Review Article

A REVIEW ON CHANDIPURA VIRUS: OUTBREAKS AND EMERGING INFECTIOUS DISEASE FOR CHILDREN IN INDIA

ABSTRACT:
Chandipura virus, also known as Chandipura vesicular virus is a rare and poorly understood virus belonging to the family Rhabdoviridae. The virus mostly affects children and is known to cause very painful and sometimes fatal brain inflammation. Chandipur disease is a disease caused by infected sandflies. The symptoms include sudden onset of fever, brain changes and seizures, often leading to encephalitis. The rapid growth and high mortality of Chandipur disease constitute a major public health problem. Diagnosing Chandipura virus infection in children involves a combination of clinical assessment and laboratory tests. Diagnostic confirmation relies on laboratory tests such as polymerase chain reaction (PCR) to detect viral RNA, and serological assays to identify specific antibodies against the virus. In some cases, viral isolation from blood or cerebrospinal fluid may be performed. Treatment for Chandipura virus infection is primarily supportive, as there are no specific antiviral therapies available. This includes fever management with antipyretics, ensuring adequate hydration, and providing supportive care for neurological symptoms such as seizures or encephalitis. In severe cases, hospitalization may be required for close monitoring and advanced supportive measures. Preventative measures, such as reducing sandfly exposure through the use of insect repellent and protective clothing, are crucial in endemic areas to reduce the risk of infection. Public health programs should focus on promoting environmental control measures to reduce sandfly populations, such as proper waste management and eliminating standing water.

KEY WORDS: Children; Virus; Encephalitis; Sand fly; Fever; Region

Fig 1- graphical abstract

INTRODUCTION:

In recently, Chandipura virus (CHPV) has emerged as an encephalitis virus and has been associated with many outbreaks in many parts of India. Children under the age of 15 are most susceptible to infection. CHPV is emerging as a major encephalitis-causing virus in the Indian subcontinent. Serious disease caused by this virus has been reported in many parts of India (Garg et al., 2024; Sarkar et al., 2024).

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This virus was first discovered in 1965 by the National Institute of Virology, ICMR-Pune in the village of Chandipur in Nagpur district of Maharashtra, India. This virus has been associated with several outbreaks of unexplained encephalitis in Central India (Kitaura et al., 2023; Dey et al., 2019).

Between June and August 2003, 329 children were affected and 183 died in the Indian states of Andhra Pradesh and Maharashtra. In 2004, an unprecedented number of child cases and deaths were recorded in the state of Gujarat.

Chandipur disease is a disease caused by infected sandflies. It has occurred a lot, especially in children. The symptoms include sudden onset of fever, brain changes and seizures, often leading to encephalitis. The rapid growth and high mortality of Chandipur disease constitute a major public health problem.

OUTBREAK OF INFECTION:

Chandipura virus outbreaks are concerning because of their capability to motive distinct essential ailments, in particular in children and immunocompromised people. The virus is thought to motive neurological complications together with seizures and coma, posing challenges for treatment and manage (Sharma et al., 2021; Mourya et al., 2019). A month for the purpose that outbreak of Chandipura Acute Viral Encephalitis (CHPV) in Gujarat, the state has noted 137 patients with suspected CHPV, amongst whom fifty-one have tested positive result for the virus and also observed cases of Viral Encephalitis spreading to 24 of the 33 districts of the Gujrat, with deaths of 56 kids being recorded. Teams from the National Institute of Virology in Pune and the National Centre for Disease Control stayed put in the state “Conducting studies” to ascertain the nature and spread of the virus. While six sufferers of viral encephalitis are from Rajasthan, where children have died, four are from Madhya Pradesh, which has suggested one death. One case has been recorded in Maharashtra. Health Minister J P Nadda informed the Rajya Sabha, fifty-three presented occurrences of Chandipura virus, 61 cases have been detected in Gujarat and three have been detected in Rajasthan.

In a written reaction to a question, Nadda said that of those fifty-three occurrences of Chandipura virus, 19 persons have died and all deaths have been mentioned from Gujarat. In the meantime, the ultra-modern bulletin from the Gujarat authorities released, the quantity of Chandipura virus cases have reached upto 64. Between early June and 15 August 2024, the Ministry of Health and Family Welfare of the Government of India reported 245 cases of AES including 82 deaths (CFR 33%). A total of 43 districts in India are currently reporting AES cases. Cases are sporadically present across various districts as in previous outbreaks. Notably, there is a rise in CHPV outbreaks every four to five years in Gujarat state.

CHANDIPURA VIRUS VECTORS AND ITS TRANSMISSION:

The CHPV infection is primarily caused by the biting of the following:

- Sandflies
- Mosquitoes
- Ticks

The Chandipura virus (CHPV) is an arthropod-borne virus that belongs to the family Rhabdoviridae and the genus Vesiculovirus. CHPV has a distinctive bullet-shaped morphology, which is characteristic of the Rhabdoviridae family. This shape is similar to a bullet or a rod with rounded ends. The virus is approximately 150-200 nanometers in length and about 50-70 nanometers in diameter.

CHPV is an enveloped virus, meaning it has an outer lipid bilayer derived from the host cell membrane. This envelope is acquired as the virus buds from the host cell. Embedded in the lipid bilayer are glycoproteins (GP), which are essential for the virus's ability to attach to and enter host cells. These glycoproteins play a crucial role in the virus’s infectivity and are the main target for the host's immune response.

Inside the envelope, CHPV has a helical nucleocapsid. This consists of a single-stranded RNA (ssRNA) genome that is tightly coiled around nucleoproteins (N) to form a helical structure. The genome of CHPV is a single-stranded RNA of negative polarity. This means that the RNA cannot be directly translated into proteins and must be converted into a positive-sense RNA by an RNA-dependent RNA polymerase (RdRp) before it can

be translated. It has Structural Proteins-Nucleoprotein (N), Matrix Protein (M), Glycoprotein (G) and Non-Structural Proteins-RNA Polymerase (L), Phosphoprotein (P).

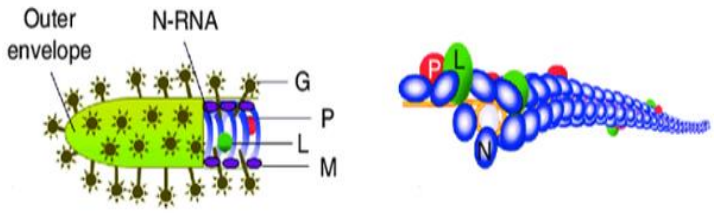

Fig 2- Chandipura virus and its helical nucleocapsid

Near residence, the authority found the presence of sandflies – the primary vector believed to be of CHPV transmission, particularly species of the genus Phlebotomus (Phlebotomus papatasi, Phlebotomus argentipes or Sergentomyia spp.). These tiny, blood-sucking insects are prevalent in tropical and subtropical regions. "Sandflies are known to be the main vectors for this virus. t is transmitted by sandflies and mosquitoes, including Aedes aegypti, which is also a vector for dengue. The virus resides in the salivary glands of these insects and can be transmitted to humans. Most of the cases are from north Gujarat, where the dry temperature is favorable for the breeding of sandflies. They are found in cracks of walls where they breed and lay their eggs and in mud houses," Dr. Pradeip Umarigar, health officer, Surat Municipal Corporation, told HT (Hindustan times).

Pathogenesis of Infection

The pathogenesis of Chandipura virus (CHPV) involves several key stages, from entry into the host to replication and the resultant clinical disease. Here's a detailed overview of how CHPV causes disease:

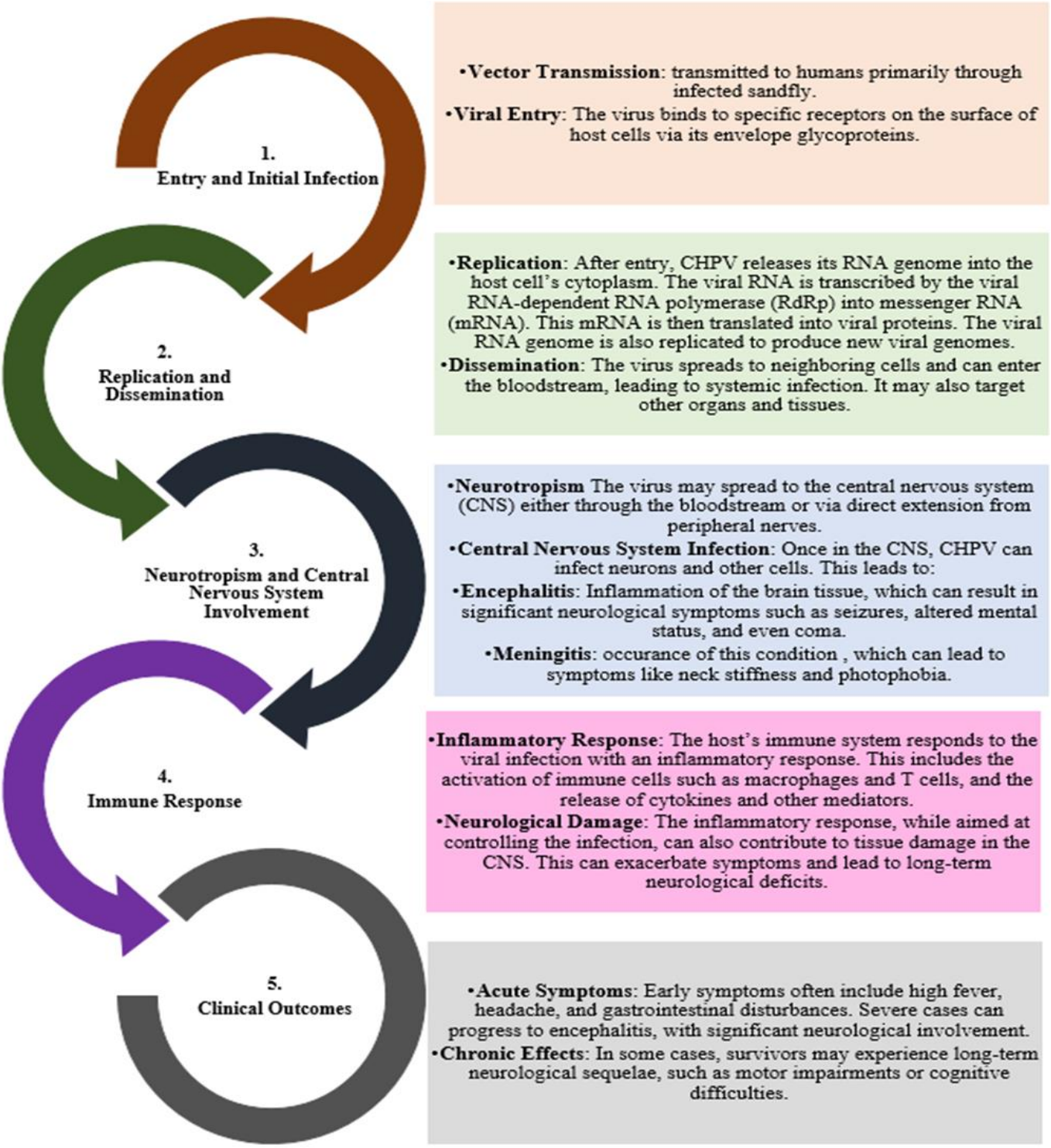

Fig 3- Detailed overview of how CHPV causes disease

CLINICAL FEATURES AND SYMPTOMS:

Chandipura virus (CHPV) infection can manifest with a range of clinical features and symptoms, often affecting the central nervous system. Here's a detailed overview of the clinical presentation of CHPV infection:

1. **Incubation Period**
    - Typical Duration: The incubation period for CHPV is generally between 2 to 14 days after exposure to the virus through mosquito bites.

2. **Initial Symptoms**
    - Fever: One of the earliest symptoms is a high fever, which can be sudden and may last for several days.
    - Headache: Severe headaches are common and can be quite debilitating.
    - Body Aches: General body aches and malaise are also frequently reported.
3. **Neurological Symptoms**
    - Seizures: Neurological involvement can lead to seizures, which are a significant clinical feature of severe CHPV infection.
    - Altered Mental Status: Patients may experience confusion, drowsiness, or agitation. In severe cases, there may be loss of consciousness or coma.
    - Meningeal Signs: Symptoms such as neck stiffness and photophobia (sensitivity to light) can indicate meningitis.
4. **Gastrointestinal Symptoms**
    - Nausea and Vomiting: These can occur alongside other symptoms, especially in the initial stages of the illness.
5. **Other Symptoms**
    - Rash: Some patients may develop a rash, although this is less common.
    - Weakness: Generalized weakness or paralysis can occur in severe cases.
6. **Severe Manifestations**
    - Encephalitis: In severe cases, CHPV infection can lead to encephalitis, which is an inflammation of the brain. This can result in significant neurological impairment and is associated with a higher risk of complications or death.
    - Severe Neurological Damage: Long-term neurological sequelae may occur, such as motor deficits or cognitive impairments, especially in severe or untreated cases.

DIAGNOSIS OF CHANDIPURA VIRUS (CHPV) INFECTION:

Clinical Diagnosis:

- Symptoms Review: Clinical diagnosis often starts with a review of symptoms, particularly in regions where CHPV is known to be endemic. Key symptoms include high fever, headache, nausea, vomiting, seizures, and neurological signs such as altered mental status.
- Neurological Symptoms: In severe cases, signs of encephalitis or meningitis, such as neck stiffness and photophobia, may be present.

Laboratory Diagnosis:

- Serology: Detection of specific antibodies (IgM and IgG) against CHPV in the blood can confirm infection. IgM antibodies are typically detectable in the early stages, while IgG indicates a past infection.
- Polymerase Chain Reaction (PCR): PCR tests can detect CHPV RNA in blood, cerebrospinal fluid (CSF), or tissue samples. This method is highly sensitive and specific for confirming the presence of the virus.
- Cerebrospinal Fluid (CSF) Analysis: In cases of suspected encephalitis or meningitis, CSF analysis may show elevated protein levels, normal glucose levels, and an increased white blood cell count. PCR can be performed on CSF for more precise diagnosis.
- Virus Isolation: Although less commonly used due to the need for specialized facilities, virus isolation from clinical samples can confirm the presence of CHPV.

Imaging Studies:

- Neuroimaging: Techniques such as MRI or CT scans can be used to assess the extent of neurological damage and to rule out other causes of neurological symptoms.

TREATMENT OF CHANDIPURA VIRUS (CHPV) INFECTION:

Supportive Care:

- Hydration and Nutrition: Ensuring adequate fluid intake and nutrition is essential to support the patient's overall health.
- Antipyretics: Medications like acetaminophen or ibuprofen can help manage fever and provide symptomatic relief.
- Seizure Management: Antiepileptic drugs may be used to control seizures, especially in patients with severe neurological symptoms.
- Monitoring: Close monitoring in a hospital setting may be required for severe cases, particularly for managing neurological symptoms and complications.

Experimental Treatments:

- Antiviral Agents: There are no specific antiviral treatments approved for CHPV. Research into antiviral drugs and therapeutic approaches is ongoing.
- Clinical Trials: Patients may be eligible for experimental treatments or clinical trials, which should be considered under the guidance of healthcare professionals.

PREVENTION OF CHANDIPURA VIRUS (CHPV) INFECTION:

1. Vector Control:

- Eliminate Breeding Sites: Reducing mosquito populations by eliminating standing water in containers, tires, and other potential breeding sites.
- Use of Insecticides: Applying insecticides to control mosquito larvae and adult mosquitoes in areas where CHPV is known to be active.
- Environmental Management: Improving sanitation and waste management to reduce mosquito breeding habitats.

2. Personal Protection:

- Insect Repellents: Using repellents containing DEET, picaridin, or other effective ingredients on exposed skin and clothing.
- Protective Clothing: Wearing long-sleeved shirts and long pants, especially during peak mosquito activity periods (dawn and dusk).
- Mosquito Nets: Sleeping under mosquito nets, particularly in endemic areas, to prevent mosquito bites.

3. Community Education:

- Awareness Programs: Educating communities about the risks of CHPV and the importance of mosquito bite prevention can help reduce transmission.
- Health Campaigns: Public health campaigns can inform people about preventive measures and symptoms of CHPV infection.

4. Surveillance and Monitoring:

- Monitoring Mosquito Populations: Regular monitoring of mosquito populations and CHPV activity can help in early detection and control of outbreaks.
- Early Detection: Surveillance systems can aid in the early identification of CHPV cases and prompt public health responses.

PUBLIC HEALTH AND AWARENESS:

Promoting public awareness of Chandipura disease is important for effective prevention and control. Health professionals and community organizations play an important role in educating the public about risk and prevention.

- ✓ Community Education Program:

- Conduct workshops and meetings in affected areas
- Provide informational materials to be distributed

✓ Educate physicians:
- Update physicians' knowledge on CHPV diagnosis and management
- Improve surveillance and reporting systems

✓ Media Collaboration:
- Work with local media to spread the right message
- Use social media to spread the word

✓ School Programs:
- Educating children and youth about infectious diseases
- Promoting hygiene and preventive measures

✓ Work with local leaders:
- Involve community leaders in spreading awareness
- Incorporate local knowledge and practices into strategy blocks

By knowing and understanding Chandipura disease, the community can better protect themselves and contribute to overall community health.

CHALLENGES WITH CHANDIPURA VIRUS IN INDIA

Chandipura virus is a significant concern in India due to its impact on public health. This virus, which belongs to the Vesiculo virus genus in the Rhabdoviridae family, primarily affects children and can cause severe neurological complications. It poses significant challenges in India, particularly in the states of Maharashtra, Gujarat, and Madhya Pradesh.

Here are some key challenges associated with this virus:

1. Geographical Distribution: Chandipura virus is primarily found in specific regions of India. Its localized nature means that outbreaks can be highly concentrated, making targeted public health interventions crucial but also complex.
2. Surveillance and Detection: Early detection of Chandipura virus is challenging due to the lack of widespread surveillance systems. The symptoms, which can include fever, headache, and encephalitis, are often non-specific and can be mistaken for other diseases, complicating diagnosis and control efforts.
3. Lack of Vaccine: As of now, there is no specific vaccine available for Chandipura virus, which means that prevention relies heavily on mosquito control measures and public awareness.
4. Public Awareness and Education: There is a need for increased public awareness about the virus and its transmission. Educating communities about prevention methods and recognizing symptoms can help in early detection and reducing transmission.
5. Vector Control: The virus is transmitted by mosquitoes, primarily the Culex species. Effective vector control measures are essential but can be challenging to implement consistently across affected areas due to factors such as climate, population density, and environmental conditions.
6. Healthcare Infrastructure: In regions where the Chandipura virus is prevalent, healthcare infrastructure may be under strain. Limited resources can delay effective diagnosis, treatment, and management of cases, leading to higher morbidity and mortality rates.
7. Research and Development: There is a need for more research to better understand the virus, its transmission dynamics, and potential vaccines or treatments. Limited research funding and infrastructure can slow progress in these areas.
8. Epidemiological Surveillance: Effective surveillance systems are necessary to track and monitor the spread of the virus. Inadequate surveillance can lead to delayed responses and uncontrolled outbreaks.

DISCUSSION

The Chandipura virus represents a significant emerging infectious disease in India, particularly for children. With the virus causing severe neurological disease and having a high mortality rate, the impact on public health is profound. However, the control of CHPV is complicated by factors such as inadequate healthcare

infrastructure, limited access to diagnostic tools, and challenges in vector control. The future of managing CHPV lies in improving surveillance, strengthening healthcare systems, investing in research for vaccines and treatments, and educating communities about prevention. A multi-pronged approach involving government, healthcare providers, and communities will be essential to reducing the burden of this disease in India and preventing future outbreaks.

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