxoviruses. They are also exceptional in their broad host range and high case fatality rates. They have a nonsegmented negative-stranded RNA genome consisting of helical nucleocapsids encased in an envelope forming spherical to filamentous, pleomorphic virus particles. Both HeV and NiV have a significantly larger genome than other paramyxoviruses. The genome encodes six structural proteins, the nucleocapsid protein, phosphoprotein, matrix protein, fusion protein, glycoprotein and large protein or RNA polymerase.

In the initial stage of illness in man, detection of NiV can be done in epithelial cells of the bronchiole. Viral antigen can be detected in bronchi and alveoli in experimental animal models, the primary targets being epithelium of bronchi and type II pneumocytes.

From the respiratory epithelium, the virus is disseminated to the endothelial cells of the lungs in the latter stage of the disease. Subsequently, the virus can gain entry into blood stream followed by dissemination, either freely or in host leukocyte bound form. Apart from lungs, spleen and kidneys along with brain may act as target organs leading to multiple organ failure. There is development of lethal infection in hamsters when leukocytes loaded with NiV are passively transferred. In pigs, there is productive infection of monocytes, natural killer (NK) cells along with CD6+, CD8+T lymphocytes [30].

A diagrammatic representation of pathogenesis of NiV has been depicted in following figure;

1. NiV can be seen in the epithelial cells of the bronchiole in the initial stage of infection.

2. NiV antigen can be detected in bronchi and alveoli.

3. Inflammatory mediators are activated as a result of infection to the airway epithelium.

4. Virus is disseminated to the endothelial cells of the lungs in the later stage of the disease.

5,6. Virus enter the blood stream followed by dissemination, either freely or in host leukocyte bound form, reach brain, spleen and kidneys.

7. Two pathways are involved in the process of viral entry into the central nervous system (CNS), via olfactory nerves.

8. The blood brain barrier (BBB) is disrupted and IL-1β alon with tumor necrosis factor (TNF)-α are expressed due to infection of the CNS by the virus which ultimately leads to development of neurological signs. Red font shows the symptoms in humans.

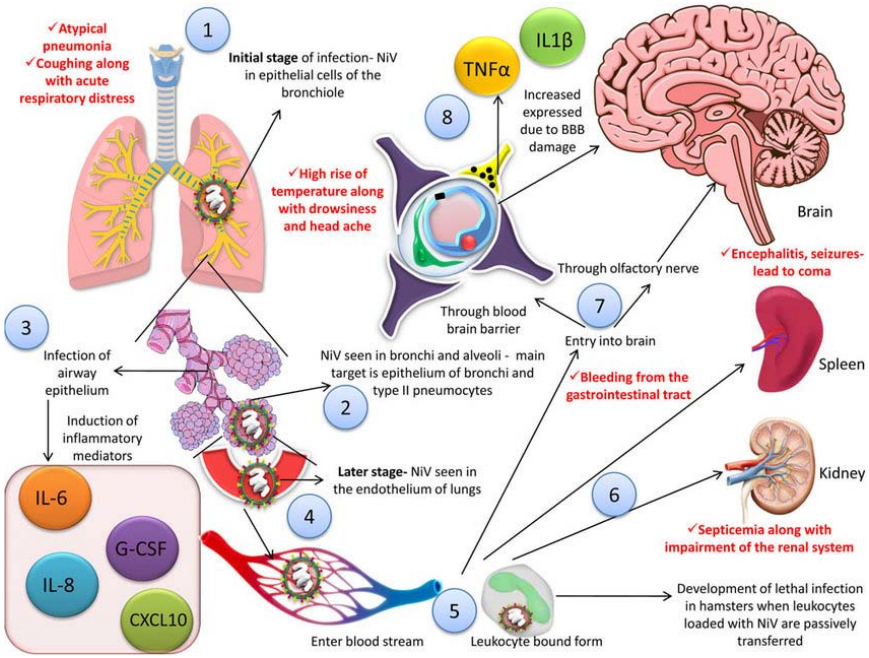

Fig. 4: Pathogenesis of Nipah virus

Clinical signs and symptoms

Highly pathogenic NiV causes symptomatic infections in pigs and humans. Respiratory symptoms are much more severe in pigs as compared to humans.

In humans

The virus is responsible for causing severe and rapidly progessing illness in humans with the respiratory system as well as the central nervous system (CNS) mainly effected. The signs and symptoms of the disease appear 3-14 d post NiV exposure. Initially, there is high rise of temperature along with drowsiness and headache. This is followed by disorientation, ultimately progressing towards coma within 1-2 d. A critical complication of the NiV infection is encephalitis. During intial phase, the respiratory problems may become evident. There is development of atypical pneumonia. Coughing along with acute respiratory distress may be evident in certain patients. There may be development of septicemia along with impairment of the renal system and bleeding from the gastrointestinal tract. In severe cases within a period of 24-48h, there may be development of encephalitis along with seizures that ultimately leads to coma. It is crucial to note that transmission of the

virus is more common from patients having labored breathing than those having no respiratory problems [31].

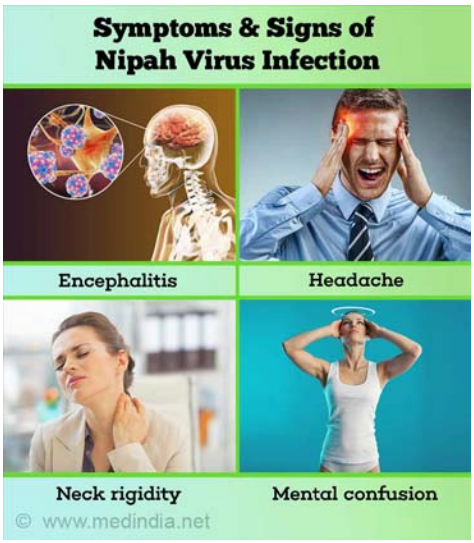

Fig. 5: Symptoms of Nipah virus

In animals

In pigs, the disease is also known as porcine respiratory and encephalitis syndrome (PRES), barking pig syndrome (BPS) (in peninsular malaysia) or one–mile cough. An acute febrile illness has been reported in pigs below 6months of age wherein there is development of respiratory illness that ranges from rapid labored breathing to non–productive cough which is harsh in nature. With the exception of young piglets, the mortality is relatively low. In animlas that are confined, morbidity may approach 100 percent. Due to involvement of nervous system, there may be twitching of muscles, weakness of hind legs, tremors, along with paresis, either flaccid or spastic, of varying degrees. There may also be nystagmus along with seizures in boars as well as sows. In dogs infected with NiV, there may be inflammation of the lungs along with necrosis of glomeruli as well as tubules with formation of syncytia in kidneys. In cats, there may be development of endothelial syncratic along with vasculapathy in multiple organs. Experimental NiV infection of various animals,viz.,hamster, guinea pig, chick embryo, as well as African green monkey, results in development of lesions in the parenchyma in the CNS along with vasculopathy. Clinical signs are, however, apparently absent in mice as well as rats for unknown reasons [32].

Diagnosis

Conformation of the human as well as animal NiV infections can be done by isolation of the virus along with performing serological tests and tests to amplify viral nucleic acids. Biosafety level-4 (BSL-4) laboratory facilities are required for NiV isolation as well as propagation. However, BSL-3 may prove to be sufficient to primarily isolate the virus from suspected clinical materials. Following confirmation of the virus in infected cells by immunofluorescent technique, there should be immediate transfer of the culture fluid in BSL-4 laboratory [33]. It is crucial to note in this aspect that international centre for Diarrhoeal Disease Research, Bangladesh (ICDDRB) along with institute of Epidermiology Disease control and Research (IECDR) are the institutes involved in handling NiV in Bangladesh. In India, BSL-4 laboratory has been established in Pune at National Institute of virology (NiV) [34].

To screen the serum samples of pigs, a recombinant N protein based–ELISA has been developed at the High Security Animal Disease Laboratory (HSADL), Bhopal. By the use of pseudptyped particles, a serum neutralization test for NiV can be performed under BSL-2 conditions. This test uses a recombinant vesicular stomatitis virus that expresse secreted alkaline phosphates (SEAP). Neutralization titer can be obatined by measurement of SEAP activity. Microsphere assay (luminex based) has been used for detection of antibodies against a glycoprotein of NiV, namely NiV sG, in the sera of pigs and ruminants like goats and cattle. Recently, ELISA has also been developed using recombinant full length N protein and truncated G protein for detecting virus specific antibodies in serum samples of porcines. NiV N ELISA was employed for initial screening of serum samples for henipavirus infection, While NiV G Elisa detected specifically the NiV infections. such ELISAs are valuable diagnostic methods for seromonitoring of swine population and probably livestock and wildlife animals.

Molecular tests such as reverse transcription polymerase chain reaction (RT-PCR) along with real-time RT-PCR (qRt-PCR)and duplex nested RT-PCR (nRT-PCr) have been found useful for detection of NiV infection, with subsequent confirmation by nucleotide sequencing of amplicons. A unique primer set targeting the N gene has been reported. Internal controls may also be included in nRT-PCR tests for detection of NiV RNA. Further, such kind of nRT-PCR has helped to detect two different viral strains from pteropus lyrei in Thailand. qRT-PCR protols have also been developed for detection of henipaviruses and found to be useful for the diagnosis of NiV infection as well. SYBR-Green I dye based qRT-PCR employing primers specific to N gene have also been reported for quantitative detection of NIV replicative viral RNA thats avoids viral mRNA amplification, and may represent a more precise assay than the conventional qRT-PCR. Advancements in the field of diagnosis of emerging zoonotic pathogens health approach need to be explored optimally. zoonotic pathogens following an integrated one Health approach need to be explored optimally [35].

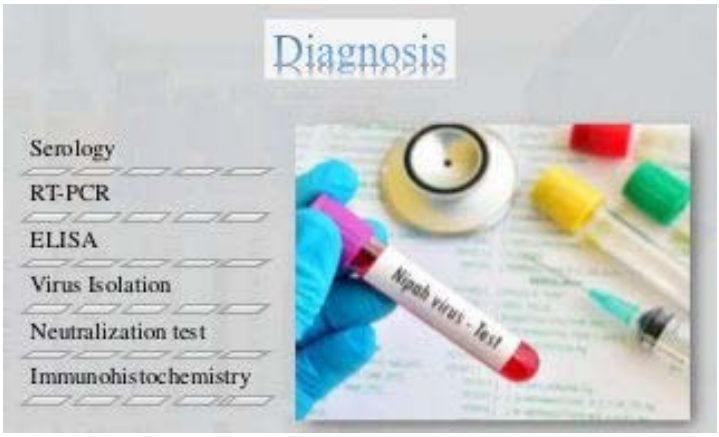

Fig. 6: Diagnosis of Nipah virus

Clinical presentation

The incubation period in humans ranged from 4d to 2 mo, with more than 90% at 2 w or less. Patients presented with fever, headache, dizziness,and vomiting, which developed into a picture of severe encephalitis. Many patients had a reduced level of consciousness and prominent signs of brain stem dysfunction including abnormal doll's eye reflex, pupillary reflexex, vasomotor changes, seizures and myoclonic jerks. neurological involvement, and focal brainstem involvement Cerebellar signs were relatively common.

A unique and interesting features of NiV infection was the developmentof relapse and late-onset encephalitis, some of which occurred months or years after the acute illness. In Tan's series 160cases who survived the initial encephalitis, 12(7.5%) suffered relapses (which occurred after recovery from acyte encephalitis), while there were 3(3.4%) cases who had late-onset encephalitis (where initial infection did not cause neurological manifestation). The longest delay in the onset of late-onset encephalitis was 11 y.

Vaccines

Vaccination of humans is an integral part of preventing infection due to NiV. Prevention also includes vaccination of livestock (especially pigs and probably horses 0 in endemic areas. Outbreak cannot be prevented amongst the livestock population in areas where contamination of date palm sap acts as major contributor to the spread of NiV infection. However, if vcaccination of livestock is made cheap it may prove to be successful in certain regions. Extensive research involving preclinical studies in a number of animals and nonhuman primates have identified multiple vaccine candidates, including vectored and subunit vaccines, offering protective immunity. Among vectored vaccines, one employing vesicular stomatitis virus has shown protection inferrets, African green monkeys, as well as hamsters. Despite these developments, funding for human clinical trials of candidate vaccines remain a problem for academic community. The pharmaceutical companies are hesitant to invest in research on development of vaccines for dideases like Nipah, which are rare occurrences, despite the high fatality.

A recombinant measles virus (rMV) vaccine that expresses envelope glycoprotein of NiV has been found to be promising for use in man. a replication–competent, recombinant VSV-vectored vaccine encoding NiV glycoprotein was reported to show high efficiency in a hamster model. A single intramuscular dose of the vaccines conferred protective immunity in African green monkeys one month after vaccination. Healthcare workers and family contacts attending Nipah cases should be considered for Nipah vaccination, in order to limit human-to-human transmission. A very strong virus-specific immune response is generated through vaccination which inhibit the virus replication and shedding. Such vaccine could provide from niV in disease outbreak. Attenuated live vaccines as well as subunit G (recombinant platforms) have also been tested [36].

Table 2: Different vaccine strategies available for Nipah virus

Vector	Antigen used	Dose for immunization	Animal model	Route if vaccination	Administration frequency
Vesicular stomatitis virus (VSV)	rVSV expressingNiVG	10^5plaque	Hamsters	Intraperitoneal	Single
	rVSV-ZEBOV-GP-NiVG	forming units.	African Green	Intramuscular	Single
	rVSV-NiVB/G	10^7PFU	Monkey	Intramuscular	Single
	Replication detective VSV.	10^7 PFU	Ferrets	intramuscular	Single
		10^6 infectious particles	Female Syrian golden hamsters		
Canarypox virus (ALVAC) vaccine	vCP2199, carrying the NiV-G and vCP2208,carrying the NiV NiV G	10^8 PFU	Landrace female pigs	Intramuscular	Boosted 14 d postvaccination
vector Adeno–associated virus (AAV)		2.1010/1.1010 genome particles	Intra muscular or intra–dermal		One Booster
Vaccinia virus	NiV G and NiV F	6.1011 genome particles 10^7 PFU	Balb/c male mice Golden hamsters BALB/c	Intra muscular Subcutaneously	Boosted with the same dose
Measles virus based–vectors (HL strain or Edmonston B strain)	NiV G	1×10^5 TCID50	African green	Subcutaneously	One booster
	NiV G	2×10^4 TCID50	monkeys	Intraperitoneal	Single
venezuelan equine encephalitis virus replicon particles		3.1×10^4 IU	Hamsters C3H/He mice	Foot pad inoculation	
Newcastle disease virus (NDV), LaSota strains	NiVG and NiVF	108 EID50	Mice	Intramuscular	Single
		2 × 109 EID50	Pig	Intramuscular	

Vaccine platforms for NiV

1. Recombinant measles virus vaccine that expresses envelope glycoprotein of NiV has been found to be effective vaccine candidate.

2. A recombinant vaccine based on vesicular stomatitis virus (replication–competent) has been developed in recent years encoding a glycoprotein of NiV.

3. Nipah virus–like particle composed of three NiV proteins G,F and M derived from mammalian cells have been produced and validated as vaccine in BALB/c mice.

4. Immunoinformatic advances have been utilized for developing peptide-based NiV vaccine by prediction and modeling of T-cells epitopes of NiV antigenic proteins.

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Surveillance

Disease surveillance is carried out regularly in the Nipah belt in Bangladesh. surveillance activities consist of event-based and sentinel surveillance. Print and electronic media surveillance is carried out in 10 national newspapers and eight national news channels and hotlines have been set up for healthcare personnel to report outbreaks. Suspected outbreaks and deaths due to unknown causes are rapidly identified through these methods. Under sentinel surveillance clusters of encephalitis are investigated. Clusters are defined as two or more cases within 21d and half an hour's walk from each other. A team of epidemiologists from the institute of Epidemiology, Disease control And Research,Bangladesh investigates any identified clusters. The team identifies suspected human cases, potential animal sources of infection, behavioural factors contributing to infection and environmental contamination. Surveillance is an important part of disease management and should be instituted in areas that have seen outbreak like india and Other countries in the region [37].

Prevention

As treatment options are limited, focus on NiV management should be on prevention. Preventive strategies include interventions to prevent farm animals from acquiring NiV by eating fruit contaminated by bats. Farms should be designed to reduce overcrowding to avoid rapid spread of disease between animals and should not be near fruit treees that attract bats.

Consumption of contaminated sap should be avoided. However, efforts to reduce fresh sap consumption in general would be unpopular, as they go against social and cultural norms. Other, more acceptable methods would include physical barriers to prevent bats from accessing and contaminating sap.

Efforts towards prevention have primarily focussed on the prevention of contamination of date palm sap, increasing awareness about the dangers of consuming date palm sap and prevention of person-to-person spread. The use of skirts to cover the sap producing areas of date palm tress has been found to effective prtevent contact with bats. In 2015, a study assessing the behaviuor of people consuming raw date palm sap, found that awareness of NiV was very low among them and even people who were aware of it were just as likely to consume it as people who did not. A randomised controlled trial assessing behaviour change communication intervention conducted in 2017 found that disseminating a message encouraging consumption of safe sap reduced exposure to potentially contaminated sap while a message discouraging consumption of sap at all did not. The WHO advices to reduce the risk of animal-to-human transmission gloves and other protective clothing should be worn while handling sick animals or their tissues and during slaughtering and culling procedures.

Prevention of person-to-person transmission includes the implementation of infection control practices such as isolation of patients, use of personal protectiveequipment and good hand hygiene practices. Hospital surfaces have been found to be contaminated by NiV around patients. Healthcare care workers exposed to a suspected NiV patient should inform the authorities and undergo testing for NiV. Contacts of infected patients are counseled to avoidprolonged close personal contact with patients [38].

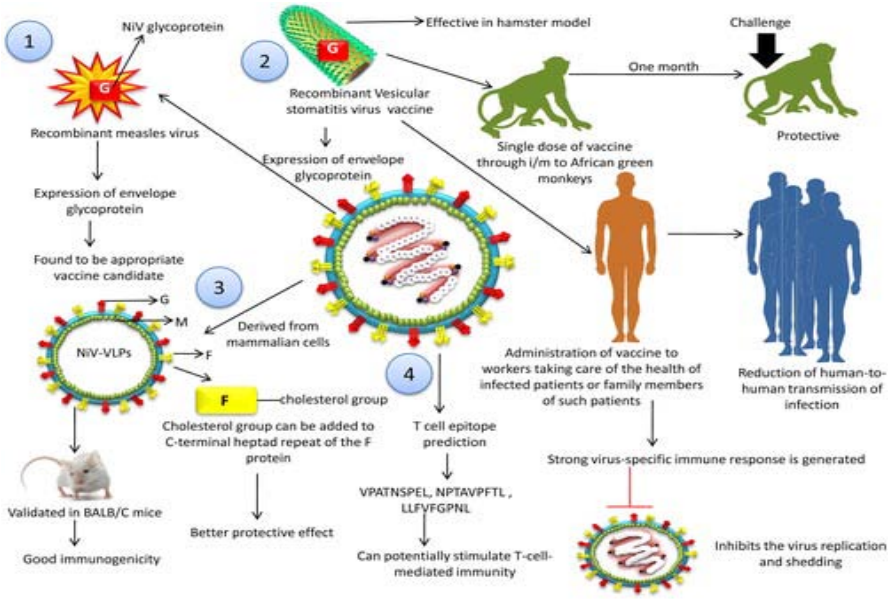

Fig. 7: Vaccination of nipah virus

Biosafety issues of nipah virus

For those who have to work in the field or on farms where Nipah infection is suspected, personal protection, such as masks, googles, gloves, gowns and boots, is advocated, together with hand washing and disinfection of equipment. With its high virulence, animal-to-human and human-to-human spread, significant morbidity and mortality, and resultant fear and panic and tremendous economic losses caused, NiV fulfils some criteria to be considered a potential agent for bioterrorism. It is thus listed as a category C agent on a list of bioterroism agents by the centres for Disease control and Prevention, and by handling has to be done in biosafety level (BSL) 4 facilities [39].

Therapeutics and treatment

The essence of treatment modalities along with effective therapeutics is understood, once there is an outbreak of an infectious disease. There is a need for administering therapeutics to manage the patients during NiV outbreaks and to prevent the mortality. No specific drug has been used yet approved for the treatment of this important disease. Limited work has been done to develop therapeutics against NiV infection. In preclinical studies, monoclonal antibodies have been used for treatment purposes. Due to the expensive nature of the drugs based on antibodies, identification of broad spectrum antiviral is essential along with focusing on small interfering RNAs(siRNAs). In animals models, the NiV pathogenesis has been understood by the shedding light on the crucial nature of phosphomatrix as well as accessory proteins. For the development of novel anti-NiV drugs, such viral proteins, fusion protein and glycoprotein of the virion surface are attractive targets. Therapeutic applications of cytokines, recombinant proteins, RNA interference technology, Toll like receptors, Avian Egg Yolk antibodies, plant based pharmaceuticals, nano medicines, immunomodulatory agents probiotics, herbs/plants extarcts and others may be explored appropriately to combat NIPAH virus as these have been found promising against other viral pathogens [40].

CONCLUSION

NIV has emerged as a deadly zoonotic disease. Bats, the natural reservoir of the virus, are effective at virus dissemination and human outbreak continue to be reported regularly. Due to world wide distribution of bats,outbreaks in New areas are likely to occur. The high case fatality rate and acute course of disease make the infection difficult to diagnose. This is further compounded by the lack of easily available low cost diagnostic test and facilities equipped to handle viral samples. Effective treatment and prophylaxis are unavailable due to a lack of studies in human subjects because the overal case burden is small and the course of infection is acute. The recent outbreak in India highlights the possibility of potential spillover events in areas where currently known risk factors do not exist. establishment of surveillance systems for NIV is necessary, particularly in South and South east Asia. There is an urgent need for countries in South and South East Asia to work together to strengthen surveillance systems in order to monitor spill over events abd prevents transmission.

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AUTHORS CONTRIBUTIONS

All the authors have contributed equally.

CONFLICT OF INTERESTS

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