

## Epidemiology and clinical characteristics of Chandipura virus

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### Abstract

Chandipura virus is an emerging arbovirus that poses significant public health challenges, especially in South Asia. Chandipura virus infection is one of the neglected diseases that is receiving limited attention. This virus primarily affects young children and has been associated with outbreaks of influenza-like illness and acute encephalitis, leading to high morbidity and mortality rates with death occurring within 48-72 h of the onset of symptoms in most of the affected populations. The outbreaks occur majorly during near-monsoon season especially in regions with favorable ecological conditions for sand fly proliferation. Currently, no vaccines or therapeutics are available, depicting the ongoing public health challenge posed by this emerging infectious virus. This review provides an overview of epidemiology, clinical features, and public health implications of Chandipura virus infections. Understanding the epidemiological patterns, clinical manifestations, and public health responses to the Chandipura virus is essential for developing effective preventive strategies and enhancing patient outcomes.

### Introduction

RNA viruses are characterized by their exceptionally high mutation rates compared to organisms with DNA genomes (1). In the past two decades, the world has witnessed the (re)emergence of several viruses, with a majority being RNA viruses. These emerging viruses include pathogens like Ebola virus, zika virus, Nipah virus, Middle

East respiratory syndrome-related coronavirus (MERS-CoV), severe acute respiratory syndrome coronavirus (SARS or SARS-CoV-1), SARS-CoV-2, Marburg virus and various strains of influenza viruses (2, 3). Many of these viruses have caused severe outbreaks posing significant threats to public health globally. These viral outbreaks showed the vulnerability of modern human civilization to

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potential viral epidemics or pandemics (4). Among these threats is Chandipura virus (CHPV), arthropod-borne virus (arbovirus) causing encephalitis in humans. The virus belongs to the family *Rhabdoviridae*, genus *Vesiculovirus*, and was first isolated in 1965 from the blood of a febrile child in Chandipura village, Maharashtra, India (5). Several arthropod-borne viruses such as the Japanese encephalitis virus, West Nile virus, zika virus, and CHPV are associated with encephalitis. Mosquitoes, ticks, sand flies, and occasionally other insects typically serve as the vectors responsible for transmitting these viruses (6, 7). CHPV was isolated from Phlebotomine sandflies captured in Aurangabad district, Maharashtra, India, between 1967 and 1969. The sand flies are the known vectors of the virus (8). In 1983, Rodrigues et al. reported the isolation of this virus from the blood of an encephalopathy patient (9). This was followed by a case in 1988, where the virus was isolated from cerebrospinal fluid (10). The cases have been reported primarily in India and the existing epidemiological information suggests that this virus causes sporadic outbreaks (11, 12), however, has the potential to cause epidemics. As it is an emerging pathogen, it is necessary to prioritize the understanding of CHPV infection in both humans and experimental animals in order to develop effective diagnostic tools, treatments, and preventive measures. This is crucial for managing potential outbreaks and reducing morbidity and mortality associated with the virus. Further, detailed analysis of CHPV can provide necessary information about its transmission mechanism, reservoir hosts, and potential for adaptation or mutation. Such knowledge is essential for implementing targeted public health strategies, including surveillance and early detection efforts. This review provides a structured overview of CHPV, emphasizing its epidemiology, clinical manifestations, and public health implications.

## Genome

The genome of CHPV is composed of a single-stranded, non-segmented, negative-sense single-stranded RNA molecule of approximately 11 kb long. The genetic material encodes for five essential proteins (3' N-P-M-G-L) crucial for the virus life cycle and pathogenesis (13-15). The 49-nucleotide leader RNA at the 3' end and a short 46 nucleotide trailer sequence at the 5' end were also present in the genome. The nucleocapsid (N) protein binds to the viral RNA and forms a protective ribonucleoprotein complex which is essential for RNA synthesis and stability. Interacting with the N protein, the phosphoprotein (P) and large (L) protein form the RNA polymerase complex, responsible for viral RNA transcription and replication. The matrix (M) protein present in the internal viral surface facilitates viral assembly and budding by interacting with both the ribonucleoprotein complex and the viral glycoprotein (G), which protrudes from the viral envelope. The G protein serves in virus absorption, assembly, and budding and also plays a major role in eliciting host immune responses, thus acting as a major antigenic determinant (16, 17). This genomic organization is characteristic of *vesiculoviruses* within the *Rhabdoviridae* family, encapsulated within a lipid envelope which is derived during viral budding from host cell membranes (13, 14).

## Epidemiology and Transmission

CHPV exhibits a seasonal pattern, with outbreaks typically occurs during the near-monsoon months typically from July to October when the sand fly populations are high. CHPV is primarily circulating across India and the sporadic outbreak has been reported in specific geographic regions of India so far (12). The virus has been detected in various states across India, with Maharashtra, Gujarat, Andhra Pradesh, and Telangana reporting the highest number of cases. The virus was first detected in 1965 in Maharashtra, India. Prior to a surge in documented cases, the virus existed with limited scientific attention. In 2003, there was a large outbreak of encephalitis in Andhra Pradesh,

India, resulting in 329 reported cases and 183 fatalities (18). Subsequently, in 2004, another outbreak in Gujarat, India was reported with over 75% fatality rates (19). After 2004, sporadic outbreaks were reported in Andhra Pradesh and Maharashtra (20, 21). The virus has also been isolated in Nigeria, Senegal (22, 23) as well as in Bhutan and Sri Lanka (11, 24), depicting the widespread presence in tropical countries and the potential for geographical spread especially within the South Asian region. The detection of anti-CHPV neutralizing antibodies in blood samples collected from pigs, buffaloes, cattle, goats, and sheep indicates the circulation of this virus (25). Further, the presence of anti-CHPV antibodies in other animals such as frogs, lizards, and rodents also suggests that the virus utilizes a wide range of hosts for multiplication and maintenance in nature (11). However, further research is essential for the detailed understanding of the susceptibility of various animal species to this virus. Recently, in 2024, 148 cases were reported in India, resulting in 59 deaths (as of July 31, 2024) (26). The factors contributing to the epidemiology of CHPV include ecological changes, urbanization, and population movement, which influence vector abundance and human exposure (27). CHPV is transmitted through the bite of infected Phlebotomine sand flies belonging to the species of genus *Phlebotomus*. These sand flies serve as vectors, acquiring the virus by feeding on viremic hosts, typically an infected human (28, 29). After ingestion, the virus replicates within the vector and the vector can transmit the virus to new hosts (30).

### Clinical Features and Treatment

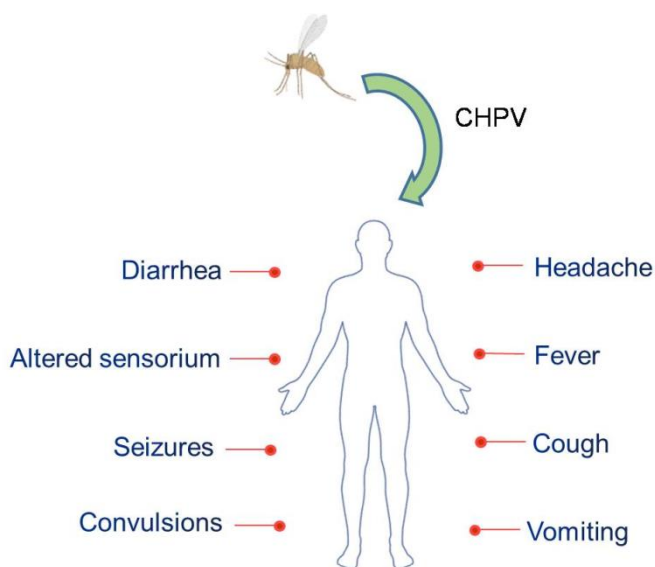
The clinical features of CHPV infection range from asymptomatic or mild febrile illness to severe encephalitis with high mortality rates. Children are particularly vulnerable, and the onset of illness is abrupt, with fever, headache, vomiting, and drowsiness being common initial symptoms (Figure 1). As the infection progresses neurological symptoms (within 24-30 hrs.) such as seizures,

altered sensorium, and coma may develop, requiring prompt medical intervention (11, 31). The diagnosis of CHPV infection can be challenging due to its similarity to other febrile illnesses and the rapid progression of severe cases. The laboratory diagnosis of CHPV involves methods such as virus identification by real-time polymerase chain reaction to amplify viral RNA from clinical specimens (32), virus isolation, antigen detection using enzyme-linked immunosorbent assay (ELISA) and immunofluorescence assay, as well as serological tests including IgM and IgG ELISA, and viral neutralization tests (18, 33).

As there are currently no specific antiviral drugs or vaccines approved for use against this virus, treatment options primarily focus on supportive care and symptomatic treatment (16). Kitaura et al. developed a novel C.B-17 severe combined immunodeficiency (SCID) mouse model for evaluating the antiviral efficacy against CHPV. The favipiravir treatment in the SCID model reduced viral load and improved survival both when administered pre-symptomatically (days 5–14) and post-symptomatically (days 9–18) (34). Venkateswarlu and Arankalle attempted to develop a candidate vaccine against CHPV using the baculovirus expression system to express the virus's G protein. The recombinant protein induced an antibody response in mice upon testing (35). Subsequently, a vero cell-based beta propiolactone (BPL) inactivated vaccine was developed and assessed for its immunogenicity in mice. Immunized mice showed neutralizing antibody responses and survived live virus challenge through intracranial route. The vaccine efficacy in combination with commercially available DPT vaccine was also tested in mice, resulting in high antibody titers and survival upon challenge with live virus (36, 37). Pavitrakar et al. identified T-cell and B-cell epitopes from various antigenic proteins of CHPV and utilized immunoinformatic approaches to design a multi-epitope peptide vaccine named MEC-CHPV. *In silico* immune-simulation indicated an immune response against

MEC-CHPV when used as a potential vaccine. However, further laboratory experiments are

necessary to validate these findings (38). Still, no vaccines have reached advanced clinical trials.



**Fig.1.** Transmission and symptoms of CHPV. CHPV is primarily spread through the bites of infected sand flies, particularly those from the *Phlebotomus* genus. The symptoms typically include a sudden onset of high fever, followed by seizures, altered sensorium, and gastrointestinal symptoms such as diarrhea and vomiting. In severe cases, the infection can progress rapidly and lead to death.

The public health impact of CHPV outbreaks is significant, necessitating the coordinated efforts in surveillance, diagnosis, and outbreak response (39). The reporting of suspected and confirmed cases to public health authorities is essential for initiating outbreak response measures. In addition, early detection of cases, vector control measures, and public awareness campaigns are essential for preventing and mitigating the outbreaks. The preventive measures focus on controlling the vectors; by reducing the vector populations in specific geographic areas, the likelihood of human exposure to pathogens can be significantly reduced (40). In addition to environmental interventions, individual protective measures also play a crucial role. The usage of insect repellents and insecticide-treated bed nets is also effective in preventing the infection (41). Further, many of the arboviral borne

diseases are symptomatically treated due to the lack of specific treatments or vaccines. Hence, the development of effective diagnostic tests, vaccines, and/or antiviral therapeutics is highly essential for significantly reducing the public health burden of CHPV. Overall, arboviral diseases pose a major threat to human health globally, yet many diseases remain neglected, highlighting the need for more research on the neglected tropical diseases. Since CHPV is one of the neglected tropical pathogens with a high fatality rate, the plant expression system can be explored to develop affordable recombinant vaccines against this pathogen. Several arboviral vaccine candidates have already been successfully expressed in plants, demonstrating their feasibility and efficacy (42). Utilizing plant system to manufacture vaccines against CHPV could potentially offer cost-effective and accessible

solutions for vulnerable populations, especially in regions with limited resources, where these diseases have the most severe impact. Additionally, capacity building in healthcare facilities, especially in endemic regions, is crucial for managing severe cases and reducing mortality rates associated with CHPV encephalitis (43, 44).

### Conclusion

CHPV continues to pose a significant public health threat in the Indian subcontinent, with sporadic outbreaks highlighting the need for continued surveillance and preparedness. The virus primarily affects regions across India, where it periodically causes outbreaks with significant morbidity and mortality, particularly among children. A comprehensive understanding of the epidemiology, clinical manifestations, and public health implications of CHPV is essential for developing effective prevention and control strategies. However, further research into vector biology, viral pathogenesis, and vaccine development is warranted in order to address the challenges posed by this emerging virus.

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### Ethical approval

Not applicable.

### Conflicts of Interest

The author declares no conflict of interest.

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