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Review of Chandipura virus-outbreaks in India

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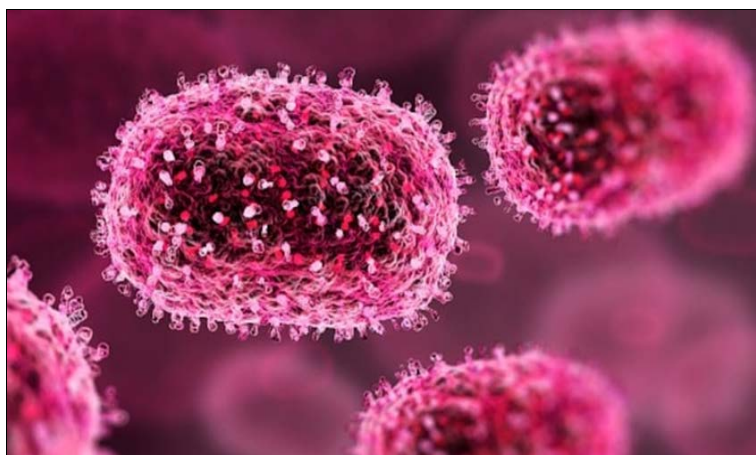
Abstract

Chandipura virus (CHPV) is a virus from the Rhabdoviridae family that causes brain infections, mainly in children. It was first found in 1965 in India and has led to deadly outbreaks with symptoms like fever, seizures, and coma. The virus is shaped like a bullet and spreads mostly through sandflies. Diagnosis is done using tests like RT-PCR. There is no specific treatment yet, and care is mainly supportive. Controlling sandflies and early detection are key to preventing outbreaks. Research for vaccines and medicines is ongoing. In this present study mainly focused on latest outbreak happens in the Months of June-August 2024 across several districts in Gujarat, India.

Keywords: Chandipura virus, RT-PCR, sandflies, siRNA, pediatric sporadic encephalitis, ribavirin, IgM Elisa

Introduction

Chandipura virus (CHPV) is a negative, single-stranded RNA virus belonging to the family *Rhabdoviridae* [1]. CHPV is transmitted by the sand fly species *Phlebotomus* sp. and *Sergentomyia* sp. as well as by the mosquito *Aedes aegypti*. Human-to-human transmissions of Chandipura Virus have not been documented. Infection of this virus can lead to pediatric encephalitis (brain inflammation especially in children) [2] thereby the mortality rate enhanced from 44% to 75% [3,4]. Other severe symptoms of CHPV Virus infections include high-grade fever, vomiting, convulsions and coma leads death also happens within 2 days of hospitalization. The most recent outbreak of CHPV took place of several districts of Gujarat in the Months of during June-August 2024, India [5, 6], where 78 cases of acute encephalitis syndrome (AES) were identified in children under the age of 15 years old. According to a press release dated on 20 July 2024 by the Ministry of Health and Family Welfare, Government of India, most of the cases (75) recorded from 21 districts of Gujarat and its corporations, two cases reported from Rajasthan, and one case was notified from Madhya Pradesh, resulting in 28 deaths happens, among which children were most effected [7]. Nine of 76 patients' samples were sent to the National Institute of Virology in Pune, India, and tested results were found positive for CHPV. All of those 9 positive patients, along with five other related deaths due to CHPV infections reported from Gujarat, India [7]. A recent report by the World Health Organization (WHO) listed the total number of confirmed and suspected virus infected cases at 245 with a case fatality rate of 33% [8].



Chandipura Virus was first discovered in India in the year of 1965 at Maharashtra state of Nagpur district, Chandipura village during outbreak and hence it was named the Chandipura virus ^[2]. CHPV was initially isolated from two cases in adult humans presenting with high grade fever and joint pain ^[2].

Outbreaks

CHPV has since caused several large outbreaks throughout India, as shown in below table

Summary of recorded outbreaks of CHPV. A total of 11 outbreaks have occurred since 1965 ^[1, 3, 9-14]. The table includes the date(s) of outbreaks, regions affected, total number of acute encephalitis syndrome (AES) cases, the age of affected patients, and the case fatality rate (CFR). Historical data (prior to 2024) adapted from reference 14.

Date	Regions	AES Cases	Ages Affected	CFR
2024	Gujarat	245	Under 15 years	33%
2016	Bihar	24	1-15 years	20.8%
2009	Odisha	21	Under 10 years to over 18 years	28.65%
2007	Maharashtra	78	Under 15 years	43.6%
2005-2006	Andhra Pradesh	52	Under 15 years	54.4%
2004	Gujarat	20	2-16 years	78.3%
2003	Andhra Pradesh	55	2.5 months to 15 years	54.9%
2002	Andhra Pradesh	surveillance	No symptomatic cases	-
1997	Andhra Pradesh	surveillance	Pre-epidemic CHPV detection	-
1980	Madhya Pradesh	1 [isolated]	Unknown	-
1965	Maharashtra	2[isolated]	Febrile patients	-

Structure

The Chandipura virus (CHPV) is a bullet-shaped virus from the Rhabdoviridae family. Its structure includes a lipid

envelope with glycoprotein G spikes that help the virus attach to and enter host cells. Beneath the envelope lies the matrix protein, which maintains the virus's shape and aids in assembly. Inside, the nucleocapsid houses the viral RNA tightly bound by nucleoprotein, which protects the RNA. The phosphoprotein acts as a cofactor for the large protein, an RNA-dependent RNA polymerase responsible for replication and transcription of the viral genome ^[15].

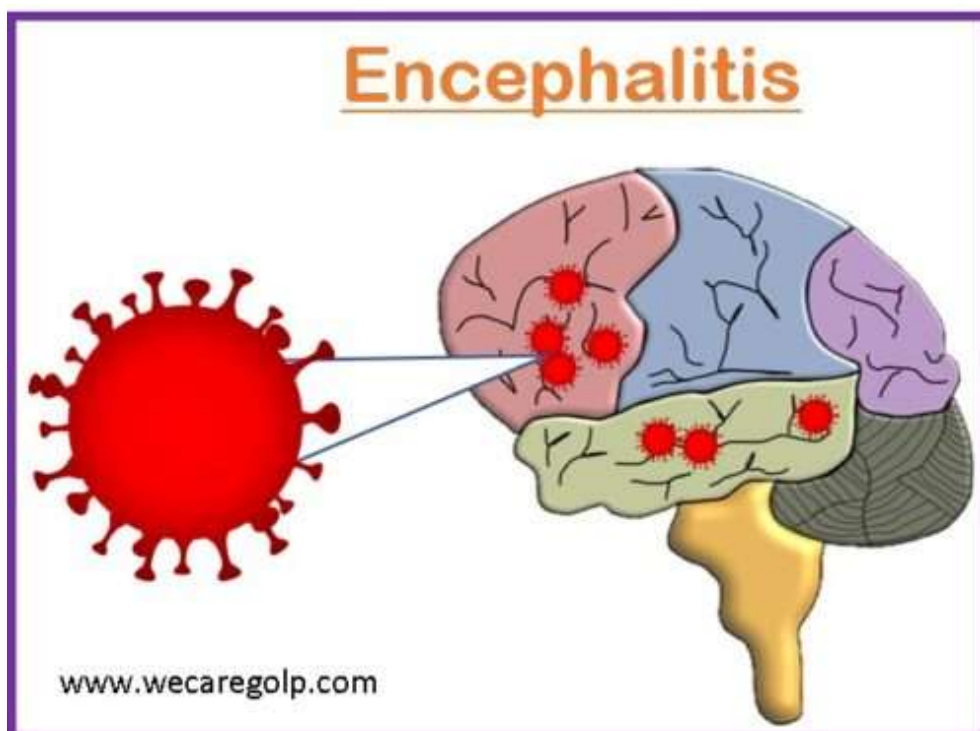
Clinical Symptoms

Initial Stage Symptoms

- **Fever:** High fever is a common initial symptom.
- **Headache:** Severe headaches often accompany the fever.
- **Fatigue:** General fatigue and weakness are common.
- **Body Aches:** Muscle aches and joint pain can be present.
- **Vomiting:** Nausea and vomiting are frequent symptoms.
- **Convulsions:** Seizures or convulsions may occur ^[16].

Progressive Stage Symptoms

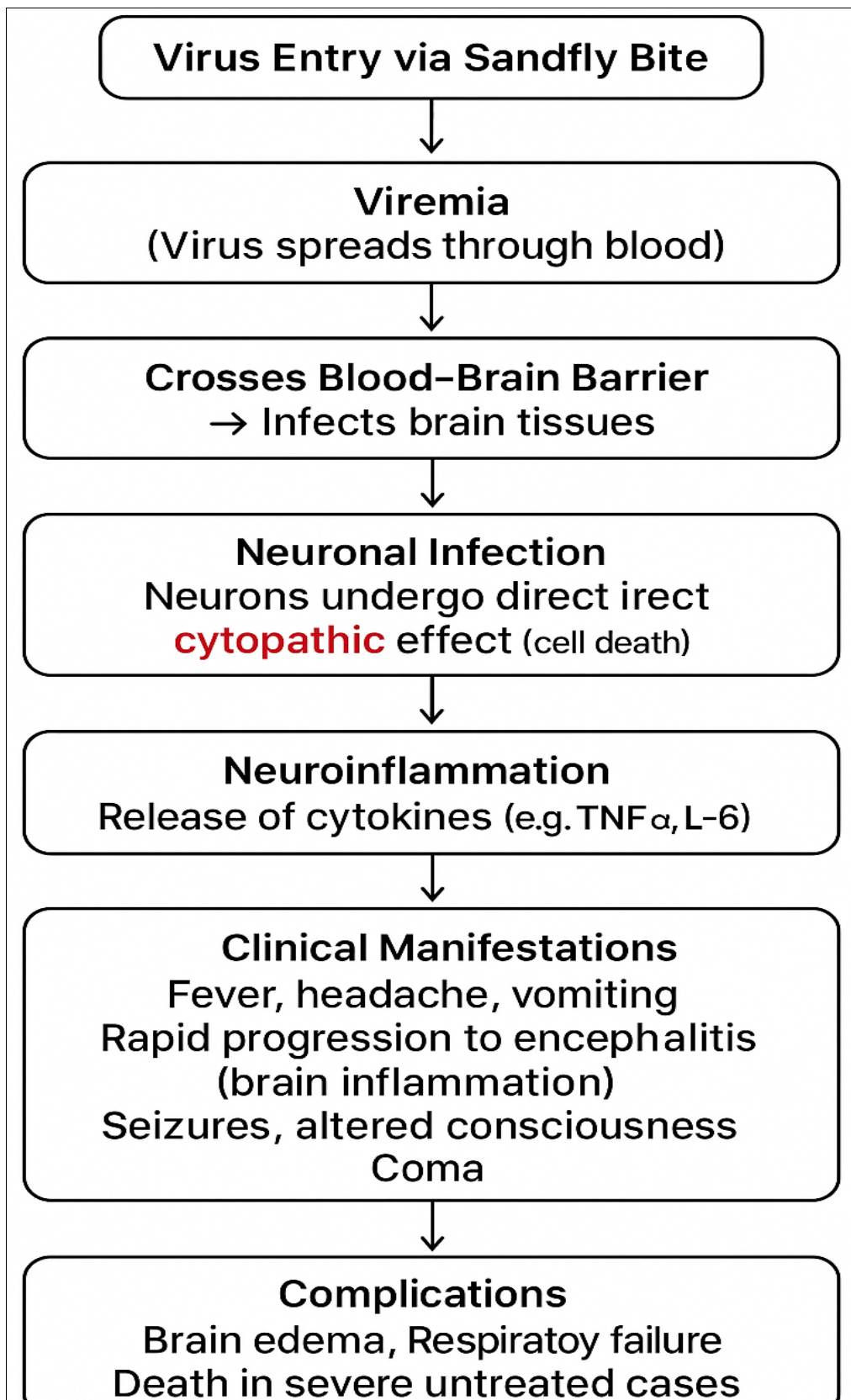
- **Altered Mental Status:** Confusion, irritability, or altered consciousness can develop.
- **Encephalitis:** Inflammation of the brain tissue, leading to severe neurological complications.
- **Neurological Deficits:** Inability to speak, loss of balance, vision changes, and other neurological impairments.
- **Meningeal Irritation:** Symptoms like neck stiffness, photophobia (sensitivity to light), and seizures may indicate meningeal irritation.
- **Coma:** In severe cases, the patient may progress to a state of coma.
- **Death:** Untreated encephalitis syndrome can have a high case-fatality rate ^[17].



Progression and Severity

Symptoms can progress rapidly, sometimes from initial symptoms to coma and death within 48-72 hours. The case-

fatality rate in outbreaks has been reported to be 56%-75%. Chandipura virus infections primarily affect children under 15 years of age ^[18, 19].

Pathogenesis ^[20-22]**Latest Case Study**

In 2024, a significant outbreak of Chandipura virus (CHPV) occurred in Gujarat, with 61 confirmed cases reported,

primarily affecting children under 15 years old ^[23]. One of the witnessed persons a resident of Vavdi village, Mandvi Mandal, Kutch District, Gujarat, described the sudden onset

of symptoms in his 7-year-old nephew, who succumbed to the disease within 24 hours.

He stated, "My nephew was playing outside in the evening and by night, he had high fever and seizures. We rushed him

to the hospital, but he passed away the next day ^[24]. The outbreak resulted in a high case-fatality ratio, ranging from 56% to 75%, with most deaths occurring within 24-48 hours of symptom onset ^[23].



The symptoms of CHPV infection include sudden onset of high fever, seizures, altered sensorium, diarrhea and vomiting followed by death in most cases ^[25]. Phlebotomine sandflies are the primary vectors of CHPV, and their predominance in endemic areas has been linked to the spread of the virus ^[26].

The Gujarat government has taken measures to control the outbreak, including deployment of a National Joint Outbreak Response Team, vector control measures, and health awareness campaigns. The World Health Organization (WHO) has also provided guidance on vector control, protection against bites, and enhanced surveillance in high-risk areas ^[23].

Mode of Transmission

Chandipura virus (CHPV) is primarily transmitted through arthropod vectors. The most important vectors identified are sandflies, particularly species such as *Phlebotomus papatasi* and *Sergentomyia* spp. These sandflies acquire the virus while feeding on infected vertebrate hosts and subsequently transmit it to humans through bites ^[27].

Mosquitoes have also been implicated in the transmission cycle of CHPV. Studies have demonstrated the presence of the virus in species such as *Aedes aegypti* and *Culex* spp suggesting their role as secondary vectors, especially in regions where sandfly populations are low ^[28, 29]. The ability of mosquitoes to harbor the virus raises concern due to their widespread distribution and breeding habits, particularly in tropical environments ^[30].

Ticks have been proposed as additional potential vectors. Though definitive evidence is limited, detection of Chandipura viral RNA in tick species indicates that ticks could contribute to the virus's maintenance in nature ^[31].

However, more studies are needed to fully establish the role of ticks in CHPV transmission.

The natural cycle of CHPV involves an inter play between vectors and vertebrate hosts. Animals such as rodents and domestic animals may act as reservoirs, maintaining the virus in an enzootic cycle. When vector populations surge during monsoon seasons, the risk of human transmission increases significantly ^[32].

Human infection typically occurs when an infected vector introduces the virus into the bloodstream during feeding. Following an incubation period of about 1-5 days, clinical symptoms such as fever, vomiting, altered sensorium, and encephalitis may rapidly develop, particularly in young children ^[33].

Mode of Transmission of Chandipura Virus Environmental factors like temperature, rainfall, and humidity influence the breeding and abundance of vectors. For instance, sandfly activity is enhanced during humid, warm conditions, leading to seasonal peaks in virus transmission ^[34].

Overall, the mode of transmission of Chandipura virus centers around vector-borne transmission through sandflies, mosquitoes, and potentially ticks, amplified by ecological and climatic conditions that favour vector proliferation ^[35, 36].

Laboratory Diagnosis

• Molecular Diagnostic Assays for CHPV

The pediatric population below 15 years of age is affected by CHPV. The Patient's Critical health problem CHPE has features of high fatality and high morbidity from severe clinical features that arise within 24 to 30 hours ^[37]. Due to the extensive clinical features and multi system neurological

illness, serological diagnostic tests are of no value [38,39]. RT-PCR assays which have the capability of detecting 10-100 pfu/ml of the virus in human clinical specimens proves the virus is present in CSF as well as sera collected during the acute phase of illness [40]. Real-time one-step RT-PCR

assays show a direct proportional relationship for a wide range of viral RNA from 102-1 x 1010 Viral RNA copies. When healthy individuals' RNA from other viruses was used, specificity is found out to be 100% [41, 42].



• Serological Diagnosis Assay for CHPV

Using specific polyclonal antibodies, a CHPV IgM capture ELISA shows polyclonal antibodies inhibiting the specificity of the assay designed to detect anti-CHPV IgM antibodies in a patient's CSF and sera [43]. Monoclonal antibodies were generated and incorporated into an anti-CHPV IgM ELISA to enhance the sensitivity and rapidity of the test [44, 45]. Neutralizing antibodies directed at Chand's virus are assessed through the plaque reduction neutralization test (PRNT), which is deemed the 'gold standard' for these tests [46].

Prevention and Control

Chandipura virus (CHPV) is transmitted primarily through sand-flies, particularly *Phlebotomus* species. Effective vector control is crucial in reducing disease transmission. Measures include indoor residual spraying of insecticides such as DDT or synthetic pyrethroids, using insecticide-treated bed nets (ITNs), and promoting environmental sanitation like clearing vegetation around homes to eliminate sandfly breeding sites [47].

Active surveillance helps in the early detection of outbreaks. Monitoring sandfly populations and conducting laboratory tests for CHPV in endemic areas can assist in initiating timely control measures. Surveillance systems need to be strengthened, especially during peak sandfly activity periods [48].

Community-level health education and awareness programs are important for prevention. Educating residents about personal protection methods, such as using repellents containing DEET, wearing protective clothing, and sleeping under bed nets, can significantly lower the risk of infection [49].

In the event of an outbreak, rapid response measures must be taken. This includes quick case identification, vector control intensification, emergency spraying operations, and public warnings to reduce exposure risk [47]. Currently, there is no licensed vaccine for Chandipura virus.

However, vaccine research is ongoing. Development focuses on creating recombinant vaccines and inactivated virus vaccines, but they are still in experimental stages [50].

Drug treatment for Chandipura virus

Currently, there is no specific antiviral drug approved for the treatment of Chandipura virus (CHPV) infection. Management is mainly supportive, aimed at relieving symptoms and preventing complications such as seizures and respiratory distress [51].

Supportive care includes the use of antipyretics like paracetamol to control fever, anticonvulsants such as phenytoin or phenobarbital for seizure management, oxygen therapy for respiratory complications, and intravenous fluids to maintain hydration and electrolyte balance [52].

Some experimental treatments have been explored. Ribavirin, a broad-spectrum antiviral, has shown limited inhibitory activity against Chandipura virus in laboratory (in vitro) studies. However, its clinical efficacy in humans has not been proven yet [53].

Monoclonal antibody therapy is under investigation. Preclinical studies suggest that neutralizing monoclonal antibodies targeting the glycoproteins of Chandipura virus could potentially provide therapeutic benefit, but this approach is still in the experimental phase [54].

Additionally, RNA interference (RNAi) approaches targeting Chandipura virus genes have shown promising results in laboratory models, indicating that gene-silencing therapies could emerge in the future. However, these are not yet available for clinical use [55].

Due to the absence of specific treatments, early detection and intensive supportive management remain the mainstay of improving survival in Chandipura virus infections [52].

Conclusion

Chandipura virus is a rare but serious virus primarily transmitted by sand-flies, causing acute encephalitis, especially in children. It has led to outbreaks with high

fatality rates in parts of India. Early detection, vector control, and public awareness are key to preventing its spread and reducing its impact.

Conflict of Interest

Not available

Financial Support

Not available

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