

REVIEW ARTICLE ON CHANDIPURA VESICULOVIRUS AND IT'S CURRENT SCENARIO IN INDIA

Rakibe Vaishali¹, Vidhate Shruti², Wankhede Komal^{3*}, Yelmate Shreyash⁴ and Yuvraj Chavan⁵

Department of Pharmaceutical Organic Chemistry¹

UG Student^{2,3,4,5}

Mahatma Gandhi Vidyamandir's Pharmacy College, Panchavati, Nashik, Maharashtra,
India.^{1,2,3,4,5}

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***Corresponding Author**

Wankhede Komal

UG Student, Mahatma

Gandhi Vidyamandir's

Pharmacy College,

Panchavati, Nashik,

Maharashtra, India.

ABSTRACT

Chandipura virus was first found in year 1965, after which it shown various outbreak in year 1980, 1995, 2003, 2004, 2010, 2014, but it catches the global attention in year 2003-04 as it's shown its major spread in various states of India mainly Gujrat, Maharashtra and Andhrapradesh. In 2003-2004 Central India faced an major outbreak witnessing case fatality rates ranging from 56-75 per cent in Rajasthan, Madhya Pradesh and Gujarat with major encephalitic symptoms. These virus belongs to the Rhabdoviridae family, and shows similarities with Rabbis virus. The main vector for this Virus is Flies, mosquito etc, Phlebotomine sandflies are implicated as the vectors due to their predominance in endemic areas, repeated virus isolations and their ability to transmit the virus by transovarial and venereal routes. The major symptoms observed are Fever, Headaches, Fatigue, Body and muscle aches, Vomiting, Convulsions. The diagnosis is done with IFA and RT- PCR.^[56] Due to unavailability of any approved vaccine for the

Chandipura Vesiculovirus, the treatment is generally based on preventive measures. Two candidate vaccines have been developed:

- 1) A recombinant vaccine and a killed vaccine.
- 2) Sirnas targeting the P and M proteins.
- 3) Glycoprotein based vaccine and they are now awaiting clinical trials.

KEYWORDS: Chandipura Vesiculovirus (CHPV), IFA, RT-PCR, Acute syphilis syndrome.

INTRODUCTION

Chandipura vesiculovirus (CHPV) is part of the Rhabdoviridae family. In people, it cause a serious condition as Chandipura encephalitis or Chandipura viral encephalitis. This virus was first found way in 1965 researchers isolated it from patients from Chandipura in Nagpur, Maharashtra, India.^[1] The Chandipura virus is a member of a group called vesiculoviruses and has recently been linked to several outbreaks across various regions in India. It's interesting to note that while this virus looks quite similar to the well-known Vesicular Stomatitis Virus, it can be easily identified because it infects humans.

This illness often starts suddenly with a high fever. Then, symptoms like seizures, confusion, diarrhea, and vomiting can occur, leading sadly to death for many affected. The rapid decline in health and death of patients remains somewhat puzzling even today, though many theories have been suggested. Typically, the disease is more common among lower-income populations. Patients range in age from just a few months to 15 years old.^[48] The virus made headlines during outbreaks in 2003-2004. In June 2024, reports surfaced about cases of Acute Encephalitis Syndrome (AES) affecting children under 15 in Gujarat.

What is chandipura virus?

Chandipura was discovered back in 1965 and got its name from the village in Maharashtra where it was found.^[3] This virus belongs to the Rhabdoviridae family, which also has other viruses like lyssavirus that lead to rabies. It's classified as follows:

Virus classification

- Unranked: Virus^[2]

Kingdom	Orthornavirae
Phylum	Negarnaviricota
Class	Monjiviricetes
Order	Mononegavirales
Family	Rhabdoviridae
Genus	Vesiculovirus
Species	Chandipura vesiculovirus

The Rhabdoviridae family fits into the Order Mononegavirales and is made up of negative-sense single-stranded viruses that have a bullet shape and are roughly 11kb long.^[6] Among ten genera, both Lyssavirus & Vesiculovirus hold significance for public health. Rabies virus

is the most important pathogen within this family and is found worldwide.^[7] Meanwhile, Vesiculovirus includes viruses that affect both humans & animals; its typical representative is vesicular stomatitis Indiana virus, which usually infects cattle, horses, & pigs, causing mild flu-like symptoms. Most viruses from this genus are spread through bites from Phlebotomine sandflies.

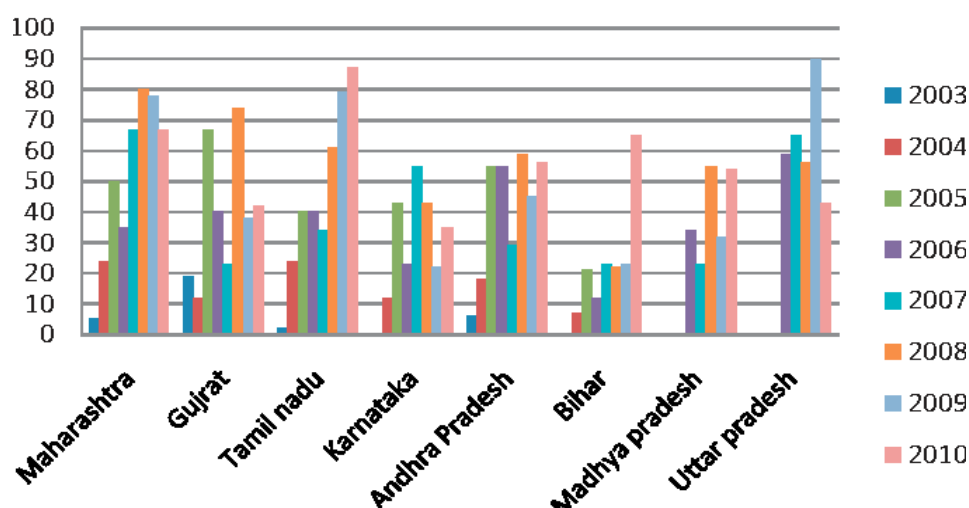
Believed to be zoonotic, Chandipura virus likely comes from animals before making its way to humans. People can get infected by directly or indirectly interacting with sandflies, ticks, or mosquitoes. However, researchers are still looking into specific animal hosts and how transmission occurs; this emphasizes how vital ongoing studies & monitoring are! Evidence shows that CHPV has been isolated from sandflies in India & West Africa; bites from these insects are thought to spread the virus.^[3,4] Although there's proof of the virus's presence in Africa, no human cases have been reported there so far.

History of the virus

In 1965, scientists first isolated this virus from two adults suffering from feverish illness in Nagpur County of Maharashtra State.^[5] Since then, it's popped up in three neighboring states: Madhya Pradesh, Maharashtra & Andhra Pradesh. This suggests that it might have been around for years and possibly triggered past outbreaks of encephalitis recorded since 1954! They even detected it among sandflies in Senegal & Nigeria.

Fast forward to 1980, when CHPV was once again isolated from a person suffering acute encephalitis in Madhya Pradesh.

From 2003 to 2010, the virus gained international attention after severe outbreaks hit India. In 2003 alone, there were reports of 329 children testing positive across Andhra Pradesh & Maharashtra; tragically, 183 of them died because of it! In years like 2005 & 2007, Maharashtra, Gujarat & Andhra Pradesh faced major challenges relating to this infection.^[19] By 2009, most patients were from Uttar Pradesh; meanwhile, 2010 saw serious outbreaks reported in Tamil Nadu, Bihar & Maharashtra as well.



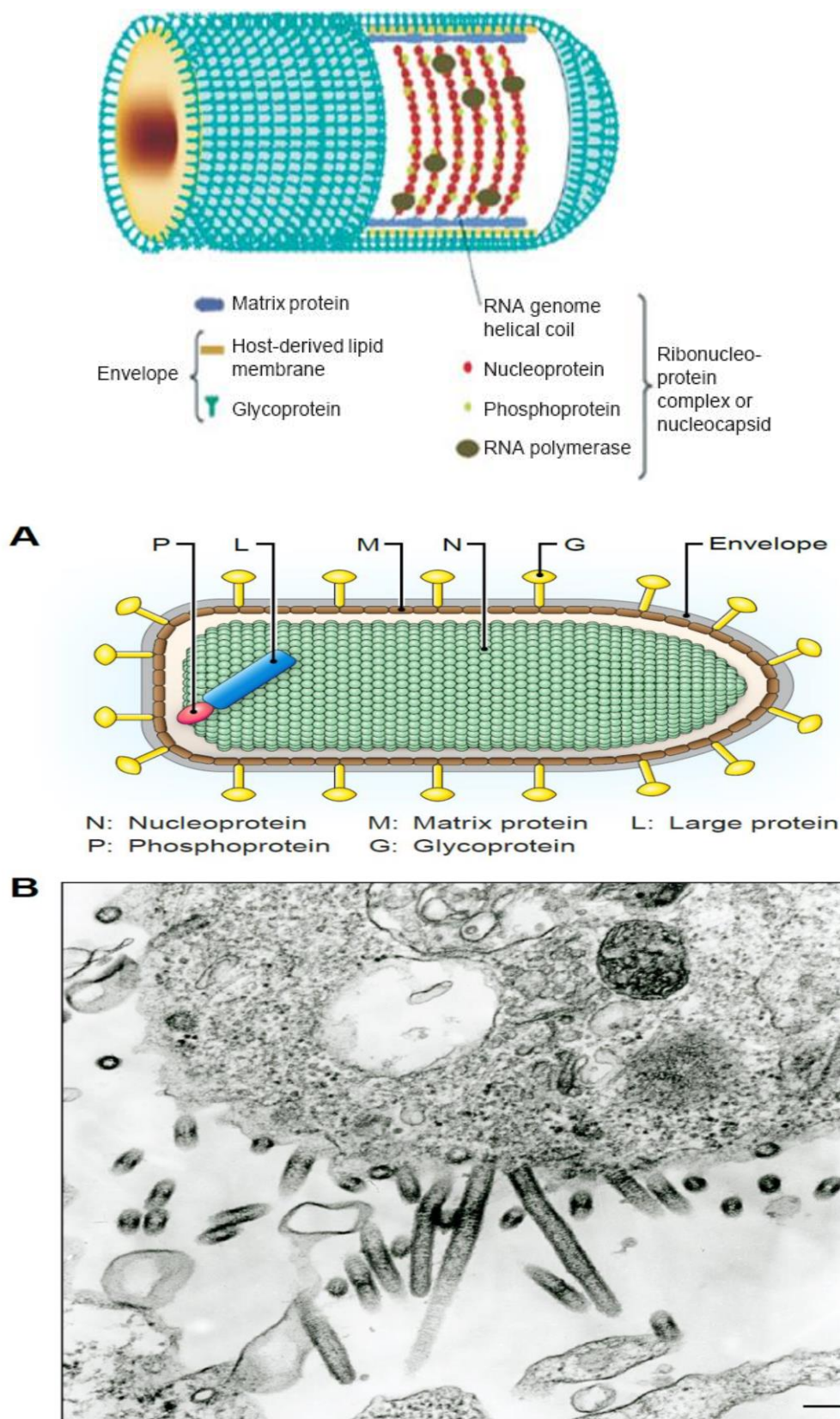
Cases of chandipura virus across various states

Some signs indicate that CHPV could have existed for more than half a century! However, it's only recently become recognized as an important emerging health concern. An outbreak investigation took place in Nagpur region during *2007,* focusing on hospitalized kids younger 15 years old where they recorded a total of *78 cases* of acute encephalitis. They tested blood samples for specific antibodies against CHPV using techniques like RT-PCR (reverse transcription-polymerase chain reaction). They also tried isolating the virus using special cell lines! Sadly, during that, around *43%* of patients didn't survive—and there were just about equal numbers of boys and girls affected! CHPV was confirmed in *39 cases.*^[10]

Structure of CHPV

There are no structural data on CHPV proteins, despite their significance for public health. Studies conducted on the prototype vesiculovirus, vesicular stomatitis virus serotype Indiana (VSVIND), have actually yielded the majority of the functional and structural information on CHPV. The fact that the amino acid (aa) sequences of the proteins from the two viruses are conserved makes this inference plausible. As an illustration, the glycoprotein G aa sequences from the two viruses are 40% identical and roughly 65% similar. Bullet-shaped structure characterizes the Chandipura virus. With a genomic length of about 11 kb, CHPV is an RNA virus that is enclosed. With discrete surface projections of 9 to 11 nm in size, it is 150–165 nm long and 50–65 nm wide.

Structure of CHPV Virus



A. Bullet shape structure of CHPV.

B. CHVP under microscope.

Transmission of CHPV^[2]

The Chandipura virus is a vector species that spreads between reservoir hosts, like humans or animals, and vector species, like sandflies.^[29] Infected sandflies reproduce or multiply the virus in their salivary glands, and these flies then bite humans while they are eating. Because of their widespread distribution in endemic locations, their frequent isolation of the virus, and their capacity to spread the virus by transovarial and venereal pathways, phthalbotomine sandflies have been identified as vectors.^[25]

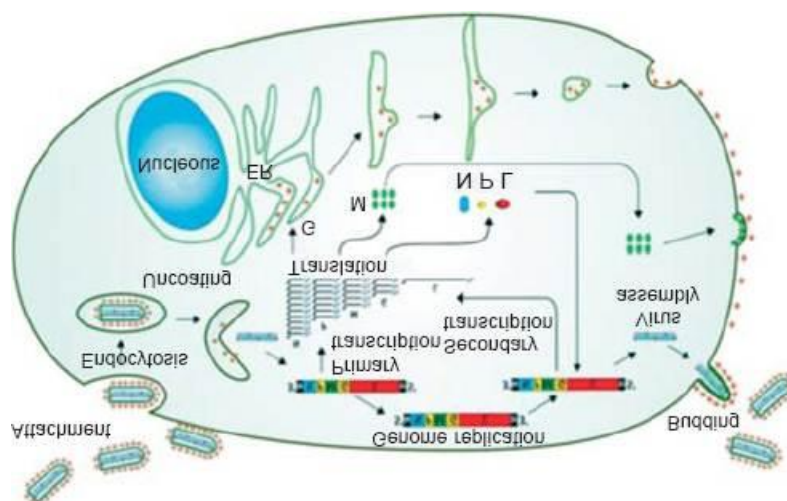
For this reason, keeping sandfly populations under control is essential to avoiding infection with the Chandipura virus. Humans can experience symptoms from an infection anywhere from a few days to a week, depending on the viral load and each person's immune system. The Chandipura vesiculovirus, which was discovered from sandflies in India and West Africa, is thought to have spread by bites.

Year of isolation	Place of isolation	Host	Reference
2012	Vidarbha region, Nagpur, India	<i>Sergentomyia</i> spp. of sandflies	Sudeep <i>et al</i> ¹¹
2007	Maharashtra, India	Human (serum)	Gurav <i>et al</i> ¹⁰
2004	Gujarat, India	Human (serum)	Chadha <i>et al</i> ⁵
2003	Andhra Pradesh, India	Human (serum)	Rao <i>et al</i> ⁴
1994-1997	Senegal, Africa	<i>Sergentomyia</i> spp. of sandflies	Ba <i>et al</i> ¹⁹
1993	Senegal, Africa	<i>Phlebotomine</i> sandflies	Fontinelle <i>et al</i> ²⁰
1980	Raipur district, Madhya Pradesh (now Chhattisgarh), India	Human (serum)	Rodrigues <i>et al</i> ¹⁷
1975	Nigeria, West Africa	Hedgehog (<i>Atelerix spiculus</i>)	Kemp ²¹
1967-1969	Aurangabad, Maharashtra, India	<i>Phlebotomine</i> sandflies	Dhanda <i>et al</i> ¹⁶
1965	Chandipura village, Nagpur district, Maharashtra, India	Human (serum)	Bhatt and Rodrigues ¹⁴

Life cycle of virus^[27]

As like many of the other virus, the virus replicates itself inside the host cell by following certain steps. The steps involved are

- 1) Adsorption of viral particle.
- 2) Penetration of virus into the host cell.
- 3) Uncoating and release of core RNP into the cytosol from late endosomal vesicles.
- 4) Transcription of the viral genome by viral polymerase.
- 5) Translation of viral mRNA, post-translational modifications of viral proteins.
- 6) The replication of viral genome, assembly of progeny particles.
- 7) Encapsulation of Genomic RNA
- 8) Finally budding and release of mature virion particles.



Life cycle of chandipura virus

Causes of chandipura virus infection

The Chandipura Virus is thought to be zoonotic, which means it starts in animal populations and can spread to human populations. Human diseases can result from direct or indirect contact with sandflies, ticks, or mosquitoes. The precise animal reservoirs and means of transmission are still being researched, emphasizing the necessity for continuing research and observation.

Preventing the transmission of the chandipura virus^[58]

Several crucial procedures are vital to preventing the Chandipura Virus infection:

- 1) Hygiene precautions: Frequent hand washing with soap and water, particularly after interacting with animals or entering possibly polluted areas.
- 2) Preserving wildlife: Reducing interactions with untamed creatures and their environments, especially in coastal regions where the virus is common.
- 3) Personal protection equipment: To lower the risk of transmission, wear the proper protective gear, such as gloves and masks, when handling potentially infected animals or their tissues.
- 4) Vector control: Utilizing mosquito nets and insect repellents might help reduce exposure, as insects may play a part in the virus's spread.
- 5) Vector Control: Using environmental management techniques and pesticide spraying to lessen sandfly breeding grounds.
- 6) Personal Safety: Promoting the usage of insect repellent and mosquito nets.

Chandipura virus infection symptoms^[61]

From minor respiratory distress to more serious problems, the Chandipura virus infection can cause a variety of symptoms.

Typical first symptoms consist of:

The illness was marked by an abrupt onset of high fever, which was followed by convulsions, altered sensorium, vomiting, diarrhea, and, in most cases, death.^[21]

- 1) High fever: Often starting suddenly, this condition can be very uncomfortable for the sufferer as it is accompanied by chills and perspiration.
- 2) Intense headache: A Chandipura virus infection is characterized by chronic, severe headaches that are extremely uncomfortable and interfere with everyday activities.
- 3) Photophobia: Photophobia is a condition of light sensitivity, whereby intense indoor lights or even moderate sunshine can hurt or irritate the eyes.
- 4) Modified sensorium: In more serious circumstances,

Diagnosis of chandipura virus

- 1) Immunofluorescent antibody technique (IFA)

IFA was effectively used to identify CHPV in brain tissues during the 2003 outbreak in Andhra Pradesh.

- 2) Diagnosis with molecular tools

Given the swift progression of the disease in children, often resulting in death within 24-48 hours of symptom onset, there was an urgent need for rapid diagnostic methods. Reverse transcriptase PCR (RT-PCR) and real-time RT-PCR have been standardized for routine diagnosis.^[53]

Management tips for chandipura virus infection^[60]

There is no specific treatment or vaccine available for the Chandipura virus infection, and hence the management focuses on supportive care and preventive measures.

Timely identification and swift medical treatment are essential for managing Chandipura Virus infections. Individuals should seek medical care immediately if they experience symptoms indicative of respiratory illness. Physician might suggest supportive care measures such as hydration, rest and treatment to relieve fever and respiratory distress.^[54]

There is no any vacancies available to treat the Chandipura virus infection hence this measure are taken to treat the infection:

Hospitalisation: Patients with severe symptoms are required to be hospitalised.

Hydration: It is important to ensure proper hydration, especially in cases where vomiting is severe.

Intensive care: In severe neurological symptoms, intensive care is often considered necessary to manage the respiratory and neurological complications of the patient.

Antipyretics: To reduce fever, proper medication is required.

Anticonvulsants: This is done to control seizures.

As we explore the complexities of the CHPV, ongoing efforts to understand its epidemiology, transmission dynamics, and potential for spread highlight the importance of collaboration across scientific fields and international borders. By staying informed and adopting preventive measures, we can collectively mitigate the impact of emerging infectious diseases like the Chandipura Virus, safeguarding both individual and community health.

Current situation of chandipura virus in india^[10,13,14]

The Chandipura virus, primarily transmitted by female phlebotomine sand flies, leads to a rapid continuation from Influenza-like symptoms to severe brain inflammation, coma, and potentially death. Symptoms include diarrhea, vomiting, high fever, headaches, delirium, and convulsions, with conditions worsening within 24 to 48 hours, necessitating urgent medical intervention.

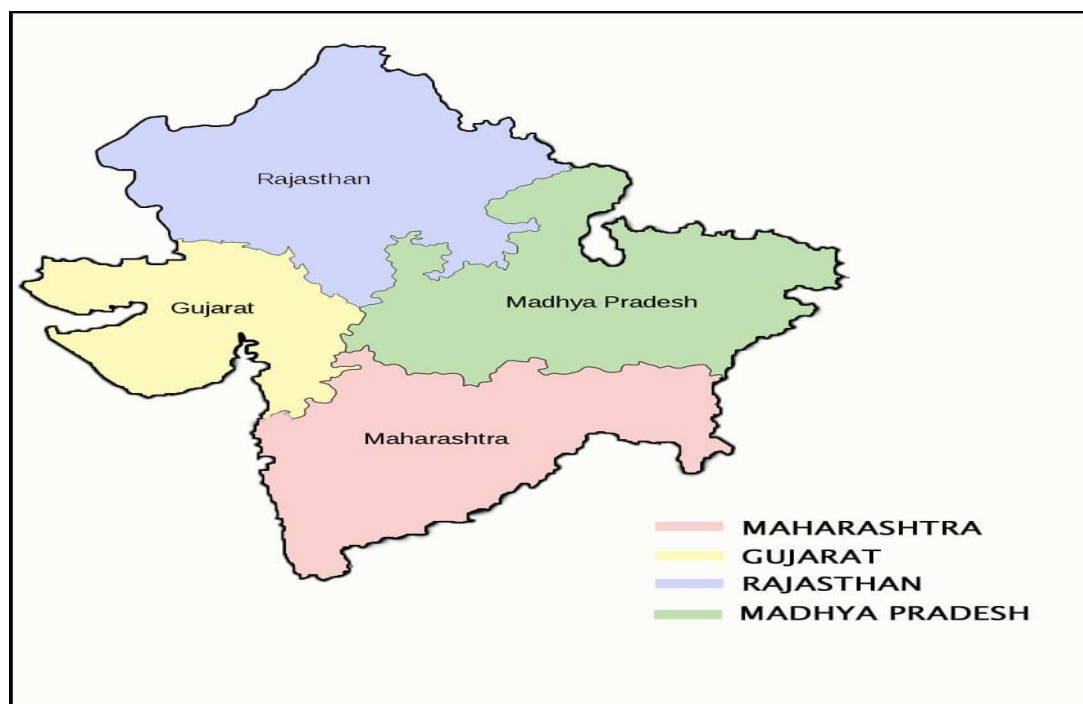
As of the report of 20 July 2024, there have been 78 reported cases of Acute Neuroinflammation, with 75 cases originating from 21 districts in Gujarat, 2 cases from Rajasthan, and 1 case from Madhya Pradesh, which of of these, 28 cases shows outcome in fatalities. Among the 76 samples was send for testing at the National Institute of Virology (NIV) in Pune, among which 9 were positive for the Chandipura virus (CHPV).

The state government has submitted samples from all patients to the NIV in Pune, where only two demices have been confirmed as being caused by the Chandipura virus. Consequently, the state government is now treating the situation as an encephalitis outbreak. Despite the terminology, the virus is spreading, with 35 cases documented in Gujarat, two in Rajasthan, and one in Madhya Pradesh during July 2024. The sand flies that transmit the virus are typically found in rural areas, but at least two deaths have also been reported in Ahmedabad

city during this outbreak. Sand fly breeding sites include crevices in walls, tree holes, dark rooms, stables, and storerooms. A similar outbreak occurred in Andhra Pradesh in 2003,^[18] resulting in several child fatalities within the initial 48 hours of infection.

A special team of epidemiologists has been deployed to the Aravalli and Sabarkantha districts, where the highest number of deaths—four—has been reported. “Approximately 11,050 households are under surveillance statewide; The Malathion powder in 4,838 raw houses and cattle sheds have been used for disease control. The first suspected case of viral encephalitis was detected on June 27 in a patient from Udaipur, Rajasthan, who was admitted to Himmatnagar Medical College in Gujarat,” stated a government release.^[13]

At the movement, there is unavailability of antiviral treatment or vaccine for the Chandipura virus, making early diagnosis and symptomatic care crucial. According to 2014 document of Gujarat government titled “Epidemiology and Management of Chandipura Encephalitis,” management strategies focus on ensuring airway, breathing, and circulation support, including oxygen therapy and potential ventilation, as well as restoring the fluid and electrolyte balance, hyperpyrexia, elevated intracranial pressure, seizures, and secondary bacterial infections. The government emphasized that all necessary facilities, including ventilators and oxygen, are available in hospitals at the district level for affected patients.^[62]



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