Unravelling Chandipura Virus: A Growing Concern in Neurotropic Infections

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Abstract:

Chandipura virus (CHPV) is a highly virulent and neurotropic pathogen that has caused significant outbreaks in India, resulting in high mortality rates, particularly among children. The virus is primarily transmitted through the bite of infected sand flies, and its rapid progression and high mortality rate make diagnosis and treatment challenging. While some progress has been made in developing diagnostic tools and vaccine candidates, further research is needed to understand the epidemiology, transmission, and pathogenesis of CHPV. Effective vector control measures, antiviral therapies, and vaccines are crucial to preventing and controlling CHPV outbreaks. Continued efforts are necessary to address the ongoing threat posed by this deadly virus.

Keywords: Chandipura virus (CHPV), Encephalitis, Sand flies, Vector control.

1. Introduction:

Chandipura virus (CHPV) emerges as new global public health concern outbreaks and improved surveillance is required immediately. In July 2024, cases of acute Encephalitis were reported from children from Gujarat, India and on further investigation CHPV causes this disorder. Those who have CHPV will have a fast-growing sort of acute encephalitis caused by this virus, which causes high fevers, severe headache, intense fatigue, vomiting, and convulsions; more than 50% of patients die [1]. Cytokine overproduction causes immune dysfunction that has produced the neurological output:a result of CHPV. Death usually occurs 24–48 h after the appearance of symptoms [1].

1.1. Chandipura Virus: Discovery and Epidemiology: Chandipura virus (CHPV) is a member of the genus Vesiculovirus in the family Rhabdoviridae. family [2], and its first isolation in India was at National Institute of Virology (NIV) in Pune in 1965 In Chandipura village in Maharashtra, the virus was by chance discovered when Researchers studying febrile illnesses first thought it was dengue or chikungunya as causes [3]. A large outbreak of CHPV caused 300 paediatric deaths in 2003 in Maharashtra and Andhra Pradesh. Though CHPV is still endemic in the region, the number of cases observed [2], has substantially decreased since the 2003-2004 outbreaks.

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1.2. Recent Outbreak and Ongoing Research on CHPV: Chandipura virus (CHPV) Following its first confirmed case in 2024 on July 14, over 20 suspected encephalitis associated deaths were reported in Gujarat [4], as well as in Rajasthan [5]. The NIV, the main referral centre, received samples from 70 cases of encephalitis, of which 14 tested positive for CHPV. Phylogenetic analysis suggests that CHPV transmission is generally via infected sand fly (mostly Phlebotomus papatasi) bites [6] and perhaps sexually through male sand flies [7]. While not infected with Leishmania, sand flies of the genus Sergentomyia that are common to endemic areas [5] have also been identified as hospitable to the L. infantum virus [8]. Although pigs, buffaloes and cattle exhibit serological signs of exposure to CHPV, the virus has not been directly detected in these animals [9]. Consequently, the complete transmission regime of CHPV is not fully elucidated. Polymerase chain reaction (PCR) allows for the detection of the virus in throat swabs, serum, and cerebrospinal fluid (CSF) [1], while it can be isolated from multiple cell lines, including Vero, MDCK, and RD [1]. More studies are needed to better understand the epidemiology, transmission, and pathogenesis of CHPV. Understanding will be crucial to the generation of diagnostics, therapeutics and control strategies to Figureht this menacing pathogen.

2. Geographic Spread of CHPV:

Since its Following its first identification in 1965, the outbreaks of the Chandipura virus (CHPV) have been limited geographically to Central India froom Figure 1, including Gujarat, Madhya Pradesh, Andhra, and Maharashtra. Nevertheless, previous examples of these types of cases were noted in areas such as Nagpur (Maharashtra), Muzaffarpur (Bihar), Warangal (now Telangana), and Vadodara (Gujarat) much before 1950 [10]. CHPV has also been detected outside India, first described in West Africa from where the virus was isolated from a hedgehog in Nigeria and wild-caught sandflies in Senegal [11,12]. In monkeys in Sri Lanka, CHPV antibodies have also been found [12]. As it has also been reported in sandflies in Nigeria and Senegal [12,13], the geographic extent of the virus may go beyond India, as it has also been identified in sandflies from Senegal and Nigeria [13,14].

Since its identification in 1965, the focus of CHPV outbreaks has remained in Concentrated in central India (including Gujarat, Madhya Pradesh and Maharashtra. However, earlier cases of the same kind were reported. In locations like Nagpur (Maharashtra), Muzaffarpur (Bihar), Warangal (now Telangana) and Vadodara (Gujarat) even before 1950 [10]. Outside India CHPV has been reported from West Africa since 1975 (the virus was isolated from a hedgehog in Nigeria) and Wild-caught sandflies in Senegal [11,12]. Additionally, in Sri Lanka, CHPV antibodies were detected in monkeys [12]. The virus's geographic range may extend further than India, as it has also been identified in sandflies from Senegal and Nigeria [13,14].

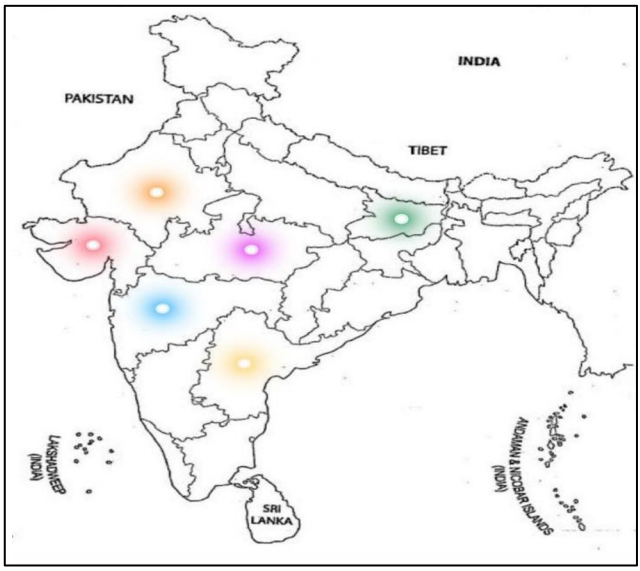

Figure 1: Spread of virus across India

3. CHPV Transmission and Vector Dynamics:

Transmission of Chandipura virus (CHPV) is mostly associated with sandflies, and the species Phlebotomus papatasi of the genus Phlebotomus is responsible for the virus [15]. Studies have shown that Phlebotomus papatasi can both multiply the virus and transmit it through vertical, venereal, and horizontal transmission pathways [16]. As the ling and subsequent investigations established Phlebotomus species were primarily responsible for CHPV transmission in India, whereas, potential virus hosts in Africa were the Sergentomyia species [17]. Additionally, CHPV can be transmitted by the venereal route, indicating that male sandflies may be a critical factor in maintaining the specific wild circulation of CHPV. CHPV has also been isolated from the very common Sergentomyia genus in endemic regions [18]. Although there is no direct evidence of human-to-human transmission, presence of CHPV antibodies have been shown in several animals in endemic regions like pigs, goats, buffaloes, sheep, and cattle. This suggests that the virus may persist in animal reservoirs, potentially causing outbreaks when sandfly populations surge in favorable conditions. Additionally, Phlebotomus argentipus, a zoophilic sandfly species, has been shown to horizontally transmit CHPV to infant mice, further highlighting the complex transmission dynamics of the virus [19].

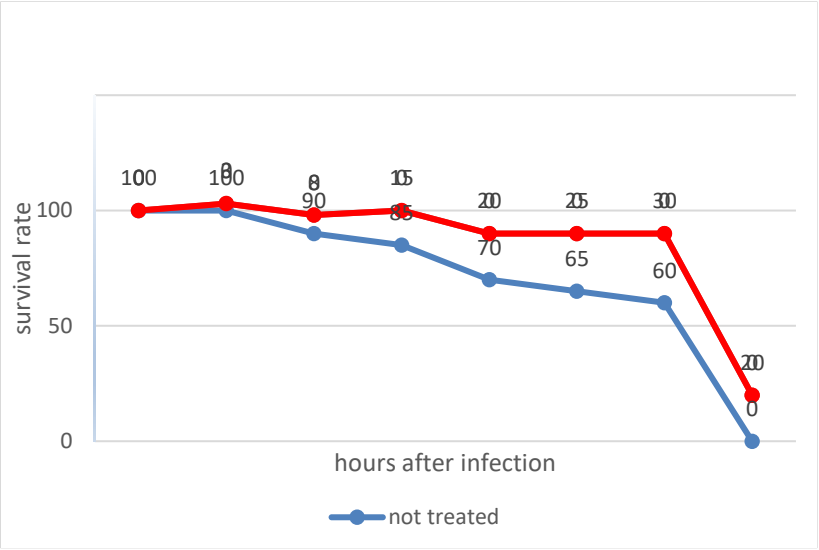

Figure 2: Evaluation of Chandipura virus in mice

Survival rate of virus-infected animal treated with the Nitric Oxide blocker, adenosineguainase. Young mice were infected with causative agent. A group of affected mice was treated with adenosineguainase. Untreated mice were used as a virus reference group. The treatment was given up to 100 hours post infection. Death rate was recorded up to 200 hours post infection. Survival rate was measured from Figure 2.

Table 1: Acute Encephalitis Syndrome (suspected Chandipura) state Gujarat

Gujarat				
S.No	**District Name**	**Suspected Cases**	**Confirm Cases**	**Death**
1	Sabarkantha	5	1	2
2	Aravali	4	1	3 (1 Confirmed)
3	Mahisagar	3	2	-
4	Kheda	2	1	-
5	Mehsana	2	1	1
6	Rajkot	2	1	2
7	Surendranagar	2	2	1
8	AMC	2	1	2
9	Gandhinagar	4	3	1
10	Panchmahal	2	2	-
11	Jamnagar	4	2	2
12	Morbi	5	4	2
13	GMC	2	1	-
	Total	41	22	16

Table 2: Acute Encephalitis Syndrome (suspected Chandipura) in India

S.No	State & District Name	Suspected Cases	Confirm Cases	Suspected Cases Death
1	Rajasthan - Udaipur	4	3	1
2	Mp – Dhar	5	2	2
3	AP	3	1	-
Total		54	28	19

From the Table 1, the data presents information on suspected and confirmed cases of Acute Encephalitis Syndrome (suspected Chandipura virus) in the state Gujarat and nearby states. In Gujarat, there are 41 suspected cases, out of which 22 are confirmed, and 16 are deaths which have been reported. The most affected districts include Morbi, Sabarkantha, Gandhinagar, and Jamnagar, each reporting multiple confirmed cases and fatalities.

From the Table 2, Other states like Rajasthan (Udaipur) and Madhya Pradesh (Dhar) have also reported cases, with Rajasthan having 4 suspected cases (3 confirmed, 1 death) and Madhya Pradesh reporting 5 suspected cases (2 confirmed, 2 deaths). Andhra Pradesh is mentioned but without specific numbers.

In total, across all regions, there are 54 suspected cases, 28 confirmed cases, and 19 deaths, indicating a high fatality rate and the need for immediate medical and preventive measures.

4. Advances in CHPV Diagnosis and Research:

Chandipura virus (CHPV) can be detected by polymerase chain reaction (PCR) from throat swabs, serum, and cerebrospinal fluid (CSF) [20]. Viral isolation can also be done in a laboratory, it can be isolated in Vero, Madin–Darby canine kidney (MDCK) and rhabdomyosarcoma (RD) cell cultures [20]. In clinical settings, traditional serological tests have very limited value in early diagnosis given the fast progression of the illness; however, some patients may have detectable IgM during the febrile stage. Notably, CHPV was verified by PCR testing in only 14 of 70 suspected acute encephalitis cases, illustrating the importance of accurate sampling and optimal time execution to increase diagnostic reliability. Additional studies are needed to improve diagnostic techniques and to assess effects of comorbidities on CHPV associated encephalitis. In recent years rapid growth has been made in improving diagnostic tools and developing measures for preventing against the virus [21].

4.1. CHPV Detection Through Advanced Diagnostic Techniques: Viral isolation in cell cultures and immunofluorescent antibody technique (IFA) based on detecting viral antigens have played a key role in the detection of Chandipura virus (CHPV). During the outbreak in 2003 in Andhra Pradesh, IFA was instrumental in demonstrating the existence of CHPV in brain tissue [22]. This first step was subsequently optimized to allow virus detection in cell culture infected with field samples. A study by Jadi et al. CHPV antigens are detectable by immunofluorescence assay (IFA) as early as two hours post inoculation and both sandfly and mosquito-derived cell lines present an efficient early detection system [23]. Additionally, cell culture-based diagnostic

methods have proven successful, as CHPV triggers specific cytopathic effects (CPE) in several vertebrate cell lines [24,25,26] which supports the virus's identification and isolation.

4.2. Molecular Diagnosis of CHPV: Considering the aggressive character of the CHPV that can kill children within 24-48 hours after appearing of the first symptoms, the need of rapid and accurate diagnostic devices has become essential. In response to this challenge, RT-PCR and real-time RT-PCR targeting human coronaviruses have undergone optimization for routine diagnostic use. The detection limit is 10-100 pfu/ml using a specific, highly sensitive RT-PCR assay targeting the N gene (527 bp) making it a reliable method for diagnosing both human and sandfly samples.

A significant advancement in the detection of CHPV was the development of a one-step real-time RT-PCR assay based on TaqMan technology that targets the virus's P gene. Comparatively, it has greatly improved the precision and speed of CHPV quantification in field samples. The assay was optimized using in vitro transcribed (IVT) RNA, and generating standard curves showed a strong linear correlation (r^2=0.99) across a broad detection range, with a maximum CV of 5.91% for IVT RNA. prominently, this method offers a detection limit when compared with nested RT-PCR and it has been proved to be more sensitive than traditional approaches, including infant mouse inoculation, embryonated egg culture, and standard cell culture techniques.

5. Current Status of CHPV Treatment and Vaccine Development:

As of now, there are no officially approved antiviral therapies for Chandipura virus (CHPV). Laboratory investigations have indicated that favipiravir [32] and ribavirin [33] exhibit antiviral activity against CHPV; however, their clinical efficacy has yet to be established. The development of therapeutics that not only inhibit viral replication but also mitigate immunopathological consequences, such as inflammation triggered by hyperketonaemia, could prove highly advantageous. Previously, scientists at the National Institute of Virology (NIV) in Pune, India, developed two vaccine candidates—an inactivated vaccine [34] and a recombinant protein-subunit vaccine targeting the envelope glycoprotein (G) [35]. Both vaccines successfully induced strong antibody responses and cell-mediated immunity, conferring complete protection against fatal CHPV infection in experimental mice. Despite these promising results, commercialization has not been pursued due to the virus's limited geographical spread and the relatively low number of reported cases.

6. CHPV Transmission and Vector Control Challenges:

Phlebotomine sandflies are the primary vectors responsible for transmitting CHPV, as demonstrated by repeated virus isolations and their ability to spread the virus through both transovarial and venereal transmission [36,37,38]. While insecticide application can substantially decrease sandfly populations, controlling these vectors in endemic areas remains challenging. Sandflies typically breed in moist environments, particularly in the crevices of construction stones, where insecticides are often ineffective. Furthermore, local residents frequently use cow dung to coat the floors and walls of their homes and store dried dung sheets for use as fodder. Research indicates that cow dung serves as a food source for sandfly larvae, contributing to the persistence of sandfly populations in these areas [39].

7. Conclusion:

A virulent, neurotropic pathogen, chandipura virus (CHPV) is the major causative agent of (outbreaks in India with high mortality, especially in children). It is transmitted through infected sand fly bites, and its rapid course and high mortality make it difficult to diagnose and treat. Diagnostic tools and vaccine candidates have been developed, but more research. Research is needed on CHPV epidemiology, transmission and pathogenesis. Effective vector control, antiviral therapies and vaccines are needed to prevent and control CHPV outbreaks we need to continue our efforts to tackle the threat of this virus.

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