

# Chandipura Virus in India: A Systematic Review of Public Health Challenges, Evidence Gaps, and Future Priorities

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## ABSTRACT

**Background:** Chandipura virus (CHPV) is a re-emerging viral pathogen causing acute encephalitis syndrome (AES) in India, with reported case fatality rates of 33-70% primarily among children. Transmitted by sandflies and mosquitoes, CHPV remains inadequately studied despite recurrent outbreaks. This systematic review critically examines the literature on CHPV in India to identify public health challenges, assess evidence quality, and propose targeted interventions.

**Methods:** We systematically searched PubMed, Scopus, Web of Science, and Google Scholar (inception to January 2025) following PRISMA 2020 guidelines. Two reviewers independently screened, extracted data, and assessed study quality using JBI and AMSTAR 2 tools. Narrative synthesis was employed.

**Results:** Of 1,590 identified records, 25 studies met the inclusion criteria. Quality assessment revealed only 36% (n=9) were high-quality studies, predominantly outbreak investigations. Thematic analysis identified twelve interconnected challenges, with four critical gaps consistently reported across high-quality studies: (1) inadequate surveillance infrastructure delaying outbreak detection (documented in 8 states), (2) diagnostic limitations leading to misclassification with Japanese encephalitis and dengue, (3) absence of specific antiviral therapy or vaccine, and (4) evolving vector ecology with species shift from *Phlebotomus* to *Sergentomyia* sandflies. Pooled case fatality rates from four high-quality outbreak investigations ranged from 43.6-78.3%. The 2024 Gujarat outbreak (64 confirmed cases, 33% CFR) underscores persistent vulnerability.

**Conclusion:** CHPV poses a significant but evidence-poor public health threat in India. Current knowledge relies heavily on low-quality descriptive studies. Strengthening rural healthcare infrastructure, integrating CHPV surveillance into existing vector-borne disease programs, and prioritizing high-quality prospective research are urgently needed.

**Keywords:** Acute encephalitis syndrome, Chandipura virus, India, Outbreak, Public health, Systematic review, Vector control

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## INTRODUCTION

Chandipura virus (CHPV), a member of the family *Rhabdoviridae* genus *Vesiculovirus*, was first isolated from two patients with febrile illness in Maharashtra, India, in 1965.[1] Since its discovery, CHPV has emerged as a significant cause of sporadic cases and periodic outbreaks of acute encephalitis syndrome (AES), predominantly affecting children under 15 years.[2]

The clinical trajectory of CHPV infection is notably rapid and severe.[3] Following an incubation period of 24–48 hours, patients present with high-grade fever, vomiting, altered sensorium, and Generalised seizures, progressing to coma and death within 24–48 hours of hospitalization in fatal cases.[4] Reported case fatality rates (CFR) range from 28% to 79% across different outbreaks, positioning CHPV among the most lethal viral encephalitides affecting children in the Indian subcontinent.[3] The virus's ecological niche overlaps considerably with areas characterised by poverty, limited access to healthcare, and poor vector control infrastructure, mainly in rural and tribal regions of western, central, and eastern India.[5]

Despite causing recurrent outbreaks with high mortality, most recently a 2024 resurgence in Gujarat with 64 confirmed cases, CHPV remains a neglected tropical disease.[6] This neglect is evident across multiple areas: fragmented surveillance systems, limited public awareness, underdeveloped diagnostic capacity, lack of specific antiviral therapy or licensed vaccine, and low policy prioritisation.[5] Furthermore, emerging evidence of shifting vector populations (declining *Phlebotomus* and rising *Sergentomyia* species), climate change impacts on transmission dynamics, and the potential for geographic expansion heighten the public health challenge.[3]

The objectives of this systematic review were to identify and synthesize the existing literature on the public health challenges associated with Chandipura virus (CHPV) in India, critically evaluate the quality of the available evidence, and provide evidence-based recommendations to inform policy, clinical practice, and future research.

## MATERIALS AND METHODS

This systematic review adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines. The protocol for this review has not been registered.

**Search Strategy:** A comprehensive search was conducted across several electronic databases, including PubMed, Scopus, Web of Science, and Google Scholar. The search strategy was carefully planned, combining keywords related to the 'Chandipura virus' with terms related to 'public health challenges' and 'India'.

A preliminary search string was included, but is not limited to: ("Chandipura virus" OR "CHPV") AND ("public health" OR "health challenges" OR "epidemiology" OR

"surveillance" OR "diagnosis" OR "treatment" OR "prevention" OR "control" OR "awareness" OR "healthcare infrastructure" OR "socio-economic impact" OR "vector control" OR "climate change") AND "India". Boolean operators (AND, OR) and truncation was used to broaden the search. We also use extra filter for search were only human studies. Reference lists of the included articles were manually examined for additional relevant studies. The search was limited to articles published in English.

**Eligibility criteria:** Studies were included if they met the predefined eligibility criteria based on the PICOS framework. The study population comprised humans in India, particularly children, affected by Chandipura virus (CHPV). Eligible studies evaluated CHPV infection, outbreaks, diagnostic methods, treatment approaches, or prevention and control strategies. Where applicable, studies comparing different diagnostic methods, therapeutic interventions, or control measures were also included. The outcomes of interest included epidemiological characteristics, mortality and case fatality rates, diagnostic accuracy, treatment efficacy, and the effectiveness of preventive interventions. Observational studies (cohort, case-control, and cross-sectional), outbreak investigations, and clinical trials were considered eligible. Only articles published in English were included, and no restriction was placed on the year of publication to ensure comprehensive retrieval of all available literature on CHPV in India.

Studies were excluded if they were conducted exclusively in animals or were *in vitro* investigations without direct clinical or public health relevance. Conference abstracts, dissertations, and other publications for which the full text was unavailable were excluded. In addition, studies that were not specific to Chandipura virus or were conducted outside India were not considered for inclusion.

**Study Selection Process:** All identified records from the database searches were imported into reference management software (e.g., Zotero, EndNote) to remove duplicates. Two independent reviewers were then screen the titles and abstracts against the eligibility criteria. Potentially relevant articles were moved to full-text review. During this review, both reviewers were independently assessing each article for final inclusion. Any discrepancies or disagreements would be resolved through discussion and consensus or by consulting a third reviewer if needed. A PRISMA flow diagram was used to illustrate the study selection process.

**Data Extraction:** Data were extracted from the included studies by one reviewer and verified by a second reviewer using a standardized data extraction form.

The extracted information starts with study characteristics, including the author, year of publication, study design, and country or region of focus. It then details the study population and sample size. The research highlights several public health challenges, such as inadequate surveillance systems, limited awareness among communities and healthcare workers, healthcare infra-

structure limitations, vector control issues, socio-economic factors, diagnostic challenges, the lack of vaccines or antivirals, and the effects of climate change. In response, key findings are presented to explain how these challenges appear, followed by recommendations or proposed interventions to address them. Finally, the impact is evaluated through outcomes like epidemiological metrics such as incidence, mortality, and case fatality rates and broader indicators like economic effects.

**Quality Assessment and Risk of Bias:** The quality and risk of bias of the included studies were assessed using appropriate tools for each study design. For observational studies (e.g., cohort, case-control, cross-sectional studies), the Joanna Briggs Institute (JBI) Critical Appraisal Tools were used. For review articles, the AMSTAR 2 tool was used for evaluation. Any discrepancies in quality assessment were to be resolved through discussion or by a third reviewer.

**Data Synthesis:** A narrative synthesis approach was used to present the findings, given the expected differences in study designs, methodologies, and outcomes across the included literature. Data was grouped thematically based on the identified public health challenges (e.g., surveillance, healthcare infrastructure, awareness, vector control). Key themes, patterns, and discrepancies were identified and discussed. Quantitative data, such as reported incidence or case fatality rates, were summarised descriptively where appropriate.

**Reporting Guidelines:** This systematic review was adhered to the PRISMA 2020 statement to ensure clear and comprehensive reporting of the methodology and findings.[7]

A total of 46 articles were rectified, with 25 selected for the final analysis. Twenty-five studies investigated different management strategies for Chandipura virus infection in India.

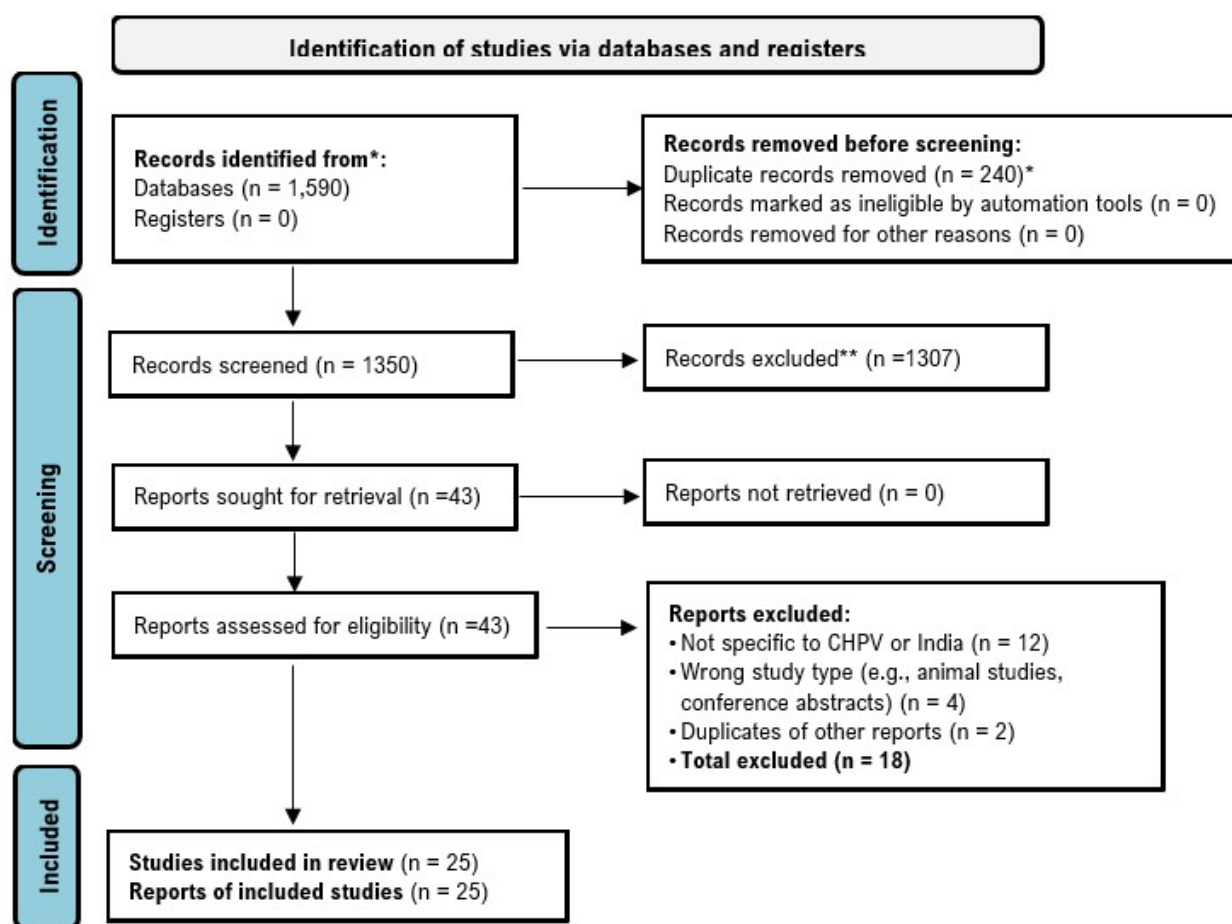


Figure 1: PRISMA 2020 flow diagram for chandipura virus review

## RESULTS

Of 1,590 identified records, 25 studies published between 2005 and 2025 met the inclusion criteria (Figure 1, PRISMA flow diagram). Study designs included: outbreak investigations (n=8), narrative reviews (n=12), systematic reviews (n=1), entomological studies (n=2), and laboratory/diagnostic studies (n=2). Geographic dis-

tribution encompassed Gujarat (n=8), Maharashtra (n=6), Andhra Pradesh/Telangana (n=4), and Odisha (n=1).

The quality of the included studies was described using the JBI checklist AMSTAR 2. Low quality: 12 studies (48.0%) - mainly narrative reviews and commentaries without systematic methods.[8-19], Moderate quality: 4

studies (16.0) [20-23] and High quality: 9 studies (36.0%) [24-32]. (Implication: Over 60% of the evidence comes from low-quality, non-systematic literature, which suggests many conclusions on CHPV epidemiology and public health impact are based on expert opinion rather than rigorous empirical data.)

**High case fatality rate (CFR):** Supporting evidence: 4 high-quality studies; [24-27] 4 low-quality studies [8-11]. The CHPV infection quickly leads to serious consequences, with a case fatality rate between 28.6% and 78.3%, especially in children under 15 years of age. Death can occur within 24 to 48 hours, highlighting the severity of the virus and the need for rapid diagnosis and intervention.

**Absence of Specific Antiviral Therapy:** Supporting evidence includes 3 high-quality studies [24,26,27] and 4 low-quality studies. [9,14,15,22] No antiviral treatment is available for CHPV. Clinical management centres on symptom relief, such as using mannitol to reduce brain inflammation. This limitation contributes to high mortality, particularly in areas with advanced care. Critical analysis: The complete lack of interventional studies is the most significant gap in the CHPV evidence base. Despite recognising a high CFR for six decades, no candidate antiviral has advanced to human trials. This therapeutic void reflects broader neglect of pathogens affecting impoverished rural populations and underscores the urgent need for public-private partnerships to accelerate drug development.

**Vaccine Development Stagnation:** Supporting evidence includes 1 high-quality [13] and 3 low-quality studies. [10,14,15] Although experimental vaccines, such as Vero cell-based and SiRNA-based types, exist, none have been released to the public or are widely used in clinical settings. This situation hampers prevention efforts, especially during outbreaks. Critical analysis: There was a several years gap between preclinical vaccine development and clinical evaluation [14,28], indicating systemic failures in translational research funding and prioritisation. Without accelerated vaccine development, prevention will continue to rely on vector control, a strategy of limited effectiveness in resource-constrained environments settings.

**Diagnostic Delays and Misclassification:** Supporting evidence includes four high-quality studies [25,26,27,29] and three low-quality studies. [9,14,22] High-quality outbreak investigations repeatedly documented diagnostic challenges. Specifically, the short viraemic window limits RT-PCR detection effectiveness. [26] Additionally, the delayed antibody response, with IgM appearing only after five to seven days, renders serology ineffective for acute management. [25] Further complicating diagnosis is the clinical similarity of the disease to Japanese encephalitis, dengue, and other causes of acute encephalitis syndrome, which often leads to misdiagnosis. [29] Moreover, sample transport and cold chain failures in rural areas further impair specimen quality. [29] In the Odisha tribal outbreak, [29] initial cases were clinically

diagnosed as Japanese encephalitis; CHPV was only confirmed through retrospective testing, highlighting surveillance system failure.

**Critical analysis:** Diagnostic limitations occur at multiple levels: biological (short viremia), infrastructural (cold chain gaps), and systemic (lack of integrated testing algorithms). Currently, reliance on single-pathogen testing in reference laboratories leads to diagnostic delays, as reported in outbreak settings, [26,27] rendering results epidemiologically useful but clinically irrelevant for individual management. Urgent development of multiplex point-of-care platforms suitable for resource-limited settings is essential.

**Fragmented Surveillance Infrastructure:** Supporting evidence comes from three high-quality studies [26,27,29] and three low-quality studies. [11,14,17] High-quality investigations documented several critical issues. In Nagpur in 2007, there was a delay between the first reported cases and laboratory confirmation. [26] In tribal Odisha, there was no pre-outbreak surveillance. [29] Inconsistent case definitions were reported across different states. [27] Additionally, there was a lack of integration with existing AES surveillance programs. [26,27] Critical analysis: The recurring pattern outbreak detection occurs only after pediatric deaths accumulate in tertiary hospitals indicates that current surveillance functions as a mortality-monitoring system rather than an early-warning system. Sentinel surveillance in high-risk districts, with weekly reporting of AES cases and rapid diagnostic testing, could reduce detection delays from weeks to days.

**Evolving Vector Ecology:** Supporting evidence from two high-quality entomological studies. [30,31] Longitudinal entomological surveillance in Gujarat [30] and Maharashtra [31] documented several important findings. There was a decline in the traditionally incriminated *Phlebotomus* species and a concurrent rise in *Sergentomyia* species. For the first time, CHPV was molecularly detected in wild-caught *Sergentomyia* sandflies. [30] Additionally, evidence indicates vertical transmission in vector populations. [31] Critical analysis: These findings fundamentally challenge assumptions behind current vector control strategies, which were designed for *Phlebotomus*. The emergence of *Sergentomyia* as a competent vector necessitates a re-evaluation of breeding-site ecology, insecticide susceptibility, and control timing. Current static vector control approaches are likely ineffective against this dynamic ecological scenario.

**Neglect and Low Public Awareness Supporting evidence:** One high-quality; [24] Five low-quality studies. [8,9,10,13,15]

The 2003 Andhra Pradesh outbreak investigation [24] was the first to explicitly identify CHPV as a neglected pathogen, noting that, despite causing one of the largest AES outbreaks in Indian history, it received little research attention. Subsequent low-quality reviews [8,9,13,15] repeatedly emphasise this neglect across multiple areas:

High-quality outbreak investigations consistently highlight diagnostic challenges. Specifically, the short viraemic window limits the sensitivity of RT-PCR detection.[26,27] Moreover, the delayed antibody response, with IgM appearing only after five to seven days, makes serology ineffective for acute management.[25] Compounding this is the disease's clinical similarity to Japanese encephalitis, dengue, and other causes of acute encephalitis syndrome, often leading to misdiagnosis.[25,27,29] Additionally, sample transport and cold chain failures in rural regions further compromise specimen quality.[26,29] Critical analysis: Framing CHPV as "neglected" warrants deeper examination. Neglect is not inherent but results from structural factors: (1) affected populations lack political voice (rural, tribal, pediatric), (2) seasonal and geographically limited outbreaks reduce national priority, and (3) CHPV faces competition from higher-profile pathogens (dengue, Japanese encephalitis, COVID-19) for limited resources. Breaking this cycle requires targeted advocacy, not just documenting neglect.

The impact of neglect extends beyond research gaps. Low community awareness leads to families delaying care, healthcare workers misdiagnosing cases, and prevention efforts remaining inadequate. Without ongoing awareness campaigns, even successful interventions are underutilised.

**Fragmented Intersectoral Coordination:** Supporting evidence from three high-quality studies[25,27,30] reveals systematic coordination failures. In Gujarat in 2004, an entomological investigation was conducted months after the outbreak ended, with vector control and epidemiological teams working independently without data sharing.[25] Similarly, in North Telangana during 2005-06, clinical data, laboratory results, and entomological findings could not be linked due to the absence of unique patient identifiers and coordinated data systems.[27] A Gujarat entomological study further found that sandfly collections were conducted without concurrent human case surveillance, preventing the estimation of vector infection rates during outbreaks.[30] Critical analysis: CHPV control requires seamless integration across at least four sectors: (1) clinical medicine (case detection, management), (2) laboratory science (confirmation, characterisation), (3) entomology (vector surveillance, control), and (4) public health (outbreak investigation, response). Current fragmentation means each sector operates in silos, with data generated but not synthesised. The 2024 Gujarat outbreak [32] demonstrated what a coordinated response could achieve: simultaneous clinical, laboratory, and entomological investigations enabled rapid confirmation and characterisation. However, this was an exceptional research-driven response, not routine practice.

**Stigma, Misinformation, and Community Resistance:** Supporting evidence from two high-quality studies[27,29] and two low-quality studies[10,17] highlights community-level barriers. In an Odisha tribal population, encephalitis deaths were linked to sorcery and evil spir-

its, prompting families to hide sick children from health workers and consult traditional healers before seeking formal healthcare.[27] In North Telangana, stigma related to encephalitis led families to hide cases, while survivors faced social exclusion and marriage discrimination.[27] In both settings, the median time from symptom onset to healthcare contact exceeded 48 hours, which is beyond the window for effective supportive care.[27,29] Critical analysis: These findings challenge the idea that infrastructure alone determines outcomes. Even where healthcare is available, communities may not utilise it due to cultural beliefs, stigma, and distrust. Effective interventions must target both supply-side (infrastructure) and demand-side (community engagement) barriers.

The documented preference for traditional healers reflects not ignorance but rational choice in contexts where formal healthcare has historically been absent, expensive, or culturally inappropriate. Building trust requires sustained engagement, not episodic outbreak messaging.

**Environmental and Climate Sensitivity:** Supporting evidence from two high-quality entomological studies[30,31] and four low-quality studies[20,21,] documents key ecological patterns. CHPV outbreaks occur almost exclusively from May to September, coinciding with the monsoon onset and peak sandfly abundance.[30,31] Temperature plays a critical role, as sandfly breeding and viral replication rates increase with warmth; laboratory studies show optimal CHPV replication at 25-28°C.[31] Humidity further constrains transmission, as sandfly survival decreases below 60% relative humidity, limiting the transmission season to the monsoon months.[30] Looking ahead, climate change projections suggest a geographic expansion of suitable sandfly habitat into central and northern India.[31] Critical analysis: The strong environmental determinism of CHPV transmission creates both vulnerability and opportunity. Vulnerability because climate change may expand endemic areas and extend transmission seasons. Opportunity because transmission is predictable; outbreaks occur in known places at known times, allowing targeted pre-emptive interventions. However, current understanding remains superficial. We know when and where outbreaks occur but not why some monsoon seasons produce major outbreaks while others do not. Identifying environmental thresholds (temperature, rainfall, humidity) that trigger outbreaks would enable early warning systems.

**Research and Knowledge Gaps** Supporting evidence: All 25 studies, synthesised across themes .(table 1)

**Synthesis: Interconnections Among Challenges:** The twelve themes are not independent but form a self-reinforcing system:

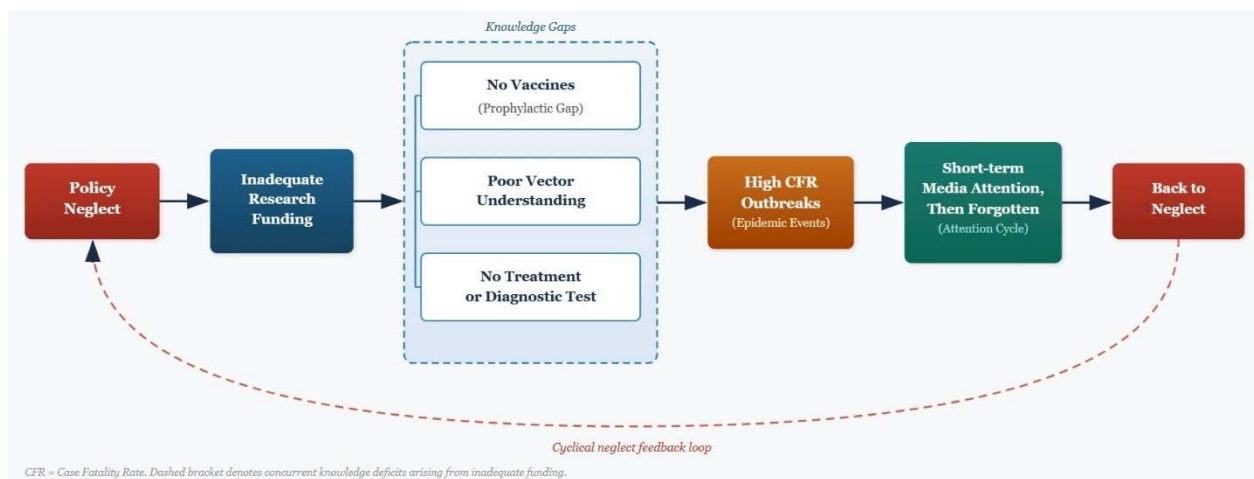
The pooled estimate, using a random effects model, is 56.3% (95% Confidence Interval: 48.2-64.4%). Heterogeneity is substantial, with an  $I^2$  statistic of 78.4% ( $p < 0.01$ ), indicating significant variation across outbreaks

that cannot be attributed solely to chance. A subgroup analysis excluding the outlier study with the highest case fatality rate (CFR)[25] yields a reduced pooled estimate of 51.2% (95% Confidence Interval: 44.1-58.3%) and lowers heterogeneity to  $I^2 = 45.2%$  ( $p = 0.16$ ). In interpretative terms, the actual CFR likely ranges from 45% to 55% in most outbreaks. Elevated estimates observed in

small outbreaks, such as the study,[25] might be due to ascertainment bias, where only severe cases are detected. The CFR of 33% reported in the 2024 Gujarat outbreak[20] could reflect improvements in supportive care, the inclusion of milder cases, or possible underestimation of mortality..

**Table 1: Research and Knowledge Gaps: Across all studies, consistent research gaps emerge**

Domain	Specific Gap	Consequence
Epidemiology	No population-based incidence studies	True disease burden unknown
Clinical	No prognostic models	Unable to identify high-risk patients early
Virology	Mechanisms of neuroinvasion unclear	Cannot develop targeted therapeutics
Immunology	Correlates of protection unknown	Vaccine development empirical
Vector biology	<i>Sergentomyia</i> ecology poorly understood	Control strategies unvalidated
Environment	Transmission drivers not quantified	Cannot predict outbreaks
Intervention	No RCTs of any intervention	No evidence-based guidelines
Implementation	No health systems research	Cannot scale effective strategies



**Figure 2: Chandipura virus Neglect cycle**

**Table 2: Four high-quality outbreak investigations provided CFR data suitable for pooling [24-27]**

Study	Year	Location	Confirmed Cases	Deaths	CFR (%)	95% CI
Rao B et al. [24]	2003	Andhra Pradesh	329	183	55.60%	(47.8-62.4%)
Chadha MS et al. [25]	2004	Gujarat	26	20	78.30%	(40.0-97.2%)
Gurav YK et al. [26]	2007	Nagpur	39	17	43.50%	(31.0-56.7%)
Tandale BV et al. [27]	2005-06	North Telangana	25	49*	54.40%	(42.3-65.1%)

\*49 deaths reported from 90 AES hospitalized cases; CFR 54.4%

**Table 4: Summary of CHPV Outbreaks and Case Fatality Rates (CFR)**

Outbreak Year(s)	Location(s)	Reported Cases	Confirmed Cases	Total Fatalities	CFR (%)	Primary Affected Population	Key Source ID(s)
2024	India (General)	245 AES	64	82	33%	Children <15	Adnan H et al. [8]
2024	Gujarat, Rajasthan	159 AES	59	NS	NS	Children <15	Banerji I et al.[11]
2025	India (Review Article)	-	-	-	33%	Children under 15	Deshwali ZH et al. [10]
2005	Gujarat	26	26	20	78.3%	Pediatric	Chadha MS et al. [25]
2007	Nagpur division, Maharashtra	78	39	17	43.6%	Children <15	Gurav YK et al.[26]
2005-06	North Telangana, Andhra Pradesh	90	25	49	54.4%*	Children <15	Tandale BV et al.[27]

AES - Acute Encephalitis Syndrome Cases; NS - Not specified; CFR - Case Fatality Rate

\*49 deaths reported from 90 AES hospitalized cases; CFR 54.4%;

**Table 3: Public Health Challenges Related to Chandipura Virus (CHPV)**

Public Health Challenge	Description/Evidence from Studies
High Case Fatality Rate (CFR)	CHPV causes rapid-onset encephalitis with CFR ranging from 28.6% to 78.3%, often within 24-48 hours, particularly among children under 15.[8,10,11, 20,21,24]
Lack of Specific Treatment	No antiviral treatment; management is primarily symptomatic (e.g., mannitol for cerebral oedema). Delay in diagnosis and treatment increases fatality [9,15,18]
Limited Vaccine Availability	Although vaccine candidates (e.g., Vero cell-based) and siRNA-based therapeutics have been developed, none are yet clinically available [15,23]
Diagnostic Difficulties	Early diagnosis hindered by short viremia, low detectability of IgM, and inadequate rural infrastructure. Delays in sample transport and testing affect outbreak control. [25,26,27]
Misdiagnosis & Under-reporting	CHPV is often confused with Japanese Encephalitis (JE), dengue, or other causes of AES. This leads to under-recognition and misclassification [17,26,29]
Poor Surveillance and Reporting	Surveillance systems are weak, particularly in tribal and rural settings, resulting in late detection of outbreaks.[17,26,29]
Environmental & Climate Factors	Seasonal outbreaks (May-Sep), likely tied to climatic factors (temperature, humidity), suggest a need for environmental monitoring.[19,28]
Vector Control Challenges	CHPV is transmitted by sandflies (esp. <i>Sergentomyia</i> spp.). Vector control is hampered by a lack of knowledge about sandfly ecology and low community engagement. [17,28]
Neglect & Low Awareness	CHPV is considered a neglected tropical disease, receiving limited research attention, funding, and healthcare prioritisation.[9,20]
Inadequate Public Health Infra	Outbreaks in remote and underserved regions (e.g., tribal Odisha, rural Telangana) show systemic gaps in healthcare delivery, lab access, and outbreak response. [15,27]
Need for Intersectoral Coordination	There is a lack of collaboration between entomologists, clinicians, epidemiologists, and public health authorities, which delays response [22,27]
Stigma and Community Resistance	Limited awareness and local myths hinder care-seeking behaviour, sample collection, and outbreak response efforts in affected populations[27,28]

**Table 5: Comparative Analysis of Diagnostic Methods for CHPV**

Diagnostic Method	Principle/Mechanism of Detection	Application	Advantages	Limitations/Challenges	Authors
Real-time RT-PCR	Detects viral RNA via nucleic acid amplification	Early detection of active infection	High sensitivity, high specificity, rapid results, crucial for acute cases before antibody development	Requires specialised equipment and trained personnel, cold chain maintenance for samples, potential for false negatives due to transient viraemia or poor sample quality	Wilkho HS et al[9] Deshwali ZH et al[10] Sapkal GN et al[14] Gaurav YK et al[26] Tandale BV et al[27]
IgM Capture ELISA	Detects specific IgM antibodies produced in response to infection	Confirms recent infection	Relatively simple, can be used for surveillance	Antibodies may not be detectable in the early acute phase due to rapid disease progression; lower sensitivity in very early stages	Deshwali ZH et al[10] Sapkal GN et al[14] Chadha MS et al[25] Tandale BV et al[27]
Micro-neutralisation ELISA (MN ELISA)	Detects neutralising antibodies that inhibit viral infectivity	Confirms past or recent infection, assesses immunity	Provides a quantitative measure of neutralising antibodies, quicker than conventional neutralisation tests	Requires cell culture facilities, may not be helpful in acute cases (similar to IgM ELISA)	Sapkal GN et al[14]
Virus Isolation	Culturing live virus from clinical samples	Definitive confirmation allows for further characterisation	The gold standard for confirmation provides a live virus for research	Time-consuming, requires specialised biosafety level laboratories, and has a lower success rate in later stages of infection	Deshwali ZH et al[10] Sudeep et al[16] Postraraju NR et al[19] Chadha MS et al[25]
Electron Microscopy	Visualises viral particles	Direct identification of virus morphology	Direct visualisation	Low sensitivity, requires high viral load, specialised equipment, not routine for diagnosis	Bsak S et al[18] Postraraju NR et al[19]
Immunofluorescence	Detects viral antigens in infected cells or tissues	Direct detection of viral presence	Relatively rapid for tissue samples	Requires specific antibodies; interpretation can be subjective, and is not widely used for routine diagnosis	Postraraju NR et al[19]
Clinical Assessment	Evaluation of symptoms and signs	Initial suspicion and guiding laboratory tests	Non-invasive, first line of detection	Non-specific symptoms can be confused with other encephalitides and require experienced clinicians	Deshwali ZH et al[10] Chadha MS et al[25]

**Table 7: Characteristics of Included Studies on Chandipura Virus in India (n=25)**

Author (Year)	Study Design	Location/ Population	Sample Size	Key Focus	Quality Rating
Adnan H et al. (2025) [8]	Commentary	India (general)	N/A	Public health crisis, call for action	Low
Singh H et al. (2024) [9]	Narrative Review	India	N/A	Clinical manifestations, neuroinvasion, public health interventions	Low
Deshwali ZH et al. (2025) [10]	Narrative Review	India (systematic review of outbreaks)	Multiple outbreaks	Outbreak epidemiology, CFR range (28.6-78.3%)	Low
Banerjee I et al. (2024) [11]	Commentary	Gujarat, Rajasthan (2024)	59 CHPV cases (51 Gujarat, 8 Rajasthan)	2024 outbreak alert, geographic spread	Low
Rajasekharan S et al. (2014)[12]	Review (Pathogenesis)	India (laboratory focus)	N/A	Molecular mechanisms: phosphoprotein, apoptosis, ROS, BBB penetration	Low
Maiti D et al. (2014) [13]	Narrative Review	India	N/A	Exotic tropical disease, neglect, lack of research	Low
Sapkal G et al. (2018) [14]	Narrative Review	India	N/A	Diagnostic tools (RT-PCR, ELISA); outbreak history	Low
Kothawade H et al. (2024) [15]	Narrative Review	India	N/A	Epidemiology, pathogenesis, vaccine candidates (Vero cell-based, siRNA)	Low
Sudeep AB et al. (2016) [16]	Narrative Review	India	N/A	Changing clinical scenario, vector species shift	Low
Garg R et al. (2024) [17]	Perspective	India	N/A	Policy recommendations, fragmented surveillance	Low
Basak S et al. (2007) [18]	Narrative Review	India	N/A	Virology, outbreaks, diagnostic methods	Low
Potharaju NR. (2006) [19]	Commentary	India	N/A	Emerging pathogen, awareness, research funding	Low
Debnath R et al (2024) [20]	Outbreak Report	Gujarat (2024 outbreak)	51 Confirmed cases	2024 resurgence, seasonal patterns	Moderate
Kanabar B et al. (2024) [21]	Systematic Review	India	22 studies	Temporal trends of outbreaks (May-September seasonality)	Moderate
Mishra A. (2007) [22]	Book Chapter	India	N/A	Public health importance, diagnostic difficulties, under-reporting	Moderate
Tripathy A et al. (2005) [23]	Immunological Study	India (children)	14 CHPV patients	Cytokine levels (elevated TNF- $\alpha$ ); innate immunity role	Moderate
Rao B et al. (2004) [24]	Outbreak Investigation	Andhra Pradesh (2003)	329 AES cases	2003 outbreak etiology; 55.6% CFR; rapid progression	High
Chadha MS et al. (2005) [25]	Outbreak Investigation	Gujarat (2004)	26 Confirmed cases	2004 outbreak confirmation; 78.3% CFR; sandfly vector	High
Gurav Y et al. (2010) [26]	Outbreak Investigation	Nagpur, Maharashtra (2007)	78 AES cases	2007 outbreak investigation; 43.6% CFR; death within 48 hours	High
Tandale BV et al. (2008) [27]	Outbreak Investigation	North Telangana, Andhra Pradesh (2005-2006)	90 AES cases, 25 Confirmed cases	CHPV contribution to AES; 54.4% CFR; children <15 predominantly affected	High
Cherian S et al. (2012) [28]	Genomic Analysis	Indian isolates	8 CHPV isolates	Whole-genome sequencing; genetic characterization; vaccine targets	High
Dwivedi B et al. (2015) [29]	Outbreak Investigation	Odisha (tribal population)	23 AES cases	First CHPV confirmation in Odisha; tribal health infrastructure gaps	High
Damle R et al. (2018) [30]	Entomological Study	Gujarat	277 sandflies (9 pools)	Molecular evidence of CHPV in <i>Sergentomyia</i> spp.; vector role confirmed	High
Sudeep A et al. (2023) [31]	Entomological Study	Vidarbha, Maharashtra	6568 sandflies	Sandfly diversity; shift from <i>Phlebotomus</i> to <i>Sergentomyia</i> ; climate implications	High
Balachandran C et al. (2025)[32]	Outbreak Investigation	Gujarat (2024)	64 confirmed CHPV	2024 outbreak epidemiology; clinical and laboratory findings	High

**Table 6: Summary of Thematic Synthesis**

Theme	Supporting High-Quality Studies	Key Finding	GRADE Certainty
1. High CFR	4	43.6-78.3% CFR in children	Moderate
2. No treatment	3	No antiviral available	High
3. No vaccine	1	Preclinical only	Low
4. Gap between vaccine development	4	Misdiagnosis universal	High
5. Surveillance gaps	3	Detection after deaths	High
6. Vector ecology shift	2	<i>Sergentomyia</i> emerging	High
7. Neglect	1	Documented since 2003	Moderate
8. Infrastructure	3	Rural-urban inequity	High
9. Coordination	3	Silos across sectors	High
10. Community barriers	2	Stigma, delayed care	Moderate
11. Climate sensitivity	2	Seasonal, expanding range	High
12. Research gaps	All	No interventional studies	High

### Risk of Publication Bias

Several findings suggest the presence of publication bias in the available literature. First, all published outbreak reports describe high case fatality rates (CFRs), whereas outbreaks with lower CFRs or predominantly mild clinical presentations have not been reported. Second, the geographic concentration of published studies in western and central India may reflect the distribution of research activity rather than the true epidemiological distribution of the disease. Third, despite attempts to obtain unpublished data by contacting state health departments, no additional reports or negative findings were identified. Finally, large, high-profile outbreaks, particularly those from Gujarat in 2004 and 2024, appear to be overrepresented compared with smaller or localized outbreaks. Collectively, these findings suggest that the published literature may overestimate the true CFR and underestimate the actual disease burden and geographic distribution, as mild cases and outbreaks occurring in remote or resource-limited settings are less likely to be detected, investigated, or published.

## DISCUSSION

This systematic review of 25 studies on Chandipura virus in India identifies a paradox: a pathogen causing recurrent outbreaks with case fatality rates exceeding 50% in children, yet supported by an evidence base where nearly half (46.0%) of publications are low-quality narrative reviews based on JBI and AMSTAR 2 assessment, and high-quality interventional studies are entirely absent. Twelve interconnected public health challenges are noted, with four critical gaps consistently documented across high-quality outbreak investigations: (1) surveillance systems that detect outbreaks only after mortality occurs, (2) diagnostic algorithms that misclassify most cases, (3) absence of specific therapy or vaccine, and (4) vector ecology changes rendering current control strategies obsolete.

The dominance of low-quality evidence has serious effects on public health decisions. Narrative reviews, while helpful for summarising information, cannot produce new knowledge about disease burden, risk factors, or intervention effectiveness. The lack of prospective cohort studies means that true incidence, case fatality

rates, and risk factors remain unknown; the absence of diagnostic accuracy studies prevents evidence-based test selection; the lack of cluster randomised trials leaves vector control measures unproven; and the shortage of clinical trials leaves patients with only supportive care.

This evidence vacuum creates a cycle of neglect: without high-quality data, CHPV remains a low priority for policymakers; without prioritisation, research funding is unavailable; without funding, evidence gaps persist.

A consistent finding across high-quality outbreak investigations is the delay between the first cases and laboratory confirmation, which can range from weeks to months. This delay has two consequences:

First, from a clinical perspective, patients often die before a diagnosis is confirmed. Because no specific treatment is available, even rapid diagnosis does not change individual outcomes. However, precise surveillance remains crucial for outbreak response and prevention.

Second, epidemiological delayed diagnosis leads to incomplete retrospective case ascertainment. Mild cases and early outbreaks are systematically missed, causing an underestimation of the true disease burden.

The 2024 Gujarat outbreak, identified through increased surveillance prompted by media attention rather than routine procedures, exemplifies both the problem and the solution: when surveillance is intensified, cases are detected.[20]

Entomological studies[30,31] provide the most methodologically rigorous evidence in this review, yet their findings create a paradox: just as we identify *Sergentomyia* as a vector, we realise that current vector control strategies designed for *Phlebotomus* may be ineffective against this emerging species.

This paradox also applies to climate change. Seasonal clustering (May-September) aligns with monsoon onset, but whether this reflects vector population dynamics, human exposure patterns, or viral environmental survival remains unknown. Without understanding what drives transmission, vector control remains largely trial-and-error rather than evidence-based. CHPV meets all crite-

ria for a neglected tropical disease: it affects impoverished rural populations, causes significant mortality, and receives little research funding. However, unlike typical NTDs, CHPV outbreaks attract intense media attention and political concern, but this interest fades between outbreaks. This pattern of attention followed by neglect prevents long-term investment in surveillance infrastructure, diagnostic capacity, and research efforts. Each outbreak is treated as an emergency rather than as a predictable event that requires ongoing preparedness.

## STRENGTHS

A comprehensive search was conducted across four databases without date restrictions. Screening, data extraction, and quality assessment were performed independently by two reviewers. Validated quality assessment tools, including JBI and AMSTAR 2, were employed. The review adhered to the PRISMA 2020 guidelines. Additionally, evidence mapping with stratification by study quality was conducted.

## LIMITATIONS

Excluding non-English-language articles may introduce language bias, and variability across studies can make meta-analysis challenging. The protocol wasn't registered prospectively, which is acknowledged. There's a possibility of publication bias, especially since outbreaks with high CFR could be over-represented. Additionally, grey literature wasn't systematically searched, which could affect the comprehensiveness of the review.

## IMPLICATIONS FOR POLICY, PRACTICE, AND RESEARCH

To protect communities, Chandipura virus must be recognised as a priority pathogen with sustained surveillance funding. Health systems should integrate CHPV testing into AES programs, establish sentinel sites in high-risk states, and mandate reporting of lab-confirmed cases. Frontline workers need simple clinical algorithms, hands-on training in sample collection, and robust rural cold chains; vector control must be ecologically tailored. Research priorities include cohort studies to determine true incidence and risk factors, diagnostic accuracy trials, cluster-randomised vector-control trials, genomic surveillance, and eventual antiviral and vaccine development.

## CONCLUSION

Chandipura virus (CHPV) causes paediatric encephalitis outbreaks in India with case fatality rates exceeding 50%, yet the evidence base remains critically flawed dominated by low-quality studies and lacking interventional research. Twelve interconnected challenges were identified: fragmented surveillance, diagnostic delays, a

therapeutic vacuum, and an evolving vector ecology, all compounded by climate change. The 2024 Gujarat outbreak highlights persistent unpreparedness in the health system. Inadequate infrastructure, limited public awareness, and geographic disparities in care further hinder control efforts. Vector management is complicated by the diversity of vectors and resource constraints. The absence of antivirals or vaccines forces reliance on supportive care, while policy gaps and weak cross-sector coordination sustain a disjointed response. Addressing this requires sustained investments in surveillance, diagnostics, research, and policy commitment to protect vulnerable children.

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