International Journal of Science and Research Archive
eISSN: 2582-8185
Cross Ref DOI: 10.30574/ijsra
Journal homepage: https://ijsra.net/

(RESEARCH ARTICLE)

Check for updates

Chandipura virus: An emerging arboviral threat in india: Epidemiology, pathogenesis, and prospects for prevention

Harshal Arun Kothawade, Prakash Pannalal Muleva *, Gayatri Sadanand Nayak and Unmesh Gulabrao Bhamare

B. Pharm, Department of Pharmacy, GES's Sir Dr M.S. Gosavi college of pharmaceutical education and research, Maharashtra, India.

International Journal of Science and Research Archive, 2024, 13(02), 3798-3807

Publication history: Received on 16 November 2024; revised on 24 December 2024; accepted on 27 December 2024

Article DOI: https://doi.org/10.30574/ijsra.2024.13.2.2607

Abstract

Chandipura Virus (CHPV), belonging to the Rhabdoviridae family, is accountable for a sudden outbreak in rural regions of India. Primarily affecting children, it manifests as an influenza-like illness and neurologic dysfunction. The transmission is facilitated by vectors such as mosquitoes, ticks, and sandflies. The adopted method for diagnosing this virus involves an effective real-time one-step reverse-transcriptase PCR assay. The genome of CHPV is comprised of a negative-sense RNA and encodes five distinct proteins: N, P, M, G, and L. The vital function in the virus's life cycle is carried out by the P protein, whereas the M protein exhibits lethal characteristics. There is currently no specific treatment, and symptomatic relief entails the utilization of mannitol to decrease brain edema. The effectiveness of a Vero cell-based vaccine candidate against CHPV was efficiently evaluated as a preventive measure. Curbing the menace of CHPV involves containing disease-transmitting vectors, ensuring good nutrition, health, hygiene, and fostering awareness in rural areas. Hence, substantial preventive measures need to be implemented to control virus transmission until an effective anti-CHPV agent is developed.

Keywords: Chandipura Virus (CHPV); Rhabdoviridae; Arbovirus; Neurological Dysfunction; Vaccine Development; Vector Control

1. Introduction

During a febrile epidemic in Nagpur, Maharashtra, India in 1965, the Chandipura virus (CHPV) was first identified. CHPV is an infant of the Rhabdoviridae family and genus Vesiculovirus. Its genome is an 11-kilobase single-stranded RNA with negative polarity. Nucleocapsid (N), phosphoprotein (P), matrix protein (M), glycoprotein (G), and large structural protein (L) are the five structural proteins that the genome codes for. Vectors for the virus are sandflies, and antibodies to the CHPV virus have been observed in a variety of vertebrate species. The virus may infect both insect and vertebrate cells, and within 24 to 48 hours, it multiplies quickly enough to destroy entire cell sheets. Clinical manifestations include a high-grade fever, vomiting, seizures, altered sensorium, and a fast descent into a coma, which frequently ends in death in less than 48 hours.[1] Virus outbreaks are possible, despite their infrequent nature. AES is not routinely detected in laboratories, and there are still unanswered problems regarding the natural cycle, the involvement of domestic animals and small mammals, and the function of sandflies as the only vector. [2] Acceptance the natural cycle is essential for forecasting epidemics and designing interventions. This review outlines the progress made in the last ten years regarding CHPV research, with an emphasis on the virus's biology, epidemiology, diagnostics, and vaccination in light of the disease's increasing significance in India. An arthropod-borne virus (Arbovirus) endemic to India, the Chandipura virus (CHPV) infection is a relatively new and often disregarded deadly disease (Mondal et al., 2010). It is a member of the Vesiculovirus family, Rhabdoviridae. Although believed to be connected to dengue or chikungunya viruses, CHPV

* Corresponding author: Prakash Pannalal Muleva

was discovered in 1966 at the Virus Research Centre (VRC) in Pune by Bhatt and Rodriguez. The virus surfaced during an investigation of fever patients in Chandipura village, Nagpur district (Bhatt and Rodrigues, 1967).[3]

CHPV is classified as an arbovirus and belongs to a taxonomically diverse group of viruses that share identical routes of transmission with vertebrate hosts (Peiris et al., 2008). Arboviruses that cause encephalitis: Togavirideae (Alpha viruses), Flaviviridae, Bunyaviradeae, and Rehoviradeae are among the families of arboviruses that are primarily spread by mosquitoes, ticks, sand flies, and occasionally other insects. When CHPV transmission progresses to encephalitis, a diffuse or focal inflammatory process in the brain parenchyma, it presents influenza-like symptoms such as nausea, vomiting, altered awareness, and neurologic impairment (Peiris et al., 2008). The two main types of encephalitis pathology are infection-related and autoimmune-mediated. The former is caused by a virus that enters the central nervous system directly, while the latter is linked to a systemic infection or vaccination and is characterized by a pathological immune response that primarily targets myelin and affects the brain and spinal cord. Since there are currently no particular treatments for arbovirus-borne illnesses, symptomatic therapy is the accepted course of action (Domingues, 2009).[4] Figure 1 illustrates the structure of CHPV.

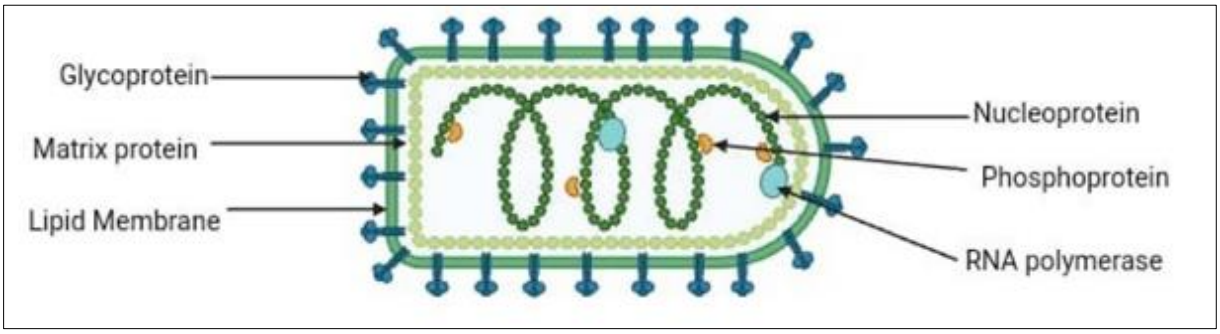

Figure 1 Structural illustration of CHPV

1.1. Pathogenesis

1.1.1. CHPV Infection in Laboratory Rodents (Mice & Rats)

After receiving a CHPV injection when they were 16 days old, the mice showed signs of hind limb paralysis on the fifth day after infection, which lasted until 7-8 PID before they recovered. Mice infected with CHPV showed ataxia, hyperesthesia, convulsions, quadriplegia, and death, although histological studies showed no alterations to any organs. Interestingly, throughout the post-infection period, notable histological changes were limited to the brain and spinal cord [1]. Two-week-old rats may be a good model to examine CHPV pathogenesis, host-virus interactions, and treatment development, according to previous studies. It was shown that chromatolysis, antigen localization, antigen detection, and neuronal degeneration occurred in Purkinje cells and choroid. The mechanism of neuronal death and the virus's pathway to the central nervous system are still unclear, despite the proven neuropathogenesis. Potential avenues of entrance include retrograde movement from olfactory or peripheral neurons, as well as cytokines and chemokines from peripheral infections that can cross the compromised blood-brain barrier. [5] The virus causes cellular stress and releases reactive oxygen species into neurons, which starts the process of neuronal death. Recent research points to microglial or death domain activation as potential pathways for virus-induced mortality.

1.1.2. Characterization and Phylogenetic Analysis of CHPV

To date, two isolates of CHPV have been found in Africa, and eight full genomes of the virus have been detected in India. These viral isolates are stable throughout a 47-year period, according to phylogenetic analysis (1965-2012). In comparison to the 1965 prototype, the percentage of nucleotide divergence in Indian CHPV genomes varied from 3.54 to 3.71.

African whole genome sequencing showed 5-6% more genetic difference from isolates from India, revealing separate evolutionary histories on the two continents. These results emphasize CHPV's autonomous evolutionary path throughout time.[6]

Bioinformatics Approach to Identify the Markers for Pathogenesis

In order to identify potential pathogenic factors, a comparison with other Rhabdoviruses was carried in order to search for potential hotspots in the full genomic sequence of CHPV. While sharing a cluster with the Isfahan virus, CHPV still

has functional reasons with other Rhabdoviruses. It is remarkable that the lining sequences of the M protein, which are essential for host protein interaction, are different from those of the prototype Vesiculovirus. Mutations in the G protein have been found to be in likely antigenic regions, whereas mutations in the N protein are linked to important N-N interactions and a potential T-cell epitope. P protein phosphorylation rates may be elevated due to a mutation in the Casein kinase II phosphorylation location. The goal of the virus's ongoing protein-protein interactions with host proteins is to understand how the virus alters host biological pathways in order to elude the immune system.[7]

Immunological Markers

Mice and humans have age-dependent sensitivity to CHPV infection, and considerable pro-inflammatory cytokine release has been seen in experimental mouse infections. B cells and monocytes both aid in the active replication of CHPV, and elevated cytokine and chemokine levels in monocytes may be a sign of pathogenicity and possible penetration into the central nervous system. Children who are recuperating have significant production of TNF-α, underscoring the significance of innate immunity in reacting to CHPV. Nitric oxide and pro-inflammatory cytokines are produced when TLR4 is activated during a CHPV infection, which aids in the pathogenesis. Young mice die despite the activation of their innate immune systems; [8] TLR4 mutant animals and wild-type mice treated with NO inhibitors show some protection. Early acute case identification of IL-2 implies a correlation with recovery. A notable decrease in CD4+, CD8+, and CD19+ cells has been observed in CHPV-infected mice, suggesting immune system control to avoid bystander host tissue damage. During an infection, regulatory cells—such as CD4+T regulatory cells that express PD-1—help to keep the body's equilibrium. Furthermore, it has been shown that CHPV infection triggers neuronal death by microglial activation.[9]

Approaches to Vaccine Developments

Mice immunized with a Vero cell-based inactivated CHPV vaccine showed good response, with effective protection after two doses and antibody titers ranging from 1:80 to 1:320 after the third treatment. Mice exposed to intracranial live virus challenges were shown to survive if their neutralizing antibody titers were higher than 1:20.[10]

Laboratory Transmission Experiments

Numerous studies have shown that arboviruses can spread venereously by arthropod vectors, which is a mechanism for horizontal transmission. Aedes aegypti lab tests verified CHPV transmission via both vertical and venereal routes, reporting a minimum infection rate of 1.2% in offspring and a venereal infection rate of 32.7% in female inseminated insects. Additional research on Phlebotomus papatasi revealed that 12.5% of uninfected female sand flies are infected with CHPV, which is spread by infected males to female sand flies during mating. [11,12] Figure 2 give the brief idea of life cycle of CHPV.

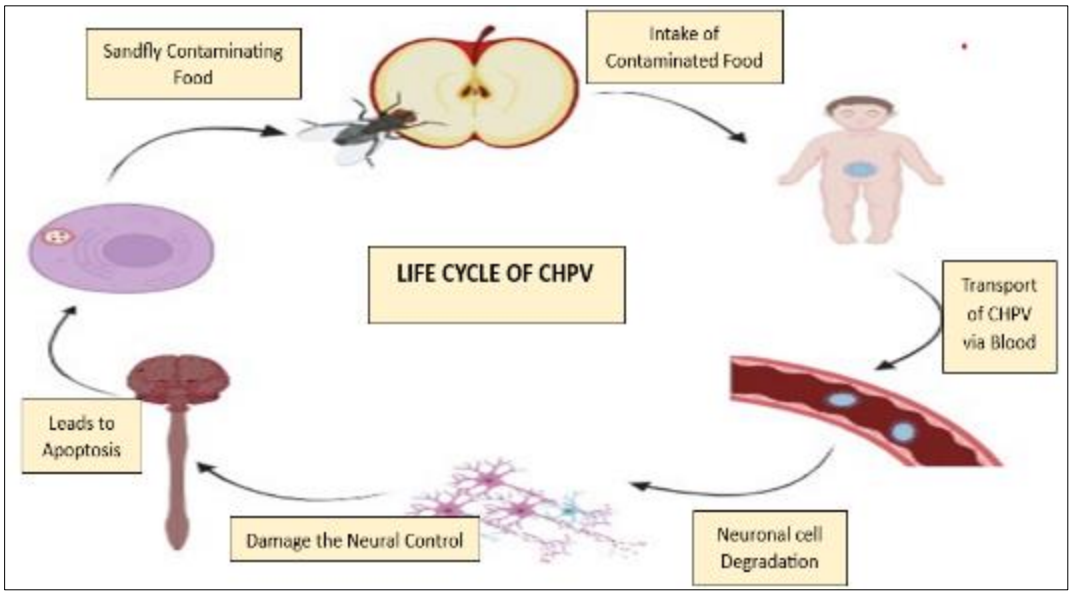

Figure 2 Life cycle of CHPV

2. Epidemiology

A new arbovirus called the Chandipura virus (CHPV) mostly affects youngsters in India and causes acute encephalitis syndrome (AES).

2.1. Important Epidemiological Aspects

- Geographic Distribution: Mainly indigenous to India, however occasional outbreaks have been documented in a few other locations.[13]
- Seasonality: There are certain times seasonal changes in the incidence of CHPV infections, with certain months having a higher incidence than others.
- Age Distribution: Children are most impacted, and younger age groups are more susceptible
- Transmission: Although the precise route of transmission is still being looked into, sandflies, ticks, and mosquitoes are thought to be the vectors.
- Clinical Manifestations: Fever, headaches, vomiting, and neurological symptoms, such as encephalitis, are the most common signs of CHPV infections. Mortality Rate: A significant number of cases end in death, especially in youngsters.
- Outbreaks: In India, CHPV has occasionally generated outbreaks that have significantly increased morbidity and mortality.[14]

189 of the 329 children in Andhra Pradesh and Maharashtra who tested positive for the virus in 2003 unfortunately lost their lives to it. There were 15 deaths and 52 positive cases in 2009. 2010 saw 16 deaths and 50 positive cases. There were three deaths and 110 positive cases between 2009 and 2011. In 2010, an epidemic in Gujarat's Panchmahal, Vadodara, and Kheda districts claimed the lives of 17 individuals. Because sandflies live in crevices in walls and in portions of mud or sand-built dwellings, their bites were held responsible for the outbreak. In Gujarat, there were isolated occurrences in 2014 and 2016. A girl from Ahmedabad passed away from the infection in 2016. A girl from Bhayli, Vadodara, passed away from the virus in 2019.[15]

In July 2024, there was an epidemic in Gujarat, India, primarily affecting children in the Sabarkantha area. Given the severity of the symptoms seen in those afflicted and the quick spread of the outbreak, serious public health concerns have been raised. There are still 48 possible deaths linked to the virus, while 38 verified deaths have been reported thus far. Given that vector-borne illnesses are still developing as a result of climate change and globalization, the importance of learning about and preparing for infections like CHPV cannot be overstated. Through the integration of ongoing scientific research with public health initiatives and community engagement, we may be able to mitigate the effects of CHPV and improve our preparedness for any future outbreaks.[16] Figure 3 represents the graphical presentation of CHPV.

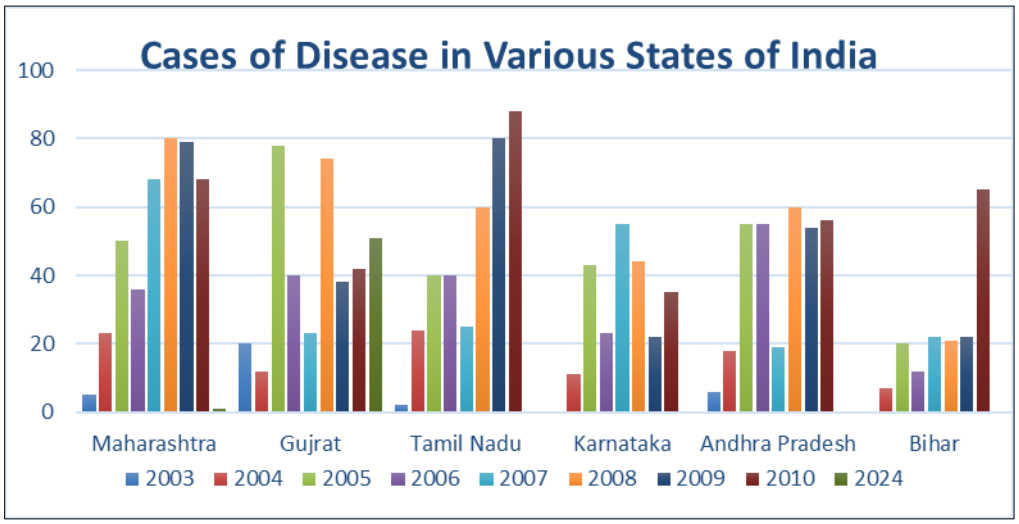

Figure 3 Graphical representation of Epidemiology of CHPV

3. Treatment

3.1. Based drugs and vaccines RNA

In Chandipura village, near Nagpur, Maharashtra, during an unidentified outbreak in 1996, the Chandipura virus was found. A virologist became aware of this virus between 2002 and 2004 after cases were reported in Andhra Pradesh, Maharashtra, and Gujarat. Since there are no particular antiviral medication for the therapy, the only option is to stop the vectors from delivering the Chandipura virus. Good health, appropriate sanitation, good hygiene, and nutrition all play a significant part in diminishing the chance of contracting the virus. The brain's microglial cells react to infections in the brain very fast. [17] This virus infection causes inflammation, stimulates microglial cells, and impairs brain function throughout the brain. High fever, vomiting, seizures, and other neurological disorders resembling those of encephalitis are among the symptoms; severely afflicted individuals may have comas or other grave consequences. The previously listed symptoms are categorized as acute encephalitis syndrome, or AES. The majority of AES cases are believed to be brought on by an infection with the Japanese Encephalitis virus (JEV) or bacterial meningitis. [18,19]

The study demonstrated how the Chandipura virus infection upregulates microRNA-21, which in turn reduces the expression of phosphatase and tensin homolog (PTEN) in cells and activates microglial cells in the infected person. As a result, human microglial cells exhibit enhanced activation of the nuclear factor kappa-light-chain enhancer of activated B cells (NF-kappa p65). The NF kappa B p65 activation triggers a response that aids in the accumulation of encephalitis-related symptoms.

A deadly encephalitis pandemic in the Indian subcontinent is known to be caused by a negative perspective single stranded RNA virus known as the Chandipura virus (CHPV). There are serious public health issues surrounding this virus, which has a preference for the pediatric population. There isn't a particular, effective medication for CHPV at the moment. In this work, pre-clinical antiviral assessment is used to assess a new CB -17 severe combined immunodeficiency (SCID) mouse model. The CHPV vaccination caused a fatal illness in the mouse. Increased viral load was discovered in a number of organs, including the brain, spinal cord, adrenal glands, and white blood cells, according to immunohistochemistry and plaque test results. Evaluation of favipiravir in the SCID mouse model. Treatment with favipiravir, both pre-symptomatic (5–14 days) and post-symptomatic (9–18 days), increased survival. When using favipiravir, lower virus loads were seen in brain tissue, kidney, or adrenal glands as well as WBC.[20]

Due to its distinct qualities and clinical effectiveness, Favipiravir has attracted a lot of interest and shown great promise in the battle against viral infections. The antiviral activity of Favipiravir against CHPV was assessed in the current study using the plaque reduction test and the viral growth kinetics assay in Vero cells. Additionally, the in vivo effect of medication therapy against fatal viral challenges was examined in 10-day-old CD1 mice. With an EC 50 of 92.26um, Vero cells treated with Favipiravir showed a dose-dependent decrease in the size and quantity of CHPV plaques. 50% cytotoxicity (CC50) at 4774um and complete suppression of CHPV reproduction at 320 um drug concentrations were noted, suggesting a high selectivity index at 51.24. When 300 mg/kg/day of Favipiravir was administered orally to mice until the seventh day post-infection, in vivo experiments revealed 100% survival. Evidence of Favipiravir's antiviral effectiveness against CHPV infection is presented in the study, and more research might reduce the related mortality.

The Baculovirus expression system was utilized to express the Glycoprotein gene (G- gene) of CHPV genome. After being purified using HPLC, the glycoprotein (rGp) was administered to mice in three dosages separated by four weeks. The ideal rGp was discovered to be one microgram. Anti-CHPV IgG antibodies were found as early as the second week, indicating sero-conversion. Antibody titres were depending on both immunogen and concentration. 90% protection was shown when the immunized mice were challenged intracerebrally with 100 LD (50) of the homologous strain. Immunized mice's antibodies were able to neutralize heterologous viruses in an in vitro neutralization procedure. In mice receiving the vaccination, T cell proliferation against rGp was found to be 60%. As demonstrated by the study, rGp induces both arms of the immune response and is a prime candidate for future testing as a vaccine.[21] Some of the common symptoms of CHPV are depicted in figure 4.

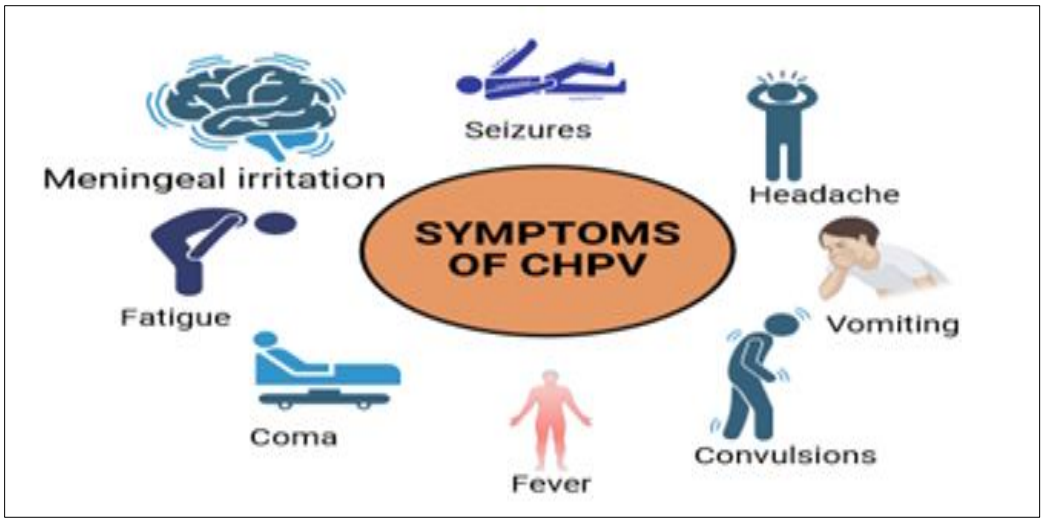

Figure 4 Symptoms of CHPV

3.2. Use of remdesivir, zidovudine (azt) and nevirapine drugs:

Ex vivo infection tests were carried out and examined to determine if the aforementioned medications have inhibitory effects on CHPV replication. These investigations involved the analysis of viral proteins and viral RNA transcripts from drug-treated and infected cells.[22]

3.2.1. Methodology

Drug treatment and virus infection

- Remdesivir, AZT, and Nevirapine at 1 Mm and 100 Mm concentrations were initially administered to Vero E6 cells. Subsequently, after two hours, cells were twice cleaned with PBS before being infected with CHPV at 0.005 Mol in serum-free DMED medium that included the same quantity of Remdesivir, AZT, and Nevirapine as before. The cells were taken out 24 hours after the therapy.[23]
- Half of collected cells had their proteins extracted, and these were subjected to Western blot analysis using anti-CHPV and anti-tubulin monoclonal antibodies
- The virus-containing supernatant was collected at -80°C and filtered using a Millipore 0.45um filtration unit. It was then utilized for Western blot analysis and the Plaque test.

3.2.2. Plaque assay

To see an example of Plaque cells were stained with crystal violet for two hours. The agarose layer was then either removed, washed, rinsed with water again, and the p value was ascertained.

3.2.3. Western blot analysis

An anti-CHPV N antibody was used to identify proteins that were deposited onto PDVF or nitrocellulose membranes from cell lysates or cell-free supernatant. Anti-beta tubulin antibody was also used to blot cell lysates, and the amounts of viral protein in drug-treated and untreated cells were compared.[24]

Vaccines for Chandipura virus

It was recently revealed that the evaluation and development of subunit vaccines achieved good immunogenicity in experimental animals. Additionally, one potential method of preventing CHPV is the development of an instigated vaccination against viruses based on tissue culture. [25]

Inactivated vaccines or killed virus vaccines

A BPL-inactivated vaccine was created using Vero E6 cells, and the immunogenicity of the vaccination in mice was examined and assessed. The investigation demonstrated that the vaccination effectively prevented mice from contracting CHPV and produced high antibody titers. and vaccination decided to use the Vero E6 cell line for large-scale virus multiplication because of its simplicity in downstream and management processing. [26] BPL, or B-propin lactone,

has grown to be a significant inactivating agent and is frequently utilized in the manufacturing of vaccines. BPL inactivated the purified viruses while preserving the immunogenicity and antigenicity of the viral proteins. Because the immunogenicity of inactivated vaccines is restricted, an adjuvant was added in order to increase the immunogenicity of the viral vaccine. The doses were planned, and the animals showed 100% seroconversion following the third dosage. Research had demonstrated that every immunized mouse with a 1:20 antibody titre survived intracerebrally acquired CHPV. A vaccination administered in two doses provided 100% protection in seroconverted mice. The vaccine candidate was determined to be promising; human clinical trials are still pending. [27]

Subunit vaccines or recombinant vaccines

The genome of CHPV encodes five polypeptides: G protein plays a crucial function as an antigenic determinant. The other four polypeptides are matrix protein M, glycoprotein G, nucleocapsid protein N, phosphoprotein P, and large protein L. G protein has been shown to have potential as a vaccine, based on research on its effects on the Rhabdoviridae family of viruses, which includes both the rabies and vesicular stomatitis viruses (VSV). Since the Baculovirus expression system was crucial in defending mice against intracerebral viral infections, the protein makes a great potential vaccination to prevent CHPV.[10] Four weeks apart, three doses resulted in 90% seroconversion and protected mice against live virus with 2 log 10 TCI 50/ml. ELISA and neutralizing antibody titres were 1:1200 and 1:320, respectively. Additionally, 60% of T cells proliferated in immunized mice. It was discovered that the recombinant G protein vaccines elicited a humoral as well as a cell-mediated immune response, which made them an excellent CHPV vaccine. Neutralizing antibodies were discovered two weeks following the first dosage, and the antibody response was found to be dose dependent. The DPT+CHPV combination produced a higher antibody response to CHPV than the CHPV vaccination alone, resulting in 90% to 100% sero-conversion and ELISA titres within the 1:1200 to 1:2400 range. A national vaccination program could effectively protect children in endemic areas, as the immunized mice demonstrated intracerebral viral survival. [28]

Antivirals

It was discovered that siRNA was a promising virus inhibitor that inhibited replication both in vitro and in vivo. The P and M proteins are important for the life cycle of viruses. Both control and siRNA-treated Vero cells showed a log reduction in viral titre. Compared to control mice, mice treated with siRNA delivered in combination showed delayed mortality. Showed a 4-log virus reduction in siRNA-treated mice compared to virus-only-inoculated mice. It was noted that anti-CHPV Ig G antibodies were not found in mice who survived on days 7, 14, and 21 after PI, indicating complete viral clearance.

3.3. Vector control

Insecticide spraying could quickly lower the population. Vectors in endemic locations are difficult to control because they breed in moist areas within the cracks and fissures of stone used in construction. Another common sight in endemic areas is cow dung smeared on walls and floors, where cow dung sheets are gathered and used as feed within homes. It was stated that the larvae of sand-fly larvae were fed cow manure.[29]

4. Advancements in diagnostics

4.1. Immunofluorescent antibody technique (ifa) and virus isolation using cell lines

In 2003, IFA had effectively used data that CHPV was present in brain tissues. IFA was also standardized to find CHPV in cell cultures had received a field sample injection. The use of cell culture techniques has been effective in isolating and detecting CHPV, leads to the distinctive CPE in vertebrate cell lines.

4.2. Diagnosis with molecular tools

Children's diseases progressed quickly, resulting in mortality within 24 to 48 hours, which made a prompt diagnosis necessary. Real-time transcriptase, or RT-PCR, and reverse transcriptase, or PCR, have been standardized for diagnosis. A very sensitive diagnostic RT-PCR targeting the N gene (527 bp) with a limit of 10 – 100 plaque forming units (pfu) had been developed for routine testing of human and sand fly samples. A significant development for the detection and measurement of CHPV from samples was the standardization and creation of one-step RT-PCR using TaqMan technology, which targets the P gene of CHPV. The detection limit was found to be on par with nested RT-PCR and to be more sensitive than convectional systems, which include cell culture, embryonated eggs, and baby mice.[26]

4.2.1. Prevention

This disease is transmitted by sandflies, which are difficult to treat since it is difficult to eradicate their breeding grounds. Sand-fly management can be accomplished by implementing the subsequent strategies:

- Pesticides: Use pesticides inside dwellings, in yards, and in dimly lit locations that have vegetation.
- Environmental Hygiene: Keep the area tidy and rid the yard of trash, waste and bushes. Household garbage must be disposed of properly, and breeding grounds, like as standing water, must be kept away from dwellings.
- Maintain a Safe Distance: Relocate animal shelters, including hen coops, from residential areas.[30]

5. Results

5.1. Remdesivir inhibits CHPV replication and virus production in VERO e6 cells

Vero E6 cells were cultured as monolayers with 1 Mm and 100um drug concentrations. Untreated cells (control samples). After 2 hours of medication treatment, cells became infected with CHPV. Later, at 24 hours post-infection, cells were examined under a microscope and the supernatants extracted. Drug-treated but uninfected cells were seen to be healthy, indicating that Remdesivir had no influence on the proliferation or shape of the cells. Drug-untreated cells displayed obvious cytopathic effects of CHPV and were rounded. Insinuating that the medication Remdesivir exhibits a notable inhibition of viral replication. Proteins from CHPV-infected cells were examined using western blot analysis to validate the results above about the treatment with 1 m AND 100 u Remdesivir. The number of N proteins in 1-millimeter Remdesivir-treated cells was significantly lower than that in 100 micrometer drug-treated cells, according to blotting with an anti-CHPV N antibody. The Plaque Assay verified the aforementioned findings and ascertained the quantity of virus particles generated in CHPV-infected Vero cells and supernatant, regardless of Remdesivir's presence or absence. observed a decrease in plaques in 1 Mm Remdesivir-treated cells as opposed to untreated cells.[25]

5.2. CHPV replication inhibited by AZT and nevirapine

The results of AZT and Nevirapine, two HIV-1 reverse transcriptase inhibitor medications, on infected CHPV Vero cells revealed that their inhibition was less than that of Remdesivir. When 1 Mm drug-treated and CHPV-infected cells were compared to drug-untreated and infected cells, no significant changes in cytopathic effects were seen. Compared to untreated cells, cell lysates from 1 Mm drug-treated and CHPV-infected cells had reduced quantities of CHPV N proteins. At 1 Mm concentrations of both AZT and Nevirapine, virus generation was similarly suppressed.[26]

6. Conclusion

The outbreak that occurred in 2003–2004 resulted in the loss of over 300 lives, making the Chhattisgarh virus (CHPV) a serious public health problem in Central India. Its significance in encephalitis or acute brain assaults is controversial, but the fact that CHPV is present in documented cases indicates that it has a role in epidemic brain attacks (EBA), which cause symptoms similar to encephalitis and quickly result in patient death. According to in vitro research, neuronal cells express more CHPV phosphoprotein, which causes apoptosis. Despite significant progress in diagnosis and prophylactic strategies, there are still unanswered questions about the inherent amplification mechanisms of the virus and the genetic components that contribute to high case fatality. Since an approved vaccination is still unobtainable despite advancements, virologists, neurologists, pediatricians, and the government must work together to address this persistent public health concern in Maharashtra and Andhra Pradesh.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

References

[1] Sapkal GN, Sawant PM, Mourya DT. Chandipura Viral Encephalitis: A Brief Review. Open Virol J. 2018 Aug 31;12:44-51.

[2] Jancarova M, Polanska N, Volf P, Dvorak V. The role of sand flies as vectors of viruses other than phleboviruses. J Gen Virol. 2023 Apr;104(4).

[3] Sudeep AB, Bondre VP, Gurav YK, Gokhale MD, Sapkal GN, Mavale MS, George RP, Mishra AC. Isolation of Chandipura virus (Vesiculovirus: Rhabdoviridae) from Sergentomyia species of sandflies from Nagpur, Maharashtra, India. Indian J Med Res. 2014 May;139(5):769-72.

[4] Qian Yang, Ben Wei,Risk factors of epilepsy secondary to viral encephalitis: A meta-analysis, Journal of Neuroimmunology,Volume 378,2023,578089,ISSN 0165-5728

[5] Loh HS, Mohd-Azmi ML, Sheikh-Omar AR, Zamri-Saad M, Tam YJ. Pathogenesis and antibody response to a cytomegalovirus infection in newborn rats. Acta Virol. 2007;51(1):27-33.

[6] Kao JH, Chen PJ, Hsiang SC, Chen W, Chen DS. Phylogenetic analysis of GB virus C: comparison of isolates from Africa, North America, and Taiwan. J Infect Dis. 1996 Aug;174(2):410-3.

[7] Verma AK, Ghosh S, Pradhan S, Basu A. Microglial activation induces neuronal death in Chandipura virus infection. Scientific reports. 2016 Mar 2;6(1):22544.

[8] Jonathan Cleaver, Katie Jeffery, Paul Klenerman, Ming Lim, Lahiru Handunnetthi, Sarosh R Irani, Adam Handel, The immunobiology of herpes simplex virus encephalitis and post-viral autoimmunity, *Brain*, Volume 147, Issue 4, April 2024, Pages 1130–1148

[9] R.S. Jadi, A.B. Sudeep, P.V. Barde, V.A. Arankalle, A.C. Mishra,Development of an inactivated candidate vaccine against Chandipura virus (Rhabdoviridae: Vesiculovirus),Vaccine,Volume 29, Issue 28,2011,Pages 4613-4617ISSN 0264-410X.

[10] Travieso T, Li J, Mahesh S, Mello JD, Blasi M. The use of viral vectors in vaccine development. npj Vaccines. 2022 Jul 4;7(1):75.

[11] Lequime S, Lambrechts L. Vertical transmission of arboviruses in mosquitoes: a historical perspective. Infection, Genetics and Evolution. 2014 Dec 1;28:681-90.

[12] Kuno G, Chang GJ. Biological transmission of arboviruses: reexamination of and new insights into components, mechanisms, and unique traits as well as their evolutionary trends. Clinical microbiology reviews. 2005 Oct;18(4):608-37.

[13] Rathore SK, Dwibedi B, Kar SK, Dixit S, Sabat J, Panda M. Viral aetiology and clinico-epidemiological features of acute encephalitis syndrome in eastern India. Epidemiology & Infection. 2014 Dec;142(12):2514-21.

[14] Asokan D, Bommu SP, Mall A, Pardeshi G. Geographic Distribution and Temporal Trends of Zika Virus Outbreaks in India (2016–2023): Insights From the Integrated Disease Surveillance Programme Data. Cureus. 2024 Aug 17;16(8):e67068.

[15] Rao BL, Basu A, Wairagkar NS, Gore MM, Arankalle VA, Thakare JP, Jadi RS, Rao KA, Mishra AC. A large outbreak of acute encephalitis with high fatality rate in children in Andhra Pradesh, India, in 2003, associated with Chandipura virus. The Lancet. 2004 Sep 4;364(9437):869-74.

[16] Adnan H, Ahmed M, Salomon IZ. Chandipura virus outbreak: a growing public health crisis that demands immediate action. Annals of Medicine and Surgery. 2024:10-97.

[17] Van Ranst M. Chandipura virus: an emerging human pathogen?. The Lancet. 2004 Sep 4;364(9437):821-2.

[18] Brisse ME, Ly H. Chandipura Virus Causing Large Viral Encephalitis Outbreaks in India. Pathogens. 2024 Dec 16;13(12):1110.

[19] Pandey, Neha & Rastogi, Meghana & Singh, Sunit. (2021). Chandipura virus dysregulates the expression of hsa-miR-21-5p to activate NF-κB in human microglial cells. Journal of Biomedical Science. 28. 52. 10.1186/s12929-021-00748-0.

[20] Garg R, Prasad AK, Agarwala P. Chandipura virus resurgence: Insights from Indian outbreaks and the path forward. Indian Journal of Medical Microbiology. 2024 Nov 1;52:100749.

[21] Pavitrakar DV, Bondre VP. Antiviral effect of Favipiravir against Chandipura virus in vitro and in vivo. Journal of Medical Virology. 2023 Jun;95(6):e28840.

[22] Basak S, Mondal A, Polley S, Mukhopadhyay S, Chattopadhyay D. Reviewing Chandipura: a vesiculovirus in human epidemics. Bioscience reports. 2007 Aug 6;27(4-5):275-98.

[23] Choy KT, Wong AY, Kaewpreedee P, Sia SF, Chen D, Hui KP, Chu DK, Chan MC, Cheung PP, Huang X, Peiris M. Remdesivir, lopinavir, emetine, and homoharringtonine inhibit SARS-CoV-2 replication in vitro. Antiviral research. 2020 Jun 1;178:104786.

[24] Shurtleff AC, Biggins JE, Keeney AE, Zumbrun EE, Bloomfield HA, Kuehne A, Audet JL, Alfson KJ, Griffiths A, Olinger GG, Bavari S. Standardization of the filovirus plaque assay for use in preclinical studies. Viruses. 2012 Dec 6;4(12):3511-30.

[25] Pruijssers AJ, George AS, Schäfer A, Leist SR, Gralinksi LE, Dinnon KH, Yount BL, Agostini ML, Stevens LJ, Chappell JD, Lu X. Remdesivir inhibits SARS-CoV-2 in human lung cells and chimeric SARS-CoV expressing the SARS-CoV-2 RNA polymerase in mice. Cell reports. 2020 Jul 21;32(3).

[26] Osborne CM, Langelier C, Kamm J, Williamson K, Ambroggio L, Reeder RW, Locandro C, Harris JK, Wagner BD, Maddux AB, Caldera S. Viral detection by reverse transcriptase polymerase chain reaction in upper respiratory tract and metagenomic RNA sequencing in lower respiratory tract in critically ill children with suspected lower respiratory tract infection. Pediatric Critical Care Medicine. 2024 Jan 1;25(1): e1-1.

[27] Pavel ST, Yetiskin H, Uygut MA, Aslan AF, Aydın G, İnan Ö, Kaplan B, Ozdarendeli A. Development of an inactivated vaccine against SARS CoV-2. Vaccines. 2021 Nov 2;9(11):1266.

[28] Heidary M, Kaviar VH, Shirani M, Ghanavati R, Motahar M, Sholeh M, Ghahramanpour H, Khoshnood S. A comprehensive review of the protein subunit vaccines against COVID-19. Frontiers in microbiology. 2022 Jul 14; 13: 927306.

[29] Qureshi A, Tantray VG, Kirmani AR, Ahangar AG. A review on current status of antiviral siRNA. Reviews in Medical Virology. 2018 Jul;28(4): e1976.

[30] Orshan, Laor & Szekely, David & Schnur, Heather & Wilamowski, Amos & Galer, Yosi & Bitton, Shimon & Schlein, Yosef. (2006). Attempt to control sandflies by insecticide-sprayed strips along the periphery of a village. Journal of vector ecology: journal of the Society for Vector Ecology. 31. 113-7. 10.3376/1081-1710(2006)31[113: ATCSFB]2.0.CO;2.