

Nipah – A Homoeopathic Perspective.*

Dr.K.Saji. MD(Hom).
Homoeopathic Medical Centre,
Perambra.
Kozhikode, Kerala.
drsajik.md@gmail.com

Nipah Virus Infection :

Nipah Virus (NiV) infection, the life threatening zoonosis with high case fatality rate, was first identified during an outbreak of the same in Kampung Sungai Nipah, Malaysia, in the year 1998. NiV is capable of causing disease in pigs, domestic animals and humans.

Natural Reservoirs and Intermediate hosts of the Virus

Natural Reservoirs : Fruit bats - Pteropodidae Family, Pteropus genus have been identified as the natural reservoir of the virus in previous outbreaks¹ (Malaysia, India, Bangladesh and Philippines)

Intermediate hosts : Pigs were the intermediate hosts in Malaysian outbreak where pigs became infected from consumption of partially bat eaten fruits. Horses were the intermediate host in Philippines.

In India and Bangladesh, there was no intermediate host and human infection was from consumption of raw date palm sap contaminated by infected bats¹.

Previous outbreaks in the world :

1. Malaysia and Singapore : Sept 1998 to June 1999. 276 cases were reported. Mortality rate was 39%.^{1,12.}
2. India (West Bengal) : 2001 & 2007 (Siliguri & Nadia) 70 people died.^{20,21}
3. Bangladesh : 11 outbreaks between 2001 & 2015, all between the months of December and May. : 260 cases were reported of which 197 died (Mortality rate 76%)¹
4. Philippines : March 3 to May 24, 2014. 11 cases. (Mortality was rate 82 %)¹¹
5. India : 2018 May. (Kozhikode & Malappuram districts, Kerala) : 19 cases were reported, 17 died. (Mortality rate 89 %)¹⁵

The months/season of outbreaks seems similar in most of the instances, ie, from December to May.

Available Details of previous outbreaks^{1,11,15,20} :

Outbreak	Natural Reservoir	Intermediate Host	Virus	Total Cases	Mortality Rate %
Malaysia	Fruit Bat	Pig	NiV ^M	276	39
India – Siliguri West Bengal	Fruit Bat	---	NiV ^B	66	74
Bangladesh	Fruit Bat	---	NiV ^B	260	76
Philippines	Fruit Bat	Horse	NiV	11	82
India – Kerala	Unknown	---	NiV ^B	19	89

Sequence of Events in Earlier Outbreaks in India^{20,21} :

Outbreak	Source	Index Case	1 st wave	2 nd Wave	Outbreak Duration
Siliguri, West Bengal	Unknown	No Info (From Hospital)	11 Cases (All infected from a hospital)	33 Cases (25 hospital staff 8 visitors)	Jan 31 to Feb 23 2001
Nadia, West Bengal	Infected Date Palm Sap ?	A Farmer 35 yrs	3 Cases (Close Relatives of Index case)	1 Case (Lab staff ?)	April 9 to 28 2007
Kozhikode & Malappuram, Kerala.	Unknown	A Plumber	3 Cases (Close Relatives of Index Case)	16 Cases (2 hospital staff, 3 patients and 12 visitors)	May 2018

Transmission :

Three routes of transmission have been identified :

- a. From natural reservoir (fruit bats) to natural hosts (pigs, horse & domestic animals) and then from natural hosts to humans. (through contact)
- b. From natural reservoir to humans (consumption of partially bat eaten fruits)
- c. From humans to humans. (through droplet infection, fomites or close physical contact, especially by contact with body fluids.)

The NiV strain which caused the previous outbreaks in India and Bangladesh produced more respiratory involvement including pneumonia and this respiratory involvement is considered as the probable reason for human to

human transmission. During the outbreak in Siliguri - West Bengal, 33 health workers and hospital visitors became ill after exposure to patients hospitalized with Nipah virus illness, suggesting nosocomial infection. The presence of virus in respiratory secretions and urine was demonstrated and this is considered as the reason for more nosocomial transmission¹. The virus of the recent outbreak of cases occurred in Kerala is reported to be similar to the NiV strain which caused outbreaks in Bangladesh⁹.

Fruit bats of the genus Pteropus have been identified as natural reservoirs of NiV. Of the 33 species of bats in Kerala, the only one under Pteropus genus is Pteropus giganteus (Indian flying fox) which is very common in every corner of the state^{2,3}. When the flying fox habitat (For eg. Large flying fox roosting trees) is destroyed by human activity the bats become stressed, their immune system weakens, their viral load increases and more virus is shed in the urine and saliva. Similar fluctuations of virus shedding may be associated with stressful physiological conditions or seasons¹.

Nipah Virus :

NiV is a paramyxovirus belonging to genus Henipavirus. It is an enveloped RNA virus. It was initially identified in 1999.

There are two distinct strains on NiV Malaysia (NiV_M) and Bangladesh (NiV_B). Bangladesh strain causes more severe disease with more case fatality rate than the Malaysian strain of the virus¹⁰.

The strains of Nipah isolates from different outbreaks of the disease showed substantial heterogeneity in their nucleotide sequences¹. This may be the reason for the variability in clinical features in different outbreaks.

The lipid envelop of NiV is susceptible to disinfectants, especially alcohol (ethanol or 2-propanol.) based ones and thus cleansing with such a disinfectant can easily destroy the virus¹³.

Pathogenesis :

The pathologic findings in the brain of Nipah encephalitis cases showed evidence of necrotizing vasculitis. The main pathology appeared to be widespread ischemia and infarction caused by vasculitis-induced thrombosis, although direct neuronal invasion may also play a major role in the pathogenesis of the encephalitis.

Alveolar hemorrhage, pulmonary edema and aspiration pneumonia were often encountered in the lungs. These may lead to pneumonia and acute respiratory distress syndrome (ARDS) ultimately.

CDC lists it as a critical potential biological weapon because of its availability, ease of production and dissemination, and high virulence in terms of high mortality and health impact¹⁴.

Incubation period^{1,18} :

The median incubation period of the primary cases in Bangladesh outbreaks was 7 days (2-12 days) and that of secondary cases who had a single exposure to Nipah case was nine days (6-11 days) but, exposure to onset of illness varies from 2 to 21 days. Incubation period of as long as 45 days has been reported in rare instances.

Infective period of the disease¹⁵ :

There is no clear cut knowledge of the exact infective period of the disease, but when reports about the case histories in the recent outbreak in Kerala are examined, it seems that the infectious period is from the second day onwards from the onset of the initial symptoms. Most of the second level victims of the outbreaks were relatives who cared for undiagnosed case-patients in their homes, patients/bystanders who unknowingly contacted the undiagnosed case-patients at hospital and health care workers who wore minimal personal protective equipment while caring for undiagnosed cases.

Duration of the disease.

Examination of the case histories in the recent outbreak in Kerala reveals that the duration of the sickness is about 3 to 14 days¹⁸. Most of the patients developed CNS symptoms in the 2nd or 3rd day of the illness.

Clinical features^{1, 16,18,19} :

Clinical presentation can range from asymptomatic infection to fatal encephalitis. Those infected initially have a sudden onset of flu-like symptoms such as fever, headaches, pain in the muscles, vomiting and sore throat, followed by dizziness, drowsiness, altered consciousness (partial or complete loss of consciousness) and focal neurological signs indicating acute encephalitis. Encephalitis and seizures occur in severe cases. This progresses to coma within 24-48 hours.

Some patients, whose respiratory functions were affected, can also present with an atypical pneumonia with fever, cough and headache. Nipah may also manifest with severe respiratory features, including acute respiratory distress; this has been observed more frequently in the outbreaks since the Malaysia outbreak.

Symptoms :

1. Fever
2. Altered mental status
3. Severe weakness
4. Headache
5. Respiratory distress
6. Cough
7. Vomiting
8. Muscle pain
9. Jerking of muscles.
10. Convulsion

11. Diarrhoea

Signs :

1. Reduced Glasgow Coma Scale/Score
2. Raised temperature
3. Increased respiratory rate (Adult: ≥ 25 /min; children of ≥ 12 months: ≥ 40 /min)
4. Increased heart rate (Adult: ≥ 100 /min; children of ≥ 12 months: ≥ 140 /min)
5. Crepitations in lung
6. Hypertension/Hypotension

Neurological signs

- i. Oculoparesis
- ii. Pupillary abnormality
- iii. Facial weakness
- iv. Bulbar weakness
- v. Limb weakness
- vi. Reduced deep tendon reflexes
- vii. Plantar-absent/extensor

Case Definitions¹⁸ :

Suspected case : Any fever case with features of encephalitis (ie, sudden onset of fever with altered sensorium or seizure) and respiratory features (shortness of breath and cough) in an area where there is history of Nipah outbreak should be considered as a suspected case.

Probable case : Any such case during a Nipah outbreak, with a history of contact with a Nipah patient should be considered as a probable case.

Confirmed Case : In these cases, Nipah infection should be ruled out by testing IgM antibody against Nipah virus (ELISA in serum or cerebrospinal fluid) or Nipah virus RNA identification (PCR from respiratory secretions, urine, or cerebrospinal fluid)

Clinical characteristics of Nipah in Previous Outbreaks :

1. Data of 4 outbreaks in Bangladesh (2001 to 2004)¹⁶ :

Total number of Cases : 92

No	Characteristic	Occurrence %
1.	Fever	100
2.	Altered mental status	90
3.	Unconsciousness	74
4.	Headache	73
5.	Severe weakness	67
6.	Cough and /or cold	62

7.	Respiratory difficulty	69
8.	Vomiting	58
9.	Diarrhoea	29
10.	Convulsion	23

2. Data of Outbreak in Siliguri, West Bengal, India, 2001²⁰.

Total Number of cases 66

No	Characteristic	Occurrence %
1.	Fever	100
2.	Altered sensorium (Confusion to Coma)	97
3.	Headache & Myalgia	57
4.	Respiratory difficulty	51
5.	Vomiting	19
6.	Involuntary movements or Convulsion	43

Diagnosis¹⁸

Initial signs and symptoms of NiV infection are non-specific. Diagnosis is often not suspected at the time of presentation and is made usually by considering the history and by doing confirmatory lab tests.

Differential Diagnosis¹ :

1. Japanese B Encephalitis
2. Bacterial Meningitis
3. Cerebral Malaria.

Clinically Nipah infection has additional segmental myoclonus (more in NiV_M)¹⁰ and respiratory features along with features of encephalitis, which differentiates it from JBE.

Investigations :

General

1. CBC : Leucopenia and lymphocytosis, thrombocytopenia
2. Chest X-ray: Diffuse infiltrates, consolidation
3. CSF study- mild pleocytosis. Normal or slightly raised protein and normal sugar level.

Confirmatory

1. IgM antibody against Nipah virus (ELISA in serum or cerebrospinal fluid)
2. Nipah virus RNA identification (Real time Polymerase chain reaction - from respiratory secretions, urine, or cerebrospinal fluid)

Prevention :

1. General : By Personal care :

- a. Isolation of cases (preferably in a separate unit)
- b. Barrier nursing e.g. personal protection using masks, gloves, gowns etc.
- c. Hand washing with an alcohol based disinfectant or soap & water before and after handling/visiting patients

2. Medicinal : By Homoeopathic prophylaxis.

There are two methods of Homoeopathic prophylaxis possible in every outbreak/epidemic^{6,7,8}.

- a. Selection of a 'Genus Epidemicus' based on the symptoms of the epidemic disease under consideration. A medicine which is proved to be capable of producing similar symptoms and disease pathology in human beings is selected as the prophylactic medicine. There are two methods of consideration of symptomatology.
 - i. Collection of generic symptoms of the disease from previous outbreaks.

This method is applied usually in for a known diseases, especially epidemic of an acute infections disease, the generic symptoms of which are almost similar in all the individuals infected.(Acute fixed miasmatic diseases like Chicken pox, Measles, Hepatitis A etc.) This could be applied in other epidemic diseases with variable symptoms too if the array of symptoms of previous episodes of the disease is known.

In this instance, we can suggest a probable GE based on the available generic symptoms, without waiting for the outbreak of the disease. (E.g.. Belladonna for scarlatina; Pulsatilla or Rhus tox for Chicken pox.; Nux vom for Hepatitis ; Camphor or Cuprum met for Cholera. Etc.)

- ii. Collection of generic symptoms of the disease from the initial cases of the specific outbreak of the acute infectious disease under consideration

For an unknown disease, or for disease which show variability in symptom totality in different individuals affected. (Acute variable miasmatic diseases)

In this instance, we must study the symptomatology of a few individuals affected with the disease, and should synthesize a totality by combining all the generic symptoms in those cases. The GE selected should be the one which covers almost all the symptoms collected under the synthetic totality.

The most important point to be noted here is that, we are looking for the generic symptoms in those cases and not for strange rare specific symptoms in individual cases.

- b. 'Homoeopathic vaccination' – ie, using a nosode prepared from the causative agent of the disease causing agent/material containing the causative agent as a prophylactic medicine. Eg. Diphtherinum for Diphtheria., Leptospira potentised preparation for Leptospirosis etc.(This method was used in Cuban Leptospirosis prevention¹⁷)

In case of Nipah, any of the GE methods could be used to find out the GE ie, by finding out a medicine similar to the collective symptoms from previous outbreaks as the disease is not a new one or by finding a similar remedy, which covers the collective symptoms from the initial few patients of a particular outbreak under consideration.

Consideration of symptoms of Nipah cases for identification of a GE

A. Symptoms from previous outbreaks.

Let us consider the symptoms and pathology listed above (from previous outbreaks) as generic symptoms of the disease and repertorise the rubric conversions to find out what medicine is coming up based on the first method of consideration of symptomatology.

Rubrics⁴ :

1. Mind; delirium; fever; during
2. Head; pain, headache; fever; during
3. Generalities; weakness; fever; during
4. Respiration; accelerated, quick; chill, during
5. Cough; fever; during
6. Fever, heat; vomiting; during
7. Generalities; pain; muscles; fever heat, during
8. Generalities; jerking; fever, during
9. Rectum; diarrhea; fever; during
10. Generalities; convulsions, fever heat, during
11. Heart & circulation; pulse, rapid, chill, during
12. Chill; respiratory complaints, with
13. Eyes; falling of lids
14. Vision; dim; chill, during
15. Extremities; weakness; fever; during
16. Extremities; reflexes; diminished
17. Head; inflammation; brain
18. Heart & circulation; inflammation; bloodvessels, arteria

Repertorial Result :

Bell	331121121321211131	30/18
Rhus-t	323121222112203021	30/16

Sulph	222121202121201031	25/15
Ars	333132302323000112	32/14
Phos	223131203131200021	27/14
Bry	222032212131100031	26/14
Acon	231131211031200031	25/14
Chin	233022302011110111	24/14

Belladonna is at the top covering all the symptoms considered.

B. Symptoms from a particular outbreak.

Now, let us consider the rubrics selected to find out the GE in the recent outbreak of Nipah in Kerala, ie by the second method – on the basis of generic symptoms of previous cases in the outbreak. Symptoms were collected from case-patients caregivers, relatives, treated doctors and from media reports. Caregivers of two deceased patients were interviewed at their home.

Rubrics⁴

1. Fever, Zymotic fevers
2. Fever, Heat, Intense heat.
3. Headache, violent, fever during.
4. Mind, coma, fever during
5. Mind, Delirium, fever during
6. Fever, Heat, alternating with chill
7. Urine, scanty, fever during.
8. Convulsions, fever during
9. Weakness, fever during
10. Brain, inflammation
11. Carditis
12. Vasculitis
13. Pulse, rapid, chill during
14. Perspiration, single parts
15. Generals, Pulsation, external, fever during
16. Vertigo, fever during
17. Generals, gait, staggering, fever during
18. Generals, trembling, chill during
19. Eye, ptosis
20. Head, brain, cerebellum

Bell	: 42/20
Bry	: 38/18
Ars	: 37/18
Nux	: 35/18

In this instance also, Belladonna is coming at the top.

According to Hahnemann, a medicine which covers the symptoms of the first stage of the disease is its best preventive. In this instance, bell covers the first stage symptoms well. In the course of treatment of Nipah, we may need other encephalitis medicines too in individual cases, depending upon the presentation⁷.

Management :

There is no proven treatment recommended for Nipah virus disease. Intensive supportive care with treatment of symptoms is the main approach to manage the infection¹⁸. But, according to the principles of Homoeopathy, there is a scope to suggest probable medicines for Nipah patients based on the available symptomatology, ie., a bunch of medicines which are proved to produce similar symptoms and pathogenesis in healthy human beings. As it is a highly virulent viral disease with high chance of human to human to spread and very high fatality rate, one should never attempt treating it in the OPD. If a suspected or probable case is identified you can prescribe a medicine based on the available symptoms but should refer the case to a higher centre with adequate facility for isolation and supportive care. During a Nipah outbreak, those practicing at the area of outbreak, should take homoeopathic preventive medicine along with other personal protective measures advocated by the health authority.

General :

Supportive care depending upon the manifestations.

Medicinal :

A Few probable medicines^{4,5} :

1. Belladonna :

Belladonna stands for suddenness of onset and violence of attack. Marked action on CNS and vascular system. High fever, sudden onset. Inflammation of brain before nervous fever. Dilated pupils during fever. Dim vision during chill. Visual hallucinations. Delirium during fever. Boring of head into pillow, drawn backward and rolls from side to side. Dryness of mouth and throat with aversion to water. No thirst with fever. Uncontrollable vomiting. Respiration oppressed, quick, unequal. Cheyne-stokes respiration. Throbbing all through body. Rapid but weakened pulse. Urinary retention with congestion of brain. Tottering gait during fever. Jerking limbs.

2. Ars alb :

Fever with great weakness. Inflammation of brain before nervous fever. Weakness out of proportion to disease. Hallucinations of smell and sight. Delirium, worse after midnight. Anxiety, fear of death. Headache relieved by cold, other symptoms worse. Nausea, retching or vomiting after eating or drinking. Diarrhoea, bloody, black stool. Suffocative catarrh. Wheezing respiration. Sepsis. Palpitation. Tachycardia during chill.

3. Opium

Stupor. Half closed eyes, pupils insensible. Cerebral depression. Delirious talking with wide open eyes. Paralysis of brain, Coma. Vomiting with colic and convulsions. Constipation during fever. Stertorous breathing. Fever with bradycardia. Great drowsiness during fever. Tottering gait during fever. Fever characterised by stupor, snoring respiration, twitching of limbs, intense thirst and sleepiness. Retention of urine during fever. General low temperature with inclination to stupor. Makes no complaints.

4. Helleborus.

Sensorial depression. Sees, hears and tastes imperfectly. General muscular weakness, which may go on to complete paralysis, accompanied by dropsical effusions. Low vitality. Severe illness. Delirium in encephalitis. Coma. Rolling of eyes. Meningo encephalitis. Dilated pupils, Respiration irregular. Chest constricted. Gasps for breath. Spasms. Myoclonus.

5. Zincum met

Epidemic encephalitis. Cerebral depression. Fever with impending brain paralysis. Seizures. Myoclonus. Rolling of eyes. Vomiting. Cold extremities during fever. Debilitating spasmodic cough.

6. Hyoscyamus

Coma vigil, tremulous weakness and twitching of tendons. Inflammation of brain before nervous fever. Constricted or dilated pupils during fever. Delirium with attempts to run away. Deep stupor with convulsions.

7. Gelsemium

Dim vision during chill. Constricted pupils during fever. Ptosis. Thirst less. Coma in encephalitis. Pulse slow, full, soft, compressible.

8. Apis

Dilated pupils during fever. Convulsion in encephalitis. Inflammation of brain with swelling and puffiness of various parts. Respiration difficult during fever. Pulse quick during fever. Shrieking during coma.

9. Stramonium

Inflammation of brain before nervous fever. Tottering gait during fever. Delirium in encephalitis. Delirium with desire to escape. Violent fever. Profuse sweat which does not relieve.

10. Bryonia.

Delirium with desire to escape, wants to go home. Aggravation by slightest motion. Vertigo during fever. Staggering gait during fever. Patient lies quietly, does not want to be disturbed. Coma during fever.

11. Nux-vom

Inflammation of brain before nervous fever. Tottering gait during fever. Chilliness in every stage of fever, must be covered. Perspiration only on one side of body.

12. Veratrum viride.

Delirium and convulsions in encephalitis. High fever. Coma in brain complaints. Dilatation of pupils during convulsions. Incipient paralysis of optic nerve. Dyspnoea during fever. Myocarditis.

One or more medicines may be needed depending upon the disease manifestation in individual cases. In the initial stage of the disease, Belladonna itself may be the medicine and may need frequent repetition of lower potencies of the medicine (3X) to effect a cure. Ars alb or Aconite also may be useful in the early stages depending on the symptoms. The other probable medicines in cases presenting with varying symptoms of encephalitis are Hyoscyamus, Gelsemium, Helleborus, Opium, Zincum met, Cuprum met, Apis, Cocculus, Stramonium, Baptisia, Bryonia. Nux-vom, Verat viride etc.

Precautions to be taken

1. Avoidance of consuming food items contaminated with body fluids of viral reservoirs ie., infected bats which could be achieved by
 - a. Avoiding partly bat eaten fruits.
 - b. Avoiding other raw food items in which there is a possibility of contamination with infected bat body fluids.
 - c. Cleaning fresh fruits and vegetables with soap before using. For Eg. In Kerala, the most important fruit item which is consumed by fruit bat is banana. Clean banana well with an alcohol containing disinfectant or soap and water before consuming, if there appears a chance for contamination.

2. Avoidance of infection from Nipah cases, which could be achieved by
 - a. Avoiding contact with body fluids of Nipah patients by using barrier nursing methods ie., personal protection using PPE, masks, gloves, gowns etc. N95 masks offer good protection especially for those who are dealing with Nipah confirmed cases.
Disposable masks should be used with great care and used masks should be disposed with at most precaution.
 - b. Hand washing with soap & water before and after handling/visiting patients.
 - c. Using PPE while handling corpse of Nipah victims.

3. Identification, close observation and follow up of contacts.

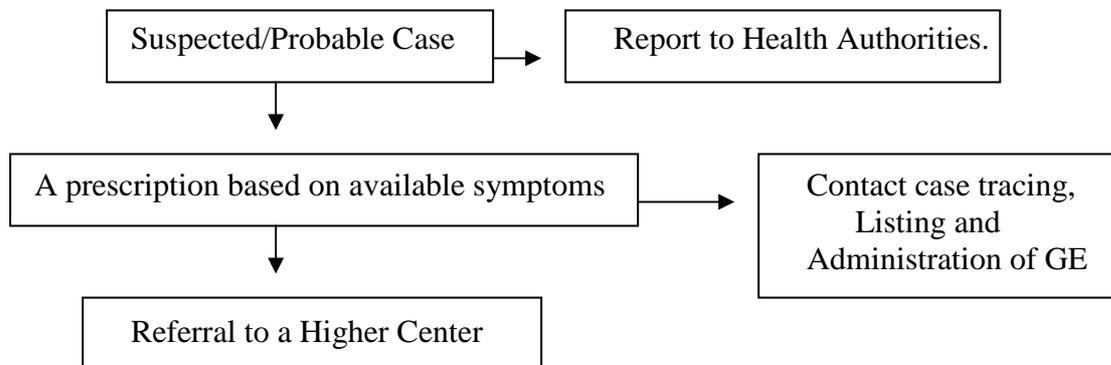
Definition of a Contact¹⁸: A Close contact is defined as a patient or a person who came in contact with a Nipah case (confirmed or probable cases) in at least one of the following ways.

- Was admitted simultaneously in a hospital ward/ shared room with a suspect/confirmed case of Nipah virus disease

- Has had direct close contact with the suspect/confirmed case of Nipah virus disease during the illness including during transportation.
- Has had direct close contact with the (deceased) suspect/confirmed case of Nipah virus disease at a funeral or during burial preparation rituals
- Has touched the blood or body fluids (saliva, urine, vomitus etc.) of a suspect/confirmed case of Nipah virus disease during their illness
- Has touched the clothes or linens of a suspect/confirmed case of Nipah virus disease

These contacts need to be followed up for appearance of symptoms of NiV for the longest incubation period (21 days).

Patient Management Flow Chart



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*This document is subject to editing as more information is obtained.