

NIPAH VIRUS INFECTION-A REVIEW¹*Kolukuluru Shivani and ²K. Sumanth Kumar¹B-Pharmacy, Ratnam Institution of Pharmacy, Nellore.²Associate Professor, Department of Pharmacology, Ratnam Institute of Pharmacy, Nellore.Article Received on
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Nipah viral ailment is a zoonotic infection because of Nipah virus (Niv), a paramyxovirus belonging to the genus Henipaviral of the circle of relatives Paramyxoviridae. First emerged in Malaysia in 1998 and has since induced outbreaks in other elements of south and south east Asia. It is an emerging bat-borne pathogen. It reasons extreme neurological and respiratory disorder that is incredibly deadly. Nipah virus is related to ingestion of infected date palm sap and human-to-human transmission. Bats are the main reservoir for this virus, that may reason disease in human beings and animals. speedy analysis and implementation of infection manipulate measures are essential to comprise outbreaks. different styles of enzyme-linked immunosorbent assays at the side of molecular strategies based on polymerase chain reaction (PCR) had been evolved for diagnostic purposes. some of

serological and molecular diagnostic techniques had been advanced for prognosis and management get up whilst a new area is affected. but no powerful remedy or prophylaxis is quite simply available, even though several methods show promise.

KEYWORDS: Nipah virus, Bats, Outbreak, Diagnosis, Treatment.**INTRODUCTION**

Nipah virus (Niv) is an RNA virus belonging to family Paramyxoviridae. It belongs to the genus Henipaviral which additionally contains Hendra Virus (HeV) and the lately defined Cedar Virus. Bats are the herbal reservoir of Henipaviral. even as cedar virus has now not been observed to be pathogenic to any animal, Niv and HeV reason deadly neurologic and respiration disorder. Niv is one of the pathogens at the WHO priority listing of pathogens probably to motive outbreaks desiring pressing studies and development action. It first

emerged in Malaysia in 1998 and has since brought about several outbreaks in South and Southeast Asia. Niv is notably pathogenic to as well as person to person transmission. An excessive percentage of victims had bodily touch with pigs, in contrast to inside the case of a mosquito-borne sickness. group of symptomatic instances among individuals of the same household become as excessive as 33%. extra than 500 stockyard workers were screened at the communicable illnesses center (Singapore) within the following week, and people with fever and symptoms and signs of breathing or neurological sicknesses have been admitted to hospital for investigation and control. an extra 7 identical sufferers, as well as the 4 index cases, have been showed to have acute Nipah virus contamination, based on raised IgM in serum. Nipah virus changed into additionally identified with the aid of reverse transcriptase PCR inside the cerebrospinal fluid and tissue of a affected person who died.

Pigs from Nipah affected regions of Malaysia had been imported and slaughtered 2 to a few w before the improvement of disorder in sufferers, which would be steady with the expected incubation length of a paramyxovirus. This, together with the nucleotide sequences of opposite transcript in-PCR (RT-PCR) products remoted from the Singaporean cases being identical to Nipah virus sequences from Malaysian cases and pigs. culmination eaten via bats may additionally had been dropped or thrown into unload areas and ultimately inflamed the pigs that ate up the contaminated fruit.

Discovery of Nipah Virus

In early March 1999, virologists from the college of Malaya had isolated a pandemic from cerebrospinal fluid of an encephalitis patient. Vero cells inoculated with cerebrospinal fluid specimens from the 3 deadly cases of encephalitis evolved syncytia. Electron microscopic studies of the virus verified features function of a virus belonging to the own family Paramyxoviridae The call Nipah virus, become proposed because the primary isolated changed into made from clinical fabric from a deadly human case from kampong Sungai Nipah, a village in Negeri Sembilan.

Classification

Niv is the second member of the genus Henipaviral is the circle of relatives Paramyxoviridae. The prototype virus of the genus is the closely associated Hendra virus (HeV), located during an research of the 1994 deadly disease outbreak in horses and people in Australia.^[10] In 2002 the global committee for Virus Taxonomy (ICTV) accredited the status quo of the new genus Henipaviral.

Morphology

similar to different paramyxoviruses, Niv debris are pleomorphic, spherical to filamentous, and range in length from 40 to 1900 nm. They comprise a unmarried layer of floor projections with an average period of 17.

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

Tho this genome size will increase in vie genome of the Malaysia Niv is 18,246 nucleotides (nt) in length, while that of the Bangladesh Niv is 18,252 nucleotides. The capacity function rues pathogenesis and interhost transmission is but to be determined.

Nipah Virus

Niv infects its host cells through glycoproteins, i.e., G and F proteins. The glycoprotein mediates attachment to host cellular floor receptors and the fusion (F) proteins makes fusion of virus–mobile membranes for cell access. The G protein of Niv binds to host ephrin B2/three receptors and induces conformational adjustments in G protein that trigger the F protein refolding have demonstrated the monomeric ephrin B2 binding that pave the manner to its full activation and receptor-activated virus access into the host cells admissions among any health care people or pathology workers. but, 3 nurses who had cared for outbreak-associated encephalitis sufferers had second serum samples that were fine for Nipah virus IgG antibodies. even though the authors concluded that these were false positives because they had no signs and symptoms of encephalitis and blood samples confirmed no IgM response and had been terrible for anti-Nipah virus neutralizing antibodies, one was a staff nurse who additionally had magnetic resonance imaging modifications much like those visible in acute Niv. when you consider that she had cared for the inflamed patients however had no preceding.

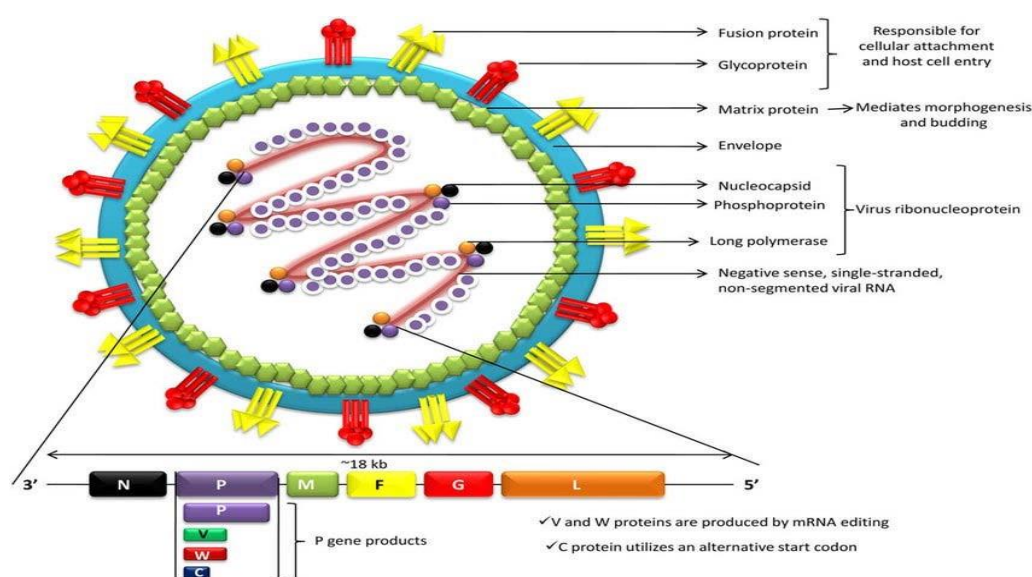


Fig 1: Structure of nipa virus.

Transmission of the Nipah virus

within the Malaysian outbreaks, there were reports of individual-to-character transmission, in particular in households of affected index case. In a look at of >300 fitness care people in the 3-health centre that had sorted eighty% of encephalitis sufferers, there have been no reviews of any severe illness, encephalitis or medical institution admissions amongst any health care workers or pathology people. however, three nurses who had cared for outbreak-related encephalitis patients had 2d serum samples that were positive for Nipah virus IgG antibodies. even though the authors concluded that those were false positives due to the fact they'd no signs and symptoms of encephalitis and blood samples confirmed no IgM response and have been bad for anti-Nipah virus neutralizing antibodies, one became a body of workers nurse who also had magnetic resonance imaging changes just like the ones seen in acute Niv. due to the fact she had cared for the infected sufferers however had no preceding touch with pigs, it's far possibly that she had an asymptomatic or slight Niv infection. The state of affairs changed into very exceptional in Bangladesh and India, wherein numerous outbreaks have resulted from person to individual transmission. approximately 1/2 of the cases identified in Bangladesh among 2001 and 2007 concerned human-to-human transmission. The clearest illustration of man or woman-to-person transmission happened during the Faridpur outbreak in 2004, in which the chain of transmission eventually concerned 5 generations and affected 34 peoples The clearest example of person-to-individual transmission happened during the Faridpur outbreak in 2004, wherein the chain of transmission finally concerned five generations and affected 34 peoples.

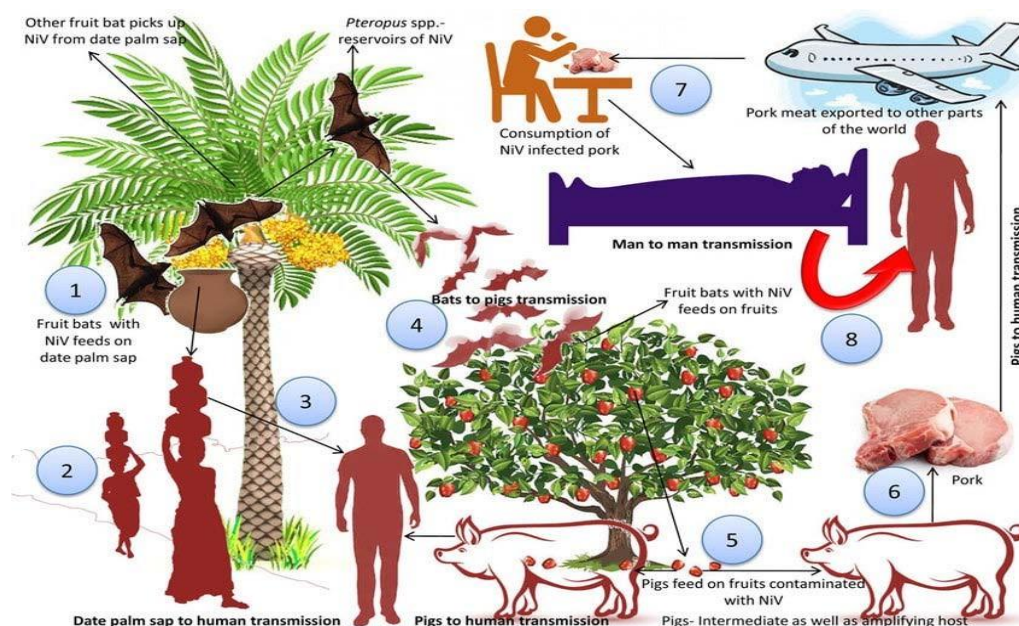


Fig 2: Transmission of Nipah virus.

Epidemiology and disease outbreaks Malaysia/Singapore

In 1998, Niv disease became diagnosed for the first time in Malaysia in people who were in contact with swine populace. In march 1999, one outbreak of acute Nipah virus contamination changed into recorded in 11 male abattoir employees (common age of 44 y) in Singapore in which pig meat became imported from Malaysia, with one lifeless. patients showed better stage of IgM in serum and some uncommon symptoms of unusual pneumonia and encephalitis with characteristic focal regions of accelerated sign intensity within the cortical white depend in MRI. The sufferers were dealt with by way of intravenous acyclovir and 8 have been cured.^[18,19] From September 1998 to June 1999, ninety-four patients (each lady and men), with a mean age of 37 y, reporting close touch with swine populace and identified with intense viral encephalitis had been investigated. consequences shoed an instantaneous transmission of Nipah virus from pigs to humans. The illness confirmed a very short incubation period and the signs and symptoms include headache, dizziness, fever, vomiting.

BANGLADESH

The epidemiology of Niv is substantially special in Bangladesh. considering 2001, seasonal outbreaks of Niv have occurred in Bangladesh in the iciness months, often in 20 districts in significant and north-western Bangladesh, in which the majority of spillover events takes place. Pteropods bats had been recognized as the reservoir. Pterocarpus bats have been discovered to go to date palm sap is the most not unusual form of transmission of

contamination from bats to people. the most important character to individual outbreak occurred in Faridpur in 2004. Niv is transmitted thru droplets infection and Niv RNA has been detected within the saliva of patients. consumption of bat bitten fruit has also been suspected of being a capacity mode of transmission, though definitive evidence has up to now been one-of-a-kind. The number one modes of transmission in Bangladesh had been located to be date palm sap intake and person-to-character transmission.

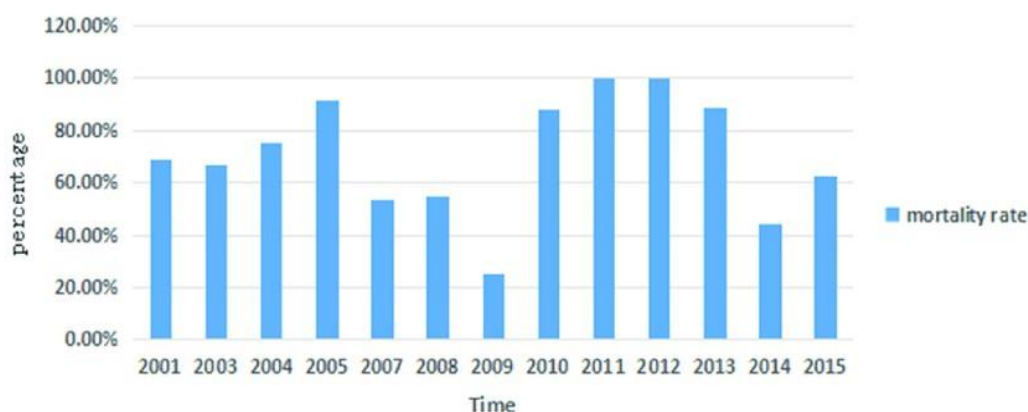


Fig 3: Mortality rate of Bangladesh.

INDIA

In India, there was a massive outbreak (sixty-six likely instances and 45 deaths) in Siliguri, West Bengal in 2001 and another smaller outbreak (five instances, one hundred% fatality) in 2007 in Nadia district, West Bengal. those outbreaks were across the border from the Nipah belt in Bangladesh. In might also 2018, a scourge of Niv became declared in Kozhikode and Malappuram districts of Kerela, a southern kingdom inside the west coast, that's geographically disconnected from formerly affected regions. Date palm sap consumption isn't always a not unusual practice in this location. There were 18 confirmed cases and 17 deaths as of one June 2018. All cases belonged to the economically efficient age institution, without a sex differential. All instances belonged to the economically efficient age institution, without an intercourse differential. In 2001 in Siliguri, the index case remained unidentified however turned into admitted to Siliguri District clinic and inflamed eleven secondary instances, all sufferers at the hospital. those patients have been transferred to others hospitals and similarly transmission inflamed 25 body of workers and eight site visitors. The 2007 outbreak consisted of one person who shrunk the sickness because of consumption of alcohol made from date palm and all of the others, including one healthcare employee, received the

disorder from the first case. at least one healthcare professional also gotten smaller the sickness in a healthcare putting inside the recent outbreak in 2018.

Philippines

an endemic of Niv contamination passed off in the Philippines in 2014. 17 instances had been showed, the case fatality rate turned into 82%. 10 sufferers had a record of near contact with horses or of horse meat intake. Deaths of 10 horses have been suggested within the equal term, of which 9 showed neurologicalsymtoms. but, samples from horses have been no longer tested for NiV.5 patients, such as 2 healthcare personnel, acquired the ailment through man or woman-to person transmission. This pressure was closely associated with the Malaysian pressure wherein definite character to character unfold had now not been formerly recognized. This suggests the possibility of co-evolution of various traces of Niv in bats or of strain mutation as the probability of mutation increases with every spillover occasion.

PATHOGENESIS

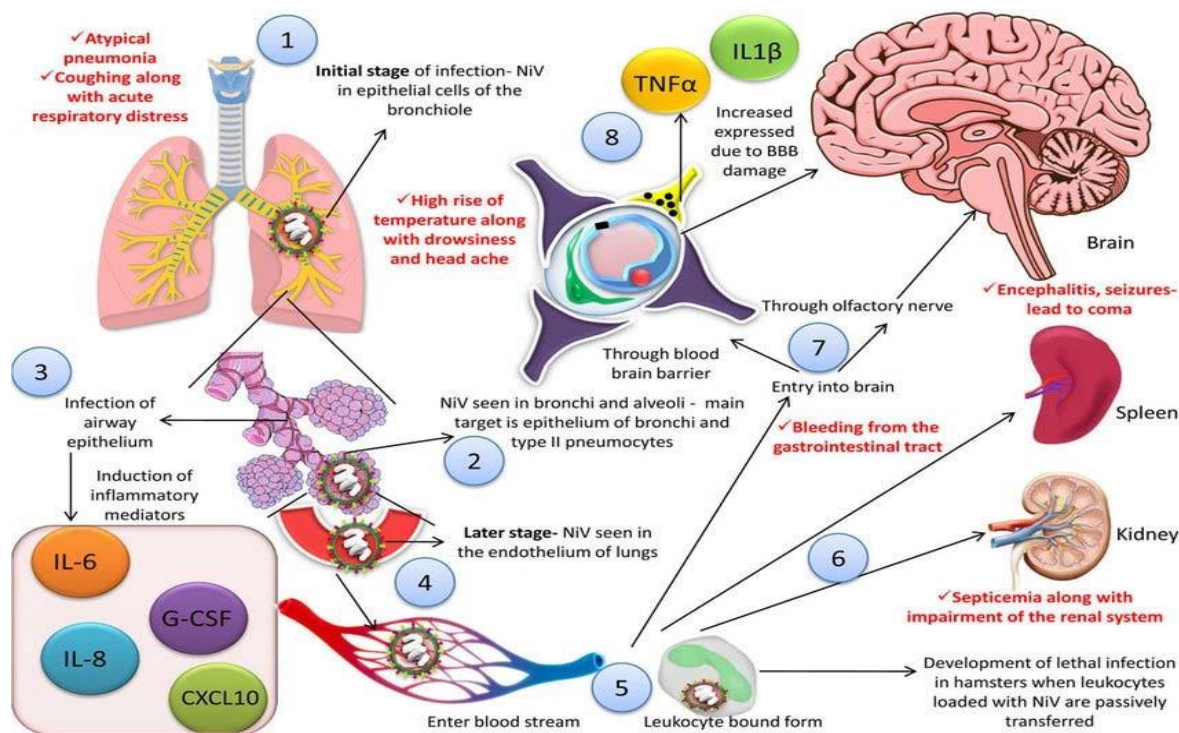


Fig 3: Pathogenesis of Nipah virus.

The Rhinoviruses are the handiest zoonotic paramyxoviruses. they're additionally great in their large host range and high case fatality prices. they have got a nonsegmental bad-stranded RNA genome inclusive of helical nucleocapsids encased in an envelope forming round to filamentous, pleomorphic virus particles. both HeV and Niv have an extensively

larger genome than other paramyxoviruses. The genome encodes six structural proteins, the nucleocapsid protein, phosphoprotein, matrix fusion protein, glycoprotein and big protein or RNA polymerase. within the preliminary degree of contamination in man, detection of Niv can be performed in epithelial cells of the bronchiole. Viral antigen can be detected in bronchi and alveoli in experimental animal fashions, the primary goals being epithelium of bronchi and sort II pneumocytes.

From the respiratory epithelium, the virus is disseminated to the endothelial cells of the lungs in the latter level of the disease.

in the end, the virus can advantage entry into blood flow observed through dissemination, both freely or in host leukocyte sure shape. other than lungs, spleen and kidneys alongside brain might also act as target organs main to multiple organ failure. there's improvement of deadly contamination in hamsters when leukocytes loaded with Niv are passively transferred. In pigs, there is productive infection of monocytes, natural killer (NK) cells together with CD6+, CD8+T lymphocytes.

A diagrammatic representation of pathogenesis of Niv has been depicted in following figure.

1. Niv may be seen inside the epithelial cells of the bronchiole in the preliminary stage of contamination.
2. Niv antigen can be detected in bronchi and alveoli.
3. Inflammatory mediators are activated due to infection to the airway epithelium.
4. Virus is disseminated to the endothelial cells of the lungs in the later degree of the disease.
6. Virus enter the blood move observed with the aid of dissemination, either freely or in host leukocyte certain form, attain brain, spleen and kidneys.
7. two pathways are worried in the technique of viral access into the principal anxious device (CNS), through olfactory nerves. Fig. four: Pathogenesis of Nipah virus.
8. The blood brain barrier (BBB) is disrupted and IL-1 β along with tumor necrosis aspect (TNF)- α are expressed due to infection of the CNS through the virus which ultimately ends in improvement of neurological symptoms. crimson font shows the signs in human beings.

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 Human

The virus is answerable for causing excessive and unexpectedly progressing infection in human beings with the respiratory device in addition to the critical nervous machine (CNS) specifically effected. The symptoms and signs and symptoms of the disease seem 3-14 d submit Niv publicity. initially, there is high upward push of temperature along with drowsiness and headache. this is followed by way of disorientation, in the end progressing closer to coma inside 1-2 d. An essential hardship of the Niv infection is encephalitis. all through initial section, the respiration issues may end up glaring. there is improvement of odd pneumonia. Coughing together with acute respiration distress can be obtrusive in certain patients. There may be improvement of septicemia alongside impairment of the renal gadget and bleeding from the gastrointestinal tract. In severe instances within a duration of 24-48h, there can be improvement of encephalitis at the side of seizures that ultimately results in coma. it's far critical to observe that transmission of the virus is greater not unusual from patients having labored respiratory than those having no respiration troubles spastic, of varying stages. There can also be nystagmus along with seizures in boars in addition to sows. In dogs inflamed with Niv, there may be irritation of the lungs at the side of necrosis of glomeruli as well as tubules with formation of syncytia in kidneys. In cats, there can be development of endothelial syncretic together with vasculopathy in a couple of organs. Experimental Niv contamination of various animals, viz., hamster, guinea pig, chick embryo, in addition to African green monkey, effects in development of lesions within the parenchyma in the CNS alongside vasculopathy. medical symptoms are, but, reputedly absent in mice as well as rats for unknown motives.



Fig 5: Symptoms of Nipa Virus.

DIAGNOSIS

To screen the serum samples of pigs, a recombinant N protein based totally-ELISA has been advanced on the high security Animal ailment Laboratory (HSADL), Bhopal. with the aid of the use of pseud typed debris, a serum neutralization check for Niv can be executed beneath BSL-2 situations. This check uses a recombinant vesicular stomatitis virus that expressed secreted alkaline phosphates (SEAP). Neutralization titer can be obtained with the aid of size of SEAP hobby. Microsphere assay (Luminex based totally) has been used for detection of antibodies in opposition to a glycoprotein of Niv, specifically Niv sag, inside the sera of pigs and ruminants like goats and cattle. these days, ELISA has also been advanced the usage of recombinant full length N protein and truncated G protein for detecting virus unique antibodies in serum samples of porcinis. Niv N ELISA became hired for initial screening of serum samples for henipaviral contamination, even as Niv G Elisa detected specially the Niv infections. such ELISAs are treasured diagnostic techniques for neuromonitoring of swine populace and possibly cattle and natural world animals.

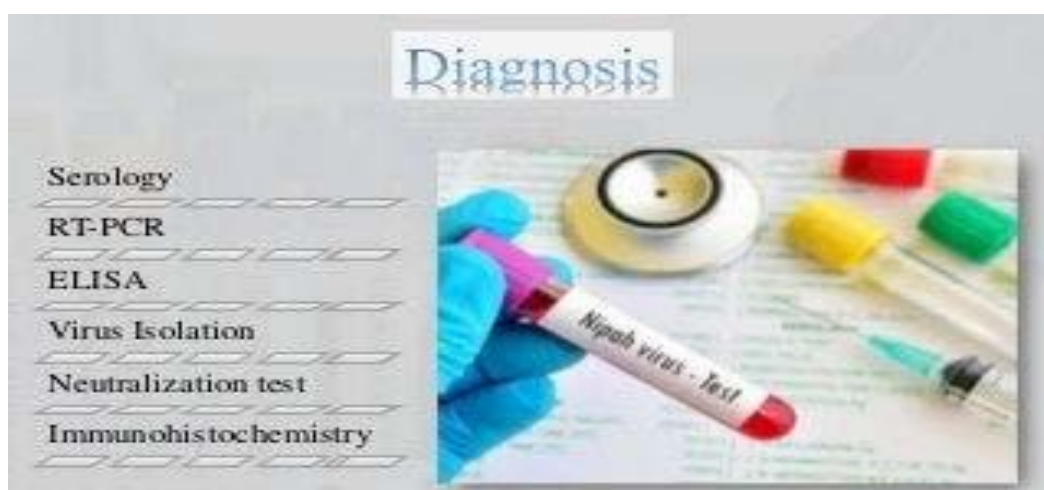


Fig 6: Diagnosis of Nipa virus.

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 trees that attract bats. intake of infected sap has to be prevented. but, efforts to lessen clean sap consumption in general might be unpopular, as they move towards social and cultural norms. other, extra

proper techniques might include physical obstacles to prevent bats from having access to and contaminating sap.

CONCLUSION

NIV has emerged as a lethal zoonotic sickness. Bats, the natural reservoir of the virus, are powerful at virus dissemination and human outbreak stay stated often. due to international wide distribution of bats, outbreaks in new regions are possibly to occur. The high case fatality fee and acute direction of ailment make the infection difficult to diagnose. that is further compounded by using the dearth of effortlessly to be had low-cost diagnostic test and centers equipped to deal with viral samples. powerful treatment and prophylaxis are unavailable due to a lack of research in human topics because the overall case burden is small and the path of contamination is acute. The current outbreak in India highlights the possibility of capacity spillover events in areas where presently regarded danger factors do now not exist. status quo of surveillance systems for NIV is necessary, particularly in South and South east Asia. there may be a pressing want for international locations in South and South East Asia to paintings collectively to bolster surveillance structures in an effort to display spill over occasions Abd prevents transmission.

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