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Research Article

CHIKUNGUNYA VIRUS INFECTION IN CHILDREN: CLINICAL SPECTRUM, NEUROLOGICAL COMPLICATIONS, AND CONTEMPORARY MANAGEMENT STRATEGIES - A SYSTEMATIC REVIEW AND UPDATE

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Abstract

Background: Chikungunya virus (CHIKV) infection is an important and expanding global health concern, with increasing recognition of severe and potentially persistent disease in pediatric populations. Although most children experience a self-limited febrile illness, neonates, young infants, and children with neurological or multisystem involvement may develop severe complications requiring intensive care. **Objective:** To systematically synthesize and critically appraise the available evidence on the clinical spectrum, neurological complications, perinatal and neonatal manifestations, management, preventive interventions, and outcomes of CHIKV infection in children, with particular emphasis on severe disease and implications for pediatric critical care. **Methods:** A systematic review was conducted and reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement. PubMed/MEDLINE, Scopus, WHO Global Index Medicus, and PAHO/IRIS were searched from inception through August 11, 2026, supplemented by backward citation searching, examination of reference lists, conference proceedings, and preprint servers. Eligible studies reported original pediatric clinical data concerning laboratory-confirmed CHIKV infection or evaluated CHIKV-specific preventive interventions in pediatric or adolescent populations. Two reviewers independently performed study selection, data extraction, and methodological appraisal using the Newcastle–Ottawa Scale, design-appropriate Joanna Briggs Institute critical appraisal tools, and the Cochrane Risk of Bias 2 tool. Owing to substantial clinical and methodological heterogeneity, findings were synthesized narratively without meta-analysis. **Results:** The searches identified 1,253 records: 1,103 through databases and registers and 150 through other methods. After duplicate and automated removal, screening, retrieval, and full-text eligibility assessment, 32 primary studies, represented by 32 reports, were included in the qualitative synthesis.Fever and rash were among the most consistently reported manifestations, whereas arthralgia was less readily recognized in infants and younger children. Severe disease occurred disproportionately among neonates, young infants, and children with neurological or multisystem involvement and included encephalitis, encephalopathy, seizures, shock, respiratory failure, cardiac dysfunction, coagulopathy, and multiorgan dysfunction. Perinatal infection was associated with substantial acute morbidity and persistent neurological, cognitive, motor, behavioral, and neurodevelopmental abnormalities in selected survivors. Management was predominantly supportive, including fluid therapy, respiratory and hemodynamic support, seizure control, and other organ support. Pediatric comparative evidence was insufficient to establish corticosteroids or intravenous immunoglobulin as CHIKV-specific therapies. No antiviral therapy with established clinical efficacy in children was identified. **Conclusions:** Pediatric CHIKV infection encompasses a broad age-dependent clinical spectrum, from self-limited febrile illness to life-threatening neurological and multisystem disease. Neonates and young infants, particularly those with perinatally acquired infection, represent the population at greatest risk of severe outcomes. Early recognition, appropriate supportive and intensive care, and structured neurological and developmental follow-up after severe disease are essential. Prospective multicenter pediatric studies are needed to improve risk stratification, define long-term outcomes, and evaluate therapeutic and preventive strategies.

Keywords: Chikungunya virus, Children; pediatrics, Neonatal infection, Perinatal transmission, Encephalitis, Neurological complications, Critical care.

INTRODUCTION

Chikungunya virus (CHIKV) infection remains a major global public health concern, particularly in tropical and subtropical regions where *Aedes aegypti* and *Aedes albopictus* are widely distributed. Since its re-emergence in the early 21st century, CHIKV has caused recurrent outbreaks across Africa, Asia, the Indian Ocean region, and the Americas, producing substantial clinical morbidity, pressure on healthcare systems, and socioeconomic disruption [1]. Recent epidemiological alerts and surveillance reports have documented sustained transmission, geographic expansion, and renewed epidemic activity, particularly in the Region of the Americas [2–4]. CHIKV infection is classically characterized by an acute febrile illness accompanied by arthralgia, myalgia, headache, fatigue, and rash. Although most infections are self-limited, the acute disease is driven by high viral replication and activation of innate immune and proinflammatory pathways, which contribute to systemic manifestations, tissue injury, and pain [5]. Neurological involvement constitutes an important form of complicated disease and encompasses encephalitis, encephalopathy, seizures, myelitis, acute flaccid paralysis, Guillain–Barré syndrome, and other central or peripheral nervous system manifestations [6]. In a subset of patients, persistent immune activation, altered inflammatory signaling, and possible retention of viral material or antigens in affected tissues contribute to prolonged arthralgia, chronic inflammatory manifestations, and functional impairment [7–9]. Clinical expression and outcomes vary substantially according to age, host characteristics, underlying vulnerability, and disease severity [10]. Neurological and multisystem involvement is particularly relevant in children. CHIKV-associated encephalitis may be accompanied by seizures, altered consciousness, focal neurological abnormalities, prolonged hospitalization, and adverse functional outcomes

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[11]. Pediatric reports demonstrate that systemic and neurological complications can occur across all age groups but are disproportionately recognized among neonates, young infants, and hospitalized children [12]. Severe or fatal disease may involve intense systemic inflammation, endothelial and microvascular injury, myocardial dysfunction, respiratory failure, hepatic injury, coagulopathy, shock, and multiorgan dysfunction [13]. These findings support considering pediatric CHIKV infection a heterogeneous clinical entity rather than uniformly characterizing it as an uncomplicated febrile illness.
No antiviral treatment with established clinical efficacy has been approved for CHIKV infection, and management remains predominantly supportive [14]. Uncomplicated disease is generally treated with adequate hydration, antipyretic therapy, rest, and symptomatic relief. Nonsteroidal anti-inflammatory drugs should usually be avoided until dengue infection has been reasonably excluded because of the potential risk of bleeding. Children with severe disease require individualized stabilization and organ support, including careful fluid administration, respiratory and hemodynamic support, seizure control, correction of metabolic and coagulation abnormalities, and close neurological and cardiovascular monitoring.

Maternal infection constitutes an additional concern because pregnant women with suspected CHIKV infection near delivery require coordinated obstetric, infectious disease, and neonatal surveillance [15]. Mother-to-child transmission occurs predominantly when maternal infection develops during the intrapartum period or in the days immediately preceding delivery, when maternal viremia is present [16]. Prospective and observational studies have demonstrated that affected neonates may initially appear clinically well and subsequently develop fever, lethargy, poor feeding, skin manifestations, thrombocytopenia, coagulopathy, respiratory distress, cardiovascular instability, seizures, encephalopathy, or multiorgan dysfunction [17–19]. Symptomatic neonatal infection frequently requires intensive care and may be followed by persistent neurological or neurodevelopmental abnormalities. Beyond severe neonatal disease, pediatric cohort studies have shown that the clinical attack rate and symptomatic expression of CHIKV infection vary according to age and epidemiological setting [20]. Persistent musculoskeletal symptoms, including recurrent arthralgia, stiffness, fatigue, and reduced physical activity, may continue beyond the acute phase, although chronic inflammatory joint disease is better characterized in adults than in children [21]. Prospective pediatric evidence from Kenya has additionally demonstrated sustained endemic CHIKV transmission and clinically relevant infection among children outside the better-characterized epidemic settings of the Americas and the Indian Ocean region [22].

Prevention remains primarily dependent on vector control, personal protection against mosquito exposure, epidemiological surveillance, and, where applicable, vaccination according to national recommendations and individual risk assessment [23,24]. The rapid development of CHIKV vaccines has expanded preventive opportunities, although implementation requires consideration of vaccine platform, population characteristics, safety, durability of protection, outbreak epidemiology, and programmatic feasibility [25]. A single-dose live-attenuated vaccine demonstrated robust immunogenicity and an acceptable safety profile in a randomized phase 3 trial involving adolescents aged 12–17 years [26].Nevertheless, pediatric vaccination policies continue to evolve, and recommendations must account for age-specific authorization, travel or occupational exposure, regional transmission, contraindications, and emerging post-licensure safety information [27,28].

Neonatal and perinatal disease remains one of the most clinically consequential pediatric presentations. Vertically transmitted infection may cause neonatal encephalitis, with abnormalities detectable on neurological examination and neuroimaging [29,30]. Latin American reports have further documented congenital and perinatal complications, fatal vertically transmitted infection, fetal loss, neonatal death, and severe multisystem disease associated with maternal infection during pregnancy [31–33]. Long-term follow-up of children exposed to perinatal infection has identified cognitive and learning difficulties that may persist into school age, reinforcing the need for structured developmental surveillance [34]. The large outbreak reported in Paraguay during 2022–2023 also demonstrated the capacity of CHIKV to produce severe disease and deaths during periods of intense regional transmission [35].

Immunomodulatory therapy has been considered in selected patients with severe neurological, inflammatory, or dermatological manifestations. Intravenous immunoglobulin (IVIG), however, is associated with potential adverse effects ranging from infusion-related symptoms to hemolysis, thrombosis, renal dysfunction, aseptic meningitis, and other uncommon but clinically important complications [36–38]. Its administration therefore requires appropriate patient selection, weight-based dosing, baseline evaluation, controlled infusion rates, hydration, monitoring, and readiness to manage adverse reactions [39–42]. Recent pediatric primary studies have instead expanded the recognized clinical spectrum by documenting neurological involvement in a child from the Brazilian Amazon [43] and frequent arthralgia among infants and young children during an outbreak in Brazil [44]. Neither study evaluated IVIG treatment. Consequently, the available evidence does not establish IVIG as an effective CHIKV-specific therapy in children, and its role in chikungunya-associated neurological disease remains uncertain [45].

Continued regional surveillance is essential because concurrent circulation of CHIKV, dengue virus, Zika virus, and other arboviruses can complicate clinical recognition, laboratory diagnosis, and public health responses. PAHO has consequently urged countries in the Americas to strengthen case detection, laboratory capacity, vector control, clinical preparedness, and epidemiological response to chikungunya and other emerging arboviral threats [46]. The pediatric evidence base has expanded considerably but remains heterogeneous. Neurological manifestations have been described in pediatric cohorts, including encephalitis, encephalopathy, seizures, altered consciousness, and other serious complications [47]. Perinatally infected children may develop persistent neurocognitive impairment, including abnormalities in language, coordination, behavior, and executive function [48]. Hospital-based studies have documented severe systemic manifestations, cardiovascular instability, respiratory compromise, coagulopathy, and intensive care requirements [49,50]. Pediatric immunological studies suggest that efficient viral clearance may be associated with a strong early innate immune response [51], whereas investigations of central nervous system infection confirm that CHIKV should be considered in children presenting with

encephalitis or acute neurological syndromes in endemic or epidemic settings [52]. Neonatal case series further demonstrate that encephalitic presentations may include seizures, feeding impairment, abnormal consciousness, and neuroimaging abnormalities [53]. Recent longitudinal studies have strengthened concern about the developmental consequences of prenatal and perinatal exposure. Neurodevelopmental abnormalities have been reported in children with intrauterine or perinatal CHIKV exposure, although their frequency and causal relationship with maternal or neonatal infection remain incompletely defined [54,55]. Studies of hospitalized children from Honduras and the Caribbean have additionally demonstrated age-dependent clinical and laboratory findings and confirmed that severe neurological disease, although uncommon, contributes disproportionately to hospitalization and adverse outcomes [56,57]. Follow-up of neonatal cases has identified developmental delay and persistent neurological abnormalities during infancy [58]. However, viral load in blood or cerebrospinal fluid has not shown a consistent association with the clinical severity of pediatric neurological manifestations, indicating that host, inflammatory, and developmental factors may also influence disease expression [59].

Evidence extending into later childhood and adolescence indicates that the consequences of perinatal CHIKV infection may persist well beyond the neonatal period, with measurable cognitive, motor, behavioral, and neurodevelopmental abnormalities reported in selected survivors [60]. Rare but severe phenotypes, including CHIKV-associated acute necrotizing encephalopathy in adolescents, further expand the recognized neurological spectrum and underscore the need for early neurocritical care assessment in rapidly deteriorating patients [61]. Despite these advances, pediatric evidence remains dominated by observational cohorts, hospital-based series, case reports, heterogeneous diagnostic criteria, and studies with variable duration and completeness of follow-up. The relative rarity of severe outcomes, potential overlap among longitudinal cohorts, limited pediatric therapeutic trials, and inconsistent reporting of intensive care interventions continue to impede precise estimates of incidence, prognosis, and treatment effectiveness.

Given the expanding burden of pediatric CHIKV infection, its heterogeneous age-dependent manifestations, and the scarcity of high-quality pediatric evidence, an updated and comprehensive synthesis is warranted. This systematic review therefore aims to summarize and critically appraise the available evidence on the clinical spectrum, neurological complications, maternal–fetal and perinatal transmission, neonatal disease, management strategies, intensive care requirements, and short- and long-term outcomes of CHIKV infection in children, incorporating evidence available through August 11, 2026. To provide an integrative overview of the pathophysiological mechanisms, clinical spectrum, and severe outcomes of CHIKV infection in children, a conceptual summary is presented in Figure 1. This figure summarizes the main elements addressed in the present systematic review, including viral transmission routes, host immune response, clinical phases of disease, multisystem involvement, and severe manifestations in high-risk pediatric populations such as neonates and infants. The diagram integrates current evidence on pathophysiological mechanisms, neurological and systemic complications, and outcomes reported in children with chikungunya virus infection.

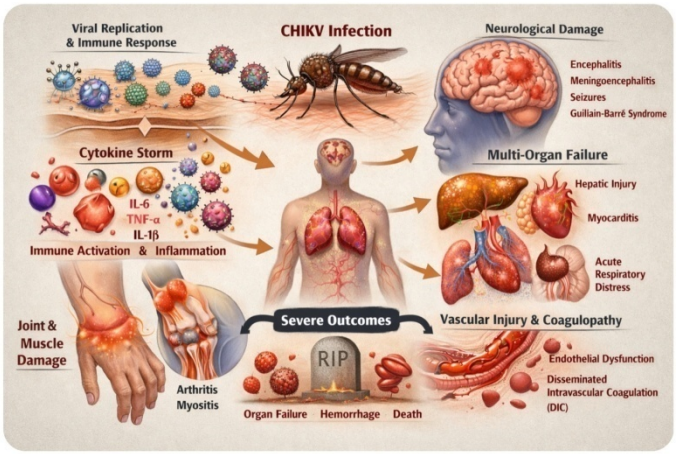

Figure 1. Conceptual overview of chikungunya virus (CHIKV) infection in children.Source: authors' own elaboration.

METHODS

Study Design and Reporting Standards

This systematic review was conducted and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement. The literature search was additionally reported in accordance with the PRISMA extension for literature searches (PRISMA-S). The review was designed to systematically identify, critically appraise, and synthesize the available evidence on CHIKV infection and CHIKV-specific preventive interventions in pediatric populations, with particular emphasis on the clinical spectrum of disease, severe and critical illness, neurological complications, maternal–fetal and perinatal transmission, neonatal disease, intensive care requirements, therapeutic and preventive approaches, and short- and long-term clinical outcomes. A prospective review protocol was not registered in PROSPERO or another publicly accessible systematic review registry. The absence of prospective protocol registration is acknowledged as a methodological limitation of the review. This systematic review therefore aims to summarize and critically appraise the available evidence on the clinical spectrum, neurological complications, maternal–fetal and perinatal transmission, neonatal disease, management and preventive strategies, intensive care requirements, and short- and long-term outcomes of CHIKV infection in children, incorporating evidence available through August 11, 2026.

Information Sources and Search Strategy

A comprehensive systematic literature search was conducted in PubMed/MEDLINE, Scopus, the World Health Organization (WHO) Global Index Medicus, and the Pan American Health Organization Institutional Repository for Information Sharing (PAHO/IRIS). Supplementary searches included backward citation searching, examination of the reference lists of included studies, conference proceedings, and preprint servers. The original search covered the period from database inception through December 2025. To ensure that the review reflected the most current evidence available, an updated search was conducted through August 11, 2026. Records identified during the updated search were subjected to the same eligibility criteria, screening procedures, data extraction process, and methodological appraisal as records identified during the original search.

The database and register searches identified 1,103 records: PubMed/MEDLINE (n = 412), Scopus (n = 568), WHO Global Index Medicus (n = 87), and PAHO/IRIS (n = 36). Searches conducted through other methods identified an additional 150 records: backward citation searching (n = 74), reference lists of included studies (n = 32), conference proceedings (n = 18), and preprint servers (n = 26). Overall, 1,253 records were identified.

The search strategy combined controlled vocabulary, where available, with free-text terms related to CHIKV infection and pediatric populations. The principal concepts included *chikungunya, chikungunya virus, CHIKV, child, children, pediatric, paediatric, infant, newborn, neonate, adolescent, neurologic, neurological, encephalitis, encephalopathy, seizure, Guillain–Barré syndrome*, *vertical transmission, maternal–fetal transmission, perinatal transmission, severe chikungunya, critical illness, intensive care, treatment, management, outcomes, vaccine, vaccination, immunization, immunogenicity, vaccine safety, vaccine effectiveness, and prevention.*

For PubMed/MEDLINE, Medical Subject Headings (MeSH) and free-text terms were combined using Boolean operators. The core pediatric search strategy was structured as follows:
("Chikungunya"[MeSH Terms] OR chikungunya[Title/Abstract] OR "chikungunya virus"[Title/Abstract] OR CHIKV[Title/Abstract]) AND ("Child"[MeSH Terms] OR "Infant"[MeSH Terms] OR "Adolescent"[MeSH Terms] OR child*[Title/Abstract] OR pediatric*[Title/Abstract] OR paediatric*[Title/Abstract] OR infant*[Title/Abstract] OR neonat*[Title/Abstract] OR newborn*[Title/Abstract] OR adolescent*[Title/Abstract])

PubMed/MEDLINE

Additional searches combined the core strategy with terms addressing neurological involvement, severe or critical disease, maternal–fetal and perinatal transmission, neonatal disease, intensive care, therapeutic interventions, clinical outcomes, vaccination, immunogenicity, vaccine safety, effectiveness, and prevention.

For Scopus, the search strategy was adapted to the database syntax using title, abstract, and keyword fields:

TITLE-ABS-KEY (chikungunya OR "chikungunya virus" OR CHIKV) AND TITLE-ABS-KEY (child* OR pediatric* OR paediatric* OR infant* OR neonat* OR newborn* OR adolescent*)

Scopus

Additional combinations incorporated terms related to neurological complications, severe disease, vertical or perinatal transmission, intensive care, treatment, management, clinical outcomes, vaccination, immunogenicity, vaccine safety, effectiveness, and prevention.

WHO Global Index Medicus y PAHO/IRIS

WHO Global Index Medicus and PAHO/IRIS were searched using combinations of terms related to chikungunya, children, pediatric populations, neonatal infection, vertical transmission, severe disease, neurological complications, management, vaccination, vaccine safety, immunogenicity, and prevention.
No publication-date restriction was applied other than the final search date. The complete source-specific search strategies, including exact syntax, date of the final search, and number of records retrieved from each source, are provided in Supplementary Table S1.

Eligibility Criteria

Studies were eligible when they reported original clinical data concerning laboratory-confirmed CHIKV infection in individuals younger than 18 years or evaluated CHIKV-specific preventive interventions in pediatric or adolescent populations and addressed at least one outcome relevant to the review objectives.

Eligible populations included neonates, infants, children, and adolescents with CHIKV infection confirmed by reverse-transcription polymerase chain reaction, virus isolation, CHIKV-specific serological testing, or another validated laboratory method. Studies evaluating maternal infection were eligible only when they reported extractable fetal, neonatal, or pediatric outcomes relevant to vertical or perinatal transmission.

Eligible outcomes included:

- Clinical manifestations and disease spectrum;
- Severe or critical CHIKV infection;
- Neurological manifestations and complications;
- Maternal–fetal, vertical, or perinatal transmission;
- Neonatal manifestations and outcomes;
- Hospitalization and pediatric intensive care unit admission;
- Respiratory, cardiovascular, neurological, or other organ-support requirements;
- Therapeutic interventions;
- Mortality;
- Neurological and neurodevelopmental sequelae;
- Persistent musculoskeletal manifestations;
- Other clinically relevant short- or long-term pediatric outcomes; and
- Vaccine safety, immunogenicity, effectiveness, and other preventive outcomes.

Eligible study designs included prospective and retrospective cohort studies, case-control studies, cross-sectional studies, observational clinical studies, case series, and clinically informative case reports. Full reports identified through conference proceedings or preprint servers were eligible when they contained sufficient original clinical and methodological information for eligibility assessment and data extraction. For studies evaluating preventive interventions, eligible populations included children or adolescents receiving a CHIKV-specific vaccine or another preventive intervention, regardless of previous CHIKV infection status. Studies containing mixed adult and pediatric populations were eligible only when pediatric data could be identified and extracted separately.

Studies were excluded when they:

1. Did not report pediatric-specific or separately extractable pediatric data;

2. Did not address outcomes relevant to the review objectives;
3. Employed a study design that did not provide eligible original pediatric clinical evidence;
4. Did not provide laboratory confirmation of CHIKV infection when laboratory confirmation was applicable to the study population and research question;
5. Contained insufficient clinical or methodological information for eligibility assessment or data extraction; or
6. Represented duplicate publications or overlapping cohort reports without distinct outcomes, follow-up periods, or clinically relevant additional information.

Systematic reviews, scoping reviews, narrative reviews, guidelines, editorials, commentaries, and other secondary sources were not included as primary studies in the qualitative synthesis. They were used for contextualization and backward citation searching. When multiple publications appeared to originate from the same underlying cohort, study setting, recruitment period, population characteristics, sample size, and reported outcomes were compared to determine the extent of participant overlap. A publication was retained only when it provided distinct outcomes, a different follow-up period, or clinically relevant additional information. Duplicate or overlapping reports without additional eligible information were excluded.

Study Selection

All records retrieved from databases, registers, and supplementary sources were compiled and assessed for duplication before formal screening. Among the 1,103 records identified through databases and registers, 380 were removed before screening: 372 duplicate records and 8 records marked as ineligible by automation tools. Consequently, 723 records underwent title and abstract screening. Study selection was performed independently by two reviewers. During the first stage, both reviewers screened the titles and abstracts of the 723 records according to the predefined eligibility criteria. A total of 556 records were excluded, and 167 reports were sought for retrieval. Of these, 21 could not be retrieved; therefore, 146 reports identified through databases and registers underwent full-text eligibility assessment.

The supplementary searches identified 150 reports through other methods. All 150 reports were sought for retrieval; 31 could not be retrieved, leaving 119 reports for full-text eligibility assessment. In total, 317 reports were sought for retrieval, 52 were not retrieved, and 265 full-text reports were assessed for eligibility.

Among the 146 full-text reports identified through databases and registers, 129 were excluded for the following reasons: wrong population (n = 28), wrong outcomes (n = 24), wrong study design (n = 20), no laboratory confirmation of CHIKV infection (n = 15), insufficient data (n = 10), and duplicate or overlapping reports (n = 32). Consequently, 17 studies identified through databases and registers were included.

Among the 119 full-text reports identified through other methods, 104 were excluded for the following reasons: wrong population (n = 20), wrong outcomes (n = 18), wrong study design (n = 15), no laboratory confirmation of CHIKV infection (n = 12), insufficient data (n = 8), and duplicate or overlapping reports (n = 31). Consequently, 15 studies identified through other methods were included.

Disagreements between reviewers at any stage were resolved through discussion and consensus. Overall, 32 studies, represented by 32 reports, were included in the qualitative synthesis. The complete study-selection process is presented in the PRISMA 2020 flow diagram (Figure 2).

Data Extraction

Data extraction was performed independently by two reviewers using a structured data extraction framework developed according to the objectives of the review.

The following information was extracted when available:

- First author and year of publication;
- Country and geographical region;
- Study design and clinical setting;
- Study period;
- Pediatric age group;
- Sample size;
- Criteria and methods used for CHIKV diagnosis;
- Mode of transmission, when relevant;
- Major clinical manifestations;
- Neurological manifestations and complications;
- Maternal–fetal, perinatal, and neonatal manifestations;
- Markers of severe or critical disease;
- Hospitalization and intensive care requirements;
- Respiratory, cardiovascular, neurological, and other organ-support interventions;
- Therapeutic interventions;
- Complications;
- Mortality;
- Neurological and neurodevelopmental outcomes;
- Persistent manifestations and other long-term outcomes; and
- Duration of follow-up.
- Characteristics of preventive interventions, when applicable;
- Vaccine platform, dose, and administration schedule;
- Vaccine safety and adverse events;
- Immunogenicity and seroresponse outcomes; andvaccine effectiveness, when reported.

Data extracted independently by the two reviewers were subsequently compared. Discrepancies were resolved through discussion and consensus, with verification against the original publication when necessary. When multiple reports appeared to originate from the same cohort or contained potentially overlapping participants, study setting, recruitment period, population characteristics, sample size, and outcomes were compared. Data from reports providing distinct outcomes or follow-up periods were synthesized according to the relevant outcome while avoiding duplicate counting of participants.

Risk-of-Bias and Methodological Quality Assessment

Risk of bias and methodological quality were assessed independently by two reviewers using appraisal tools appropriate to the design of each of the 32 included studies. Cohort and case-control studies were evaluated using the Newcastle–Ottawa Scale. Case series and case reports were assessed using the corresponding Joanna Briggs Institute Critical Appraisal Checklists. Cross-sectional studies were

evaluated using the Joanna Briggs Institute Critical Appraisal Checklist for Analytical Cross-Sectional Studies. Randomized clinical trials were assessed using the Cochrane Risk of Bias 2 (RoB 2) tool. The appraisal considered study-design-specific domains, including participant selection, ascertainment of CHIKV infection, comparability where applicable, outcome measurement, adequacy and completeness of follow-up, reporting quality, and potential sources of selection, measurement, and reporting bias.

Disagreements between reviewers were resolved through discussion and consensus.

Because the appraisal instruments differ in structure, domains, and interpretation, results from the different tools were not combined into a single numerical score across study designs or converted into arbitrary categories such as “high,” “moderate,” or “low” quality. Instead, methodological limitations were interpreted within the framework of the relevant instrument and considered when evaluating the reliability and applicability of individual study findings.

The study-level methodological assessments for the 32 included studies are summarized in Table 1.

Data Synthesis

Clinical and methodological heterogeneity was evaluated across the 32 included studies, with particular consideration of differences in age distribution, geographical setting, study design, diagnostic methods, disease severity, clinical definitions, neurological syndromes, therapeutic interventions, duration of follow-up, and outcome reporting. Because substantial heterogeneity was identified across these domains and much of the available pediatric evidence consisted of observational studies, case series, and case reports, statistical pooling was considered inappropriate for the principal outcomes. Therefore, a quantitative meta-analysis was not performed.

Findings were synthesized narratively and organized into the following clinically relevant domains:

Findings were synthesized narratively and organized into the following clinically relevant domains:

1. Overall clinical manifestations and disease spectrum;
2. Severe and critical CHIKV infection;
3. Neurological manifestations and complications;
4. Maternal–fetal and perinatal transmission;
5. Neonatal disease;
6. Hospitalization and intensive care requirements;
7. Therapeutic approaches;
8. Vaccination and other preventive interventions;
9. Mortality and acute clinical outcomes; and
10. Neurological, neurodevelopmental, musculoskeletal, and other long-term outcomes.

Where studies provided sufficiently comparable numerical information, findings were summarized descriptively using reported frequencies, proportions, ranges, and other relevant measures without statistical pooling. Particular attention was given to consistency across studies, study design and methodological limitations, population characteristics, geographical setting, diagnostic certainty, potential overlap among cohorts, and directness of the evidence to pediatric clinical practice.

Certainty and Interpretation of the Evidence

A formal Grading of Recommendations Assessment, Development and Evaluation assessment was not undertaken because the review was primarily intended to characterize and synthesize a clinically and methodologically heterogeneous body of pediatric evidence rather than estimate pooled intervention effects or formulate graded clinical practice recommendations. The strength and clinical relevance of the evidence were interpreted qualitatively by considering study design, risk of bias, sample size, consistency of findings, directness to pediatric populations, diagnostic certainty, duration and completeness of follow-up, and reproducibility across different geographical settings. Greater interpretative weight was given to prospective cohorts, comparative studies, larger observational studies, and findings replicated across independent populations. Evidence derived exclusively from small case series or individual case reports was interpreted as hypothesis-generating or supportive of uncommon clinical manifestations rather than as evidence of incidence, treatment efficacy, or causal association. Therapeutic interventions supported primarily by observational evidence, uncontrolled case series, or individual case reports were described as potential, adjunctive, or investigational approaches and were not presented as established evidence-based recommendations.

Ethics

This systematic review analyzed data from previously published studies and did not involve direct recruitment of human participants, intervention in patient care, or access to identifiable individual-level information. Therefore, institutional review board or research ethics committee approval and individual informed consent were not required.

RESULTS

Study Selection

The study-selection process is summarized in the PRISMA 2020 flow diagram (Figure 2). The systematic search, updated through August 11, 2026, identified 1,103 records through databases and registers: PubMed/MEDLINE (n = 412), Scopus (n = 568), WHO Global Index Medicus (n = 87), and PAHO/IRIS (n = 36). An additional 150 records were identified through other methods: backward citation searching (n = 74), reference lists of included studies (n = 32), conference proceedings (n = 18), and preprint servers (n = 26). Overall, 1,253 records were identified. Before screening, 380 records were removed from the database and register searches, including 372 duplicate records and 8 records marked as ineligible by automation tools. The remaining 723 records underwent title and abstract screening, of which 556 were excluded. Consequently, 167 reports were sought for retrieval; 21 could not be retrieved, leaving 146 reports for full-text eligibility assessment. All 150 reports identified through other methods were sought for retrieval. Of these, 31 could not be retrieved, leaving 119 reports for full-text eligibility assessment. Overall, 317 reports were sought for retrieval, 52 were not retrieved, and 265 full-text reports were assessed for eligibility.

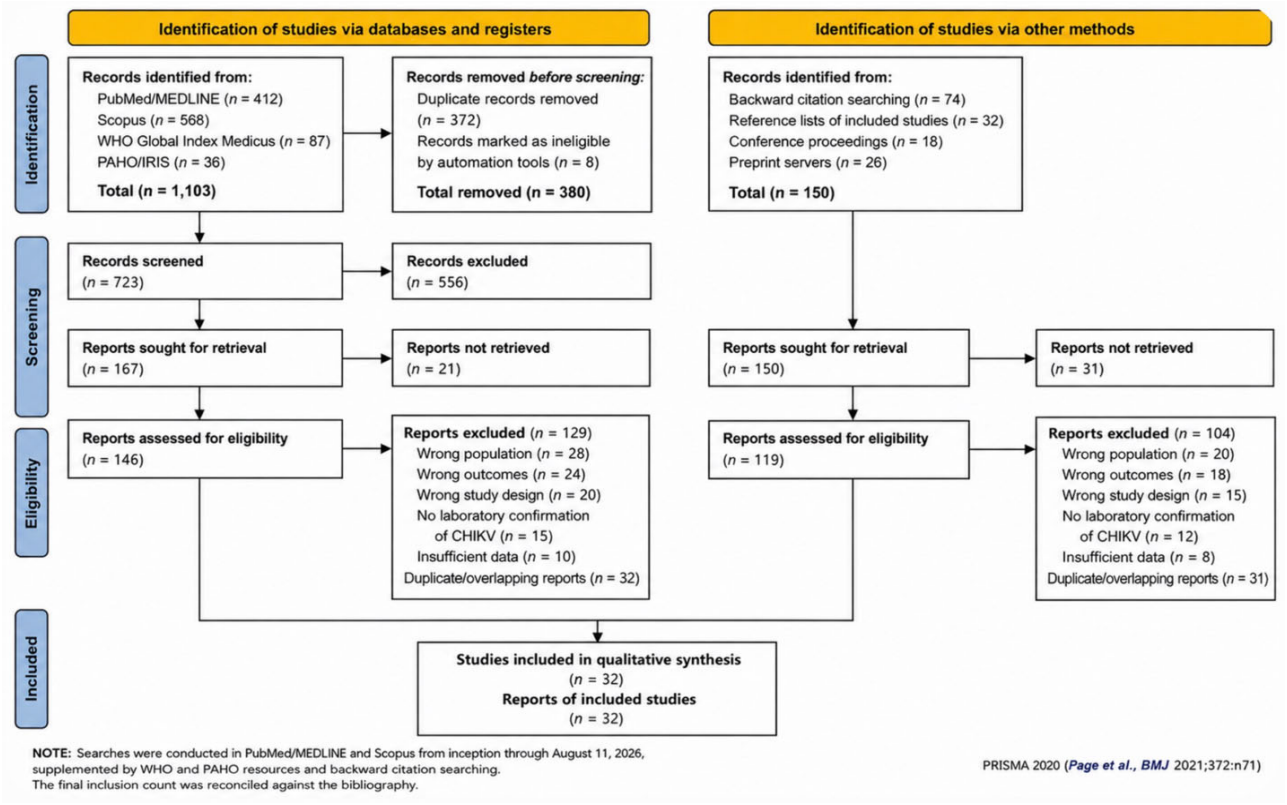

Figure 2. PRISMA 2020 flow diagram of the study-selection process

\Among the 146 reports identified through databases and registers, 129 were excluded because of wrong population (n = 28), wrong outcomes (n = 24), wrong study design (n = 20), absence of laboratory confirmation of CHIKV infection (n = 15), insufficient data (n = 10), or duplicate or overlapping publication (n = 32). Consequently, 17 studies identified through databases and registers were included.

Among the 119 reports identified through other methods, 104 were excluded because of wrong population (n = 20), wrong outcomes (n = 18), wrong study design (n = 15), absence of laboratory confirmation of CHIKV infection (n = 12), insufficient data (n = 8), or duplicate or overlapping publication (n = 31). Consequently, 15 studies identified through other methods were included. Following the updated eligibility assessment, 32 primary studies, represented by 32 reports, were included in the qualitative synthesis.The complete study-selection process and reasons for full-text exclusion are shown in Figure 2. Flow diagram illustrating the identification, screening, retrieval, eligibility assessment, and inclusion of studies in the systematic review. A total of 1,253 records were identified: 1,103 through databases and registers and 150 through other methods. After removal of 372 duplicate records and 8 records marked as ineligible by automation tools, 723 records underwent title and abstract screening. Overall, 317 reports were sought for retrieval, 52 were not retrieved, and 265 full-text reports were assessed for eligibility. Following exclusion of 233 reports, 32 studies, represented by 32 reports, were included in the qualitative synthesis. The literature search was updated through August 11, 2026.

Abbreviations: PAHO, Pan American Health Organization; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; WHO, World Health Organization.

Characteristics of Included Studies

The 32 included primary studies comprised prospective and retrospective cohort studies, cross-sectional and other observational studies, case series, clinically informative case reports, outbreak-surveillance research, and one randomized vaccine trial [11,13,17–20,22,26,29–35,43,44,47–61]. Study populations ranged from neonates to adolescents younger than 18 years and included community-based pediatric cohorts, hospitalized children, patients with severe or critical illness, children with neurological manifestations, neonates exposed to maternal infection, infants with vertically or perinatally acquired CHIKV infection, survivors undergoing long-term neurological or neurodevelopmental follow-up, and adolescents participating in vaccine research [13,17–20,22,26,29–34,43,44,47–61]. Diagnostic confirmation was predominantly based on reverse-transcription polymerase chain reaction during the acute viremic phase, CHIKV-specific serological testing, virus isolation, or combinations of validated molecular and serological methods [17–19,29–33,47,49–61]. Diagnostic approaches varied among studies and across epidemic periods.Laboratory confirmation of acute CHIKV infection was not applicable to uninfected participants enrolled in the preventive vaccine trial [26]. Several publications originated from established maternal–neonatal and longitudinal cohorts conducted on Réunion Island [17,18,34,48,60].Reports from the same underlying population were retained only when they provided distinct outcomes, different follow-up intervals, or clinically relevant additional information. Duplicate or overlapping reports without additional eligible information were excluded, and potentially overlapping participants were not interpreted as independent populations when synthesizing the cumulative evidence. The methodological characteristics, risk-of-bias assessments, and principal limitations of the 32 included primary studies are summarized in Table 1.

Table 1. Methodological Characteristics, Risk-of-Bias Assessment, and Principal Limitations of the 32 Primary Studies Included in the Qualitative Synthesis

Study, year; country/setting	Study design and population	Principal domain	Appraisal tool	Methodological appraisal and principal limitations
Gérardin et al., 2016; Réunion Island	Retrospective cohort including pediatric patients with CHIKV-associated encephalitis	Neurological disease	NOS	Standardized case identification and detailed neurological characterization. Limitations included retrospective data collection, a mixed-age population, possible referral bias, and a relatively small pediatric subgroup.
Beserra et al., 2019; Brazil	Retrospective case series of 14 hospitalized children with severe CHIKV infection	Severe pediatric disease	JBI case series checklist	Laboratory-supported diagnoses and detailed clinical and laboratory descriptions. Limited by the small hospital-based sample, retrospective design, absence of a comparison group, and limited generalizability.
Gérardin et al., 2008; Réunion Island	Prospective multidisciplinary cohort of mothers and neonates exposed to peripartum CHIKV infection	Mother-to-child transmission	NOS	Prospective recruitment, maternal–neonatal assessment, and laboratory confirmation strengthened the study. Limitations included the outbreak-specific setting, relatively few transmission events, and possible residual confounding.
Ramful et al., 2007; Réunion Island	Hospital-based case series of neonates with vertically transmitted CHIKV infection	Neonatal disease	JBI case series checklist	Consistent clinical characterization and laboratory-supported infection. Limited by the small sample, descriptive design, absence of an uninfected comparison group, and limited control of confounding.
Ferreira et al., 2024; Brazil	Case series of perinatal and neonatal CHIKV transmission	Perinatal transmission and neonatal outcomes	JBI case series checklist	Contemporary diagnostic evaluation and detailed maternal–neonatal information. Limitations included the small selected sample, lack of a comparison group, and incomplete standardization of follow-up.
Balmaseda et al., 2016; Nicaragua	Prospective community-based pediatric cohort	Pediatric attack rate and epidemiology	NOS	Active surveillance and a clearly defined pediatric cohort reduced selection and measurement concerns. Estimates were outbreak-dependent, mild or asymptomatic infections may have been missed, and follow-up was relatively short.
Nyamwaya et al., 2021; Kenya	Prospective cohort of children living in a region with endemic CHIKV transmission	Endemic pediatric infection and epidemiology	NOS	Prospective surveillance and laboratory investigation supported exposure ascertainment. Limitations included the geographically circumscribed population, possible infections between assessments, and limited evaluation of severe and long-term outcomes.
Buerger et al., 2026; Brazil	Double-blind, randomized, placebo-controlled phase 3 vaccine trial in adolescents aged 12–17 years	Vaccine safety and immunogenicity	RoB 2	Randomization, masking, placebo control, and prespecified outcomes supported a low overall risk of bias. Applicability was limited to adolescents and immunogenicity; the study did not assess treatment of established infection or adequately characterize very uncommon adverse events.
Bandeira et al., 2016; Brazil	Case report of neonatal encephalitis following vertical CHIKV transmission	Neonatal neurological disease	JBI case report checklist	Laboratory-supported infection and detailed neurological characterization. Limited by the single-patient design, absence of a comparator, restricted causal inference, and publication bias.
Corrêa et al., 2020; Brazil	Retrospective neuroimaging case series of children with perinatal CHIKV infection and neurological complications	Neuroimaging and neurological complications	JBI case series checklist	Detailed magnetic resonance imaging characterization was provided. Limitations included the small clinically selected sample, retrospective design, heterogeneous imaging intervals, and absence of a control group.
Torres et al., 2016; Latin America	Multicountry descriptive case series of congenital and perinatal CHIKV complications	Congenital and perinatal disease	JBI case series checklist	The study documented uncommon outcomes across several Latin American settings. Heterogeneous case ascertainment, a small sample, nonstandardized follow-up, and possible referral and reporting biases limited interpretation.
Evans-Gilbert, 2017; Jamaica	Case report of fatal vertically transmitted neonatal CHIKV infection	Fatal neonatal infection	JBI case report checklist	The report provided a detailed clinical course and a biologically plausible transmission pathway. Its single-case design, lack of a comparator, limited generalizability, and publication bias were major limitations.
Do Monte and Lacerda, 2025; Brazil	Case series of fetal and neonatal deaths associated with maternal CHIKV infection	Fetal and neonatal mortality	JBI case series checklist	Clinically important fatal outcomes were described. The small selected series, incomplete exclusion of alternative causes, absence of a comparison group, and inability to estimate incidence limited the evidence.
Sarton et al., 2025; Réunion Island	Long-term follow-up study of children from the CHIMERE perinatal cohort	Cognitive and learning outcomes	NOS	Extended follow-up and structured neurocognitive assessment were strengths. Limitations included attrition, survivor bias, a relatively small sample, possible overlap with earlier cohort reports, and limited adjustment for social and environmental determinants.
Centers for Disease Control and Prevention, 2023; Paraguay	Descriptive outbreak-surveillance study	Outbreak epidemiology and severe outcomes	JBI analytical cross-sectional checklist	The study provided standardized public health surveillance during a major outbreak. Passive reporting, incomplete case ascertainment, limited pediatric stratification, and underrecognition of mild disease were important limitations.
Oliveira et al., 2024; Brazilian Amazon	Case report of a pediatric patient with neurological CHIKV infection	Neurological manifestations	JBI case report checklist	Laboratory-supported diagnosis and detailed neurological evaluation strengthened the report. The single-patient design, absence of a comparison group, restricted causal inference, and publication bias limited interpretation.

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Gomes et al., 2022; Brazil	Observational study of infants and children evaluated during the 2019 CHIKV outbreak	Arthralgia and age-dependent manifestations	JBI analytical cross-sectional checklist	Systematic pediatric assessment provided clinically relevant information about arthralgia in infants. Limitations included the single-region outbreak sample, cross-sectional assessment, potential selection bias, and limited long-term follow-up.
Robin et al., 2008; Réunion Island	Retrospective pediatric case series	Pediatric neurological manifestations	JBI case series checklist	Focused neurological characterization in children was provided. Limitations included retrospective data collection, a small hospital-based sample, variable diagnostic evaluation, absence of a comparison group, and referral bias.
Gérardin et al., 2014; Réunion Island	Comparative cohort of children exposed to perinatal mother-to-child CHIKV transmission	Neurocognitive outcomes	NOS	The use of a comparison group and standardized developmental assessment strengthened the evidence. Attrition, modest sample size, residual confounding, and overlap with earlier CHIMERE reports remained concerns.
Sharma et al., 2018; India	Hospital-based case series of children with severe CHIKV infection	Severe systemic disease	JBI case series checklist	The study described uncommon severe manifestations using clinical and laboratory information. Limitations included the small selected sample, lack of a comparison group, incomplete denominator information, and referral bias.
Tavares et al., 2025; northeastern Brazil	Retrospective observational cohort of hospitalized children and adolescents	Clinical and epidemiological characteristics	NOS	A defined hospitalized pediatric population and contemporary clinical data were included. Limitations were retrospective data collection, single-region recruitment, preferential inclusion of severe cases, incomplete control of confounding, and limited follow-up.
Simarmata et al., 2016; Singapore	Prospective pediatric cohort with serial virological and immunological assessments	Viral clearance and innate immune response	NOS	Serial sampling and integration of virological and immunological measurements were strengths. The sample was relatively small, severe disease was underrepresented, and the observational associations could not demonstrate causality.
Lewthwaite et al., 2009; India	Hospital-based observational study of children with central nervous system infections	Neuroinvasive CHIKV disease	NOS	Systematic investigation of CHIKV among children with CNS infection supported diagnostic ascertainment. The selected hospital population, limited sample, possible diagnostic misclassification, and incomplete long-term follow-up reduced generalizability.
Maria et al., 2018; India	Case series of neonates with encephalitic CHIKV presentation	Neonatal encephalitis	JBI case series checklist	Detailed descriptions of neurological presentation and short-term clinical evolution were provided. Limitations included the small sample, absence of a comparator, selected tertiary-care population, and limited long-term assessment.
Ferreira et al., 2025; Brazil	Longitudinal cohort of children with intrauterine or perinatal exposure to CHIKV	Neurodevelopmental follow-up	NOS	Longitudinal developmental assessment and clearly characterized exposure groups were strengths. Limitations included a modest sample, attrition, heterogeneous timing of exposure, and possible residual confounding.
Quintans et al., 2025; Brazil	Two-year longitudinal cohort of children vertically exposed to CHIKV	Neurodevelopmental outcomes	NOS	Prospective follow-up and standardized developmental evaluation supported outcome measurement. Limitations included the limited sample, losses to follow-up, variation in diagnostic certainty, and residual socioeconomic confounding.
Samra et al., 2017; Honduras	Retrospective hospital-based pediatric cohort	Clinical and neurological complications	NOS	Pediatric-specific hospital data and detailed neurological characterization were available. Retrospective design, a selected hospitalized population, relatively small sample, and incomplete diagnostic testing were principal limitations.
Kumar et al., 2017; Caribbean	Observational pediatric cohort during the first Caribbean CHIKV epidemic	Epidemiology, clinical manifestations, and laboratory findings	NOS	A defined pediatric cohort and systematic clinical and laboratory characterization strengthened the study. Limitations included the outbreak-specific setting, possible underascertainment of mild infection, and limited evaluation of chronic outcomes.
Shukla et al., 2021; India	One-year follow-up case series of neonatal CHIKV survivors	Long-term neurodevelopmental outcomes	JBI case series checklist	Longitudinal assessment provided information beyond the acute neonatal period. The very small sample, lack of a comparison group, survivor bias, and limited duration of follow-up restricted interpretation.
Najioullah et al., 2026; French Caribbean	Observational pediatric study assessing CHIKV viral load in blood and cerebrospinal fluid in relation to neurological severity	Viral burden and neurological disease	NOS	Paired virological assessment and clinically relevant severity evaluation were strengths. Limitations included the selected neurological population, limited sample, observational design, and possible variation related to the timing of specimen collection.
Sarton et al., 2026; Réunion Island	Matched long-term CHIK13+ cohort of children with perinatal CHIKV infection	Long-term neurodevelopmental outcomes	NOS	The matched design and follow-up extending into later childhood strengthened the evidence. Attrition, survivor bias, a modest sample, residual confounding, and overlap with historical Réunion cohorts remained limitations.
Gaur et al., 2026; India	Case report of CHIKV-associated acute necrotizing encephalopathy in an adolescent	Rare neurological complication	JBI case report checklist	Detailed clinical, neuroimaging, and diagnostic information documented a rare neurological phenotype. The single-patient design, absence of a comparator, inability to establish causality, and publication bias limited the evidence.

Clinical Spectrum of Chikungunya Virus Infection in Children

Across the included studies, fever and rash were among the most consistently reported manifestations of acute pediatric CHIKV infection. Headache, myalgia, fatigue, irritability, gastrointestinal manifestations, and musculoskeletal symptoms were also frequently described, although their clinical expression varied substantially according to age [10,20,47,49–53,56,57].Arthralgia, which represents a hallmark manifestation of CHIKV infection in adults, was less consistently recognized in infants and younger children. In these age groups, musculoskeletal discomfort was sometimes expressed indirectly through irritability, reduced spontaneous movement, refusal to walk, decreased feeding, or inconsolable crying rather than through clearly reported joint pain [10,12,20,47,50,57]. Nevertheless, although arthralgia may be difficult to recognize in infants, prospective clinical assessment indicates that musculoskeletal involvement can be frequent in this age group [44]. Common laboratory abnormalities included leukopenia or lymphopenia, mild-to-moderate thrombocytopenia, and transient elevations in hepatic transaminases. Other abnormalities varied according to disease severity and organ involvement [20,49–53,56,57]. Most pediatric infections followed a self-limited course. Nevertheless, a clinically important subset developed moderate or severe disease characterized by neurological involvement, hemodynamic instability, respiratory compromise, cardiac involvement, coagulopathy, hepatic dysfunction, or multiorgan failure [10–13,31,32,47,49,50,52,53,56,61].

The principal clinical phases of CHIKV infection and their associated pathophysiological mechanisms are summarized in Table 2 [5,7–10,13,16–19].

Severe Disease and Intensive Care Admission

Severe pediatric CHIKV infection was reported disproportionately among neonates, young infants, children with neurological involvement, and patients with underlying clinical vulnerability [10–12,17–19,31–33,47,49,50,53,56]. Severe presentations included hemodynamic instability, shock, respiratory failure, severe dehydration, myocarditis or cardiac dysfunction, coagulopathy, hepatic involvement, neurological deterioration, and multiorgan dysfunction [10,13,17–19,31–33,49,50,53,56]. Admission to pediatric or neonatal intensive care units was required in selected patients with severe disease. Reported intensive care interventions included intravenous fluid resuscitation, vasoactive support, invasive or noninvasive respiratory support, mechanical ventilation, seizure management, correction of metabolic and coagulation disturbances, cardiovascular monitoring, and other forms of organ support [17–19,31–33,47,49,50,53,56]. Mortality was uncommon among children with uncomplicated CHIKV infection but was disproportionately represented among neonates and patients with severe neurological, cardiovascular, or multiorgan disease [10–13,17,18,31–33,49,56]. The available evidence did not permit reliable pooled estimates of pediatric mortality because of marked heterogeneity in study populations, admission criteria, disease severity, outbreak settings, and study design [10,12,16].

Neurological Manifestations

Neurological involvement represented one of the most clinically important forms of severe pediatric CHIKV infection. Encephalitis, encephalopathy, seizures, altered consciousness, focal neurological deficits, acute flaccid paralysis, and other central nervous system abnormalities were reported across pediatric cohorts and individual cases [6,11,12,43,47,52,53,56,59].

Table 2. Clinical Phases and Pathophysiology of Chikungunya Virus Infection

Clinical phase or manifestation	Approximate interval	Predominant pathophysiology	Key clinical manifestations
Acute phase	0–14 days	High viremia; infection of susceptible stromal and immune cells; activation of innate immunity, interferon pathways, and proinflammatory cytokines [5,7,8,51]	Fever, rash, headache, myalgia, arthralgia or age-dependent manifestations of musculoskeletal pain, gastrointestinal symptoms, lymphopenia, thrombocytopenia, and elevated transaminases [10,13,20,22,44,49–53,56,57]
Subacute phase	15–90 days	Declining systemic viremia with persistent inflammatory activation and, in some patients, persistence of viral material or antigens in affected tissues [5,7–9]	Recurrent arthralgia, periarticular discomfort, fatigue, reduced physical activity, and persistent musculoskeletal symptoms [7–10,21,44]
Chronic phase	>3 months	Persistent inflammatory responses, altered immune signaling, and mechanisms implicated in chronic post-CHIKV musculoskeletal disease [7–9,21]	Persistent arthralgia, inflammatory joint manifestations, functional limitation, fatigue, and reduced quality of life in a subset of patients [7–10,21]
Neurological involvement	Acute or delayed	Direct or indirect neuroinflammatory injury, blood–brain barrier dysfunction, viral neuroinvasion in selected cases, systemic inflammatory responses, and postinfectious immune-mediated mechanisms [5,6,11,12,45,59]	Encephalitis, encephalopathy, seizures, altered consciousness, focal neurological deficits, acute flaccid paralysis, Guillain–Barré syndrome, and rare severe encephalopathic syndromes [6,11,12,43,47,52,53,56,59,61]
Cardiovascular involvement	Usually acute	Myocardial injury, systemic inflammation, endothelial dysfunction, altered vascular permeability, and hemodynamic compromise [5,10,13]	Myocarditis, myocardial dysfunction, arrhythmias, hypotension, and shock in severe disease [10,13,49,50,56]
Neonatal/perinatal involvement	Usually following maternal infection around delivery	Vertical or peripartum transmission during maternal viremia, followed by high neonatal viral burden in the setting of immunological immaturity and vulnerability of the developing nervous system [16–19,29–33]	Fever, lethargy, poor feeding, skin manifestations, seizures, respiratory distress, coagulopathy, cardiovascular instability, multiorgan dysfunction, and risk of persistent neurological or neurodevelopmental sequelae [17–19,29–34,48,53–55,58,60]

This table summarizes the principal clinical phases and major organ-specific manifestations of CHIKV infection together with the predominant pathophysiological described in the literature.

Abbreviation: CHIKV, chikungunya virus.

Source: Authors' own elaboration based on references 5–13, 16–22, 29–34, 43–45, 47–61.

Guillain–Barré syndrome and other immune-mediated neurological syndromes were less frequent but were also documented in selected pediatric reports [6,12,45]. The neurological phenotype varied with age. Neonates and young infants frequently presented with seizures, lethargy, irritability, altered responsiveness, or encephalopathy, whereas older children could demonstrate more readily identifiable focal deficits, behavioral changes, cerebellar manifestations, or altered consciousness [17–19,29–32,47,52,53]. Neuroimaging findings were heterogeneous. Some patients had normal imaging despite clinically significant neurological disease, whereas others demonstrated cerebral edema, white-matter abnormalities, inflammatory or encephalitic changes, or other structural alterations [29,30,47,52,53]. Recent pediatric studies have further explored the relationship between viral burden in blood or cerebrospinal fluid and the severity of neurological manifestations, supporting continued investigation of virological and host determinants of neuroinvasive disease [59]. Rare but particularly severe neurological phenotypes, including acute necrotizing encephalopathy, have also been reported, emphasizing the breadth of neurological complications potentially associated with pediatric CHIKV infection [61]. Neurological involvement was associated with increased hospitalization, intensive care requirements, prolonged recovery, and a greater risk of persistent neurological or neurodevelopmental impairment, particularly following severe neonatal or perinatal infection [17–19,29,30,34,47,48,53–55,58,60].

Neonatal and Perinatal Infection

Vertical and perinatal transmission represented a distinct and particularly severe form of pediatric CHIKV infection. Transmission was most consistently documented when maternal infection occurred in close temporal proximity to delivery, particularly during maternal viremia [16–19,31–33]. Affected neonates could initially appear clinically well before developing systemic illness during the first days of life. Reported manifestations included fever, lethargy, irritability, poor feeding, skin manifestations, thrombocytopenia, coagulopathy, seizures, encephalopathy, respiratory distress, cardiovascular instability, and multiorgan dysfunction [17–19,29–33,53].

A substantial proportion of symptomatic neonates described in hospital-based series required neonatal intensive care, including respiratory support, hemodynamic stabilization, neurological monitoring, and treatment of seizures and other organ dysfunction [17–19,31–33,53].

The consequences of perinatal infection extended beyond the acute illness. Longitudinal cohorts demonstrated persistent neurological, cognitive, developmental, behavioral, and motor abnormalities in selected survivors [30,34,48,54,55,58,60]. Updated evidence available through 2026 further strengthens concern that severe perinatal CHIKV infection may be associated with alterations detectable into later childhood and adolescence, including persistent neurodevelopmental and structural neurological abnormalities [34,54,55,60].

However, the magnitude of long-term risk could not be precisely quantified because several follow-up publications originated from the same historical cohorts, sample sizes remained limited, and attrition increased with longer observation periods [34,48,54,55,58,60].

Management Strategies

Management of pediatric CHIKV infection was predominantly supportive. Children with uncomplicated disease were generally managed with antipyretic therapy, adequate hydration, symptomatic treatment, and clinical surveillance [1,3,12,14,24]. Children with severe disease required individualized organ support according to the clinical presentation. Reported interventions included intravenous fluid therapy, vasoactive medications, respiratory support, mechanical ventilation, seizure control, correction of electrolyte and metabolic abnormalities, treatment of coagulation disturbances, and intensive neurological and cardiovascular monitoring [12,17–19,31–33,47,49,53,56]. Corticosteroids and intravenous immunoglobulin (IVIG) have been described as adjunctive interventions in selected severe neurological or inflammatory presentations of CHIKV infection. However, the available evidence is derived predominantly from adult reports, secondary reviews, and uncontrolled observations, with insufficient pediatric-specific evidence to establish efficacy, indications, optimal dosing, or timing of administration [12,45]. Accordingly, neither corticosteroids nor IVIG can currently be considered an established CHIKV-specific treatment in children [12,45]

No specific antiviral therapy with demonstrated clinical efficacy against pediatric CHIKV infection was identified among the included primary studies [1,3,12,14].

Short-Term and Long-Term Outcomes

Short-term outcomes were favorable in most children with uncomplicated infection, with complete or near-complete clinical recovery [10,20,50,51,57]. Nevertheless, patients with severe neurological, neonatal, cardiovascular, or multiorgan disease experienced longer hospitalizations, greater need for intensive care, and occasional mortality [11,17–19,31–33,47,49,53,56]. Persistent musculoskeletal symptoms were documented in a subset of pediatric patients. These included recurrent arthralgia, fatigue, decreased physical activity, and functional limitations during the subacute or chronic phase [7–10,21]. The reported frequency varied considerably according to age, study population, follow-up duration, and methods used to ascertain persistent symptoms [10,21]. Long-term neurological and neurodevelopmental outcomes were of particular concern following severe neonatal and perinatal infection. Longitudinal studies documented developmental delay, cognitive impairment, behavioral abnormalities, motor deficits, and other persistent neurological sequelae in selected survivors [30,34,48,54,55,58,60]. More recent follow-up studies extending into later childhood and adolescence have expanded the available evidence on long-term outcomes after perinatal CHIKV infection. These findings suggest that neurological consequences may persist well beyond the acute and infant periods and may include measurable neurodevelopmental and neuroimaging abnormalities [34,54,55,60]. Interpretation of these findings requires caution because the long-term evidence remains based on relatively small cohorts, several publications involve overlapping historical populations, follow-up attrition is substantial in some studies, and neurodevelopmental assessment methods are heterogeneous [34,48,54,55,58,60]. The principal clinical, epidemiological, management, and outcome-related findings from the included primary studies are summarized in Table 3.

Table 3. Summary of the main findings from the primary studies included in the qualitative synthesis

Domain	Main findings
Study design and setting	The evidence base consisted predominantly of observational cohort studies, cross-sectional studies, case series, and case reports. Studies were conducted mainly in regions affected by epidemic or endemic CHIKV transmission, including Latin America, the Caribbean, South and Southeast Asia, Africa, and island outbreak settings [13,17–20,22,29–34,43,44,47–61].
Age groups	Study populations ranged from neonates to adolescents younger than 18 years. Neonates and young infants were disproportionately represented among patients with severe disease, whereas adolescents were also represented in vaccine research [13,17–19,26,31–33,43,44,47,49,53,56].
Clinical presentation	Fever and rash were consistently reported. Headache, myalgia, gastrointestinal manifestations, irritability, fatigue, and musculoskeletal symptoms were also frequent. Arthralgia may be difficult to recognize in infants and younger children, although systematic clinical assessment indicates that it can be frequent in this age group [10,13,20,22,44,47,49–53,56,57].
Laboratory findings	Leukopenia or lymphopenia, thrombocytopenia, and transient elevations of hepatic transaminases were commonly reported. Additional hematological, biochemical, and inflammatory abnormalities occurred according to disease severity and organ involvement [13,20,22,49–53,56,57].
Severity and hospitalization	Although most pediatric infections were self-limited, severe disease included shock, respiratory compromise, myocarditis or other cardiac dysfunction, neurological deterioration, coagulopathy, hepatic involvement, and multiorgan dysfunction [10–13,17–19,31–33,43,47,49,50,53,56,61].
Intensive care	Pediatric or neonatal intensive care was required principally in neonates, young infants, children with neurological complications, and patients with cardiovascular, respiratory, or multiorgan involvement. Reported interventions included respiratory support, mechanical ventilation, hemodynamic stabilization, seizure control, and other forms of organ support [13,17–19,31–33,43,47,49,50,53,56].
Neurological complications	Encephalitis, encephalopathy, seizures, altered consciousness, focal neurological deficits, acute flaccid paralysis, and, less frequently, Guillain–Barré syndrome were reported. Individual pediatric reports also demonstrate the diversity of central nervous system involvement, and rare severe encephalopathic phenotypes, including acute necrotizing encephalopathy, have been documented [6,11,12,43,47,52,53,56,59,61].
Neonatal and perinatal infection	Maternal infection close to delivery, particularly during maternal viremia, was strongly associated with perinatal transmission. Symptomatic neonates frequently developed neurological and multisystem disease and often required neonatal intensive care [16–19,29–33,53].
Vaccination	Randomized clinical evidence in adolescents indicates that a single-dose live-attenuated CHIKV vaccine can induce a robust immune response. Nevertheless, vaccine findings should be interpreted separately from evidence concerning treatment of established pediatric infection [23–28].
Management strategies	Treatment of pediatric CHIKV infection was predominantly supportive and included hydration, antipyretic therapy, clinical surveillance, seizure control, respiratory or hemodynamic support, and management of organ dysfunction when required. Pediatric-specific evidence is insufficient to establish corticosteroids or IVIG as CHIKV-specific therapies, and no antiviral treatment with proven pediatric clinical benefit was identified [1,3,12,14,24,45].
Short-term outcomes	Most children with uncomplicated disease recovered completely or nearly completely. Adverse acute outcomes, including prolonged hospitalization, intensive care admission, and mortality, were concentrated primarily among neonates and critically ill children with neurological or multisystem involvement [10,13,17–20,22,31–33,43,47,49,50,53,56,57].
Persistent musculoskeletal outcomes	A subset of children developed prolonged arthralgia, fatigue, reduced physical activity, or other musculoskeletal symptoms. The reported frequency varied according to age, study population, follow-up duration, and methods used to identify joint manifestations, particularly in infants [7–10,21,44].
Long-term neurological outcomes	Persistent cognitive, motor, behavioral, neurological, and neurodevelopmental abnormalities were reported primarily following severe perinatal or neonatal infection. Follow-up evidence extending into later childhood and adolescence has expanded understanding of the potential duration of these sequelae [30,34,48,54,55,58,60].
Evidence limitations	The evidence base was dominated by observational designs, small severe-disease cohorts, selected hospital populations, heterogeneous diagnostic and clinical definitions, and variable follow-up methods. Several longitudinal publications involved potentially overlapping historical cohorts, limiting the calculation of independent cumulative estimates [10,12,16,34,48,54,55,58,60].

Abbreviations: CHIKV, chikungunya virus; IVIG, intravenous immunoglobulin.
This table summarizes the principal clinical, epidemiological, preventive, therapeutic, and outcome-related findings identified across the primary studies included in the qualitative synthesis.

Source: Authors' own elaboration based on the studies included in the systematic review.

DISCUSSION

This systematic review provides an updated synthesis of evidence from 32 primary studies on chikungunya virus (CHIKV) infection in pediatric populations, incorporating literature available through August 11, 2026. The findings demonstrate a broad age-dependent clinical spectrum, ranging from uncomplicated acute febrile illness to severe neurological, cardiovascular, respiratory, and multisystem disease. Although most pediatric infections are self-limited, neonates, young infants, and children with neurological or multiorgan involvement consistently emerge as the populations at greatest risk of critical illness and adverse outcomes [10–13,17–20,29–33,43,47,49–61]. The clinical phenotype of CHIKV infection differs substantially across pediatric age groups. Fever and rash were among the most consistently reported manifestations, whereas arthralgia the characteristic manifestation of adult chikungunya was less readily recognized in infants and younger children [10,12,20,44,47,49–53,57].

In these patients, musculoskeletal discomfort may instead manifest as irritability, reduced spontaneous movement, refusal to walk, decreased feeding, or inconsolable crying [10,12,44,47,50,57]. Nevertheless, systematic clinical assessment indicates that arthralgia may be frequent even among infants, despite the difficulty of recognizing and documenting joint pain in this age group [44]. This age-dependent expression has important diagnostic implications, particularly in areas where dengue, Zika, and other acute febrile illnesses circulate simultaneously. Clinical suspicion therefore requires integration of age-specific manifestations with epidemiological exposure and appropriate molecular or serological testing [1,3,10,12,24]. Neurological disease represents one of the most consequential findings of the review. Encephalitis, encephalopathy, seizures, altered consciousness, focal neurological deficits, acute flaccid paralysis, and, less frequently, Guillain–Barré syndrome have been documented across pediatric cohorts and individual reports [6,11,12,43,47,52,53,56,59,61]. Rare severe phenotypes, including acute necrotizing encephalopathy,

further illustrate the breadth of neurological involvement [61]. The mechanisms underlying these manifestations are probably heterogeneous and may include direct viral neuroinvasion, disruption of the blood–brain barrier, systemic and local inflammatory responses, and postinfectious immune-mediated injury [6,11,12,45]. Recent investigation of CHIKV viral load in blood and cerebrospinal fluid did not demonstrate a direct association with the severity of neurological manifestations, indicating that viral burden alone may not explain the neurological phenotype and that host and inflammatory factors probably contribute substantially [59].

The clinical importance of neurological involvement extends beyond acute disease. Children with encephalitis, encephalopathy, or seizures were more likely to require prolonged hospitalization and intensive care, and neurological complications were disproportionately associated with persistent sequelae [11,17–19,29,30,43,47,48,52–55,58,60]. These observations support systematic neurological assessment during acute severe infection and structured post-discharge follow-up, particularly for neonates and infants who experience seizures, encephalopathy, or other evidence of central nervous system involvement [12,30,34,48,54,55,58,60]. Perinatal CHIKV infection constitutes a particularly important pediatric phenotype. The evidence consistently indicates that the risk of vertical or peripartum transmission is greatest when maternal infection occurs close to delivery during the viremic period [16–19,30–33]. Symptomatic neonates may initially appear clinically stable before developing fever, lethargy, poor feeding, thrombocytopenia, coagulopathy, seizures, respiratory distress, cardiovascular instability, encephalopathy, or multiorgan dysfunction [17–19,29–33,53,58]. The frequent requirement for neonatal intensive care among symptomatic vertically infected neonates underscores the importance of coordinated obstetric, neonatal, and infectious-disease management when maternal chikungunya occurs near delivery [16–19,29–33,53].

Importantly, the consequences of perinatal infection cannot be evaluated solely in terms of survival from the acute episode. Earlier cohorts identified neurodevelopmental impairment among survivors [30,48,58], and longitudinal evidence extending into later childhood has strengthened concern regarding persistent cognitive, motor, behavioral, neurological, and structural brain abnormalities following severe perinatal infection [34,54,55,60]. Nevertheless, the magnitude of this risk remains uncertain because the available longitudinal studies include relatively small populations, several reports originate from overlapping historical cohorts, and attrition becomes increasingly important with prolonged follow-up [34,48,54,55,58,60]. These limitations should not obscure the clinical signal but indicate the need for larger prospective cohorts using standardized neurodevelopmental and neuropsychological assessments.

Severe systemic disease outside the nervous system was less common but clinically relevant. Shock, respiratory failure, myocarditis or myocardial dysfunction, coagulopathy, hepatic involvement, and multiorgan dysfunction were reported primarily among neonates, young infants, and critically ill hospitalized patients [10,13,17–19,31,32,49,50,53,56]. The concentration of adverse outcomes within these groups suggests that pediatric risk stratification should emphasize age, neurological involvement, hemodynamic status, organ dysfunction, and the trajectory of illness rather than relying solely on the presence or intensity of arthralgia or other manifestations traditionally associated with adult disease [10,12,13,49,50,56]. Management remains predominantly supportive. Adequate hydration, antipyretic treatment, clinical surveillance, and escalation to respiratory, cardiovascular, neurological, or other organ support when required constitute the principal therapeutic approach [1,3,12,14,24]. No specific antiviral therapy with established clinical efficacy for pediatric CHIKV infection was identified in the included primary studies [1,3,12,14].

Corticosteroids and intravenous immunoglobulin (IVIG) have been described in the broader literature as adjunctive interventions for selected severe neurological or immune-mediated manifestations associated with CHIKV infection. However, the available evidence is derived predominantly from adult case reports, uncontrolled observations, and secondary sources rather than from comparative pediatric studies [12,45]. None of the pediatric primary studies included in this review provided sufficient comparative evidence to establish the efficacy, optimal timing, dosage, or safety of corticosteroids or IVIG as CHIKV-specific therapies. Accordingly, neither corticosteroids nor IVIG can currently be recommended as routine disease-specific treatment for pediatric CHIKV infection. When immunomodulatory therapy is considered for a clearly defined immune-mediated neurological or inflammatory syndrome, its use should be guided by the established indications for that syndrome, specialist assessment, and careful consideration of treatment-related risks rather than by CHIKV infection alone [36–42,45].

The available evidence also indicates that pediatric disease does not invariably terminate with resolution of the acute febrile episode. Arthralgia may be clinically relevant even in infants, while persistent arthralgia, fatigue, reduced physical activity, and functional musculoskeletal complaints have been reported in subsets of children [7–10,21,44]. Although chronic rheumatologic manifestations remain less comprehensively characterized than in adults, their occurrence supports clinical reassessment when musculoskeletal symptoms persist beyond the acute phase [7–10,21,44]. Adult therapeutic approaches to chronic post-chikungunya arthritis, including disease-modifying antirheumatic drugs, should not be extrapolated directly to children without pediatric rheumatology evaluation and an appropriate differential diagnosis [9,21]. These findings have several implications for pediatric and critical care practice. First, neonates and young infants should be regarded as a high-risk population, particularly following maternal infection near delivery [16–19,29–33]. Second, neurological manifestations should prompt early assessment and appropriate escalation of monitoring and supportive care [6,11,12,43,47,52,53]. Third, children surviving severe neurological or perinatal disease warrant longitudinal developmental and neurological surveillance rather than follow-up limited to resolution of the acute infection [30,34,48,54,55,58,60]. Finally, clinical management should remain proportionate to the strength of the evidence: supportive care is established, whereas CHIKV-specific immunomodulatory strategies remain insufficiently supported by pediatric comparative evidence [1,3,12,14,45]. From a public health perspective, prevention remains fundamental because specific pediatric antiviral treatment is unavailable [1,3,14,24]. Measures directed at reducing exposure to *Aedes* mosquitoes remain applicable to children living in or traveling to areas with CHIKV transmission [1,3,14,24].

Prevention is particularly important during pregnancy because maternal infection around delivery can result in severe neonatal disease [15–19,29–33]. Vaccine development and implementation represent an evolving component of chikungunya prevention. Randomized phase 3 evidence is now available regarding the safety and immunogenicity of a live-attenuated vaccine in adolescents aged 12–17 years [26]. Nevertheless, vaccine indications, age eligibility, contraindications, and safety recommendations remain product- and jurisdiction-specific and continue to evolve [23,25–28]. Consequently, pediatric vaccination recommendations should follow current regulatory authorization and public health guidance rather than being extrapolated from adult indications [23,26–28].

Strengths and Limitations

This review has several strengths. It incorporates 32 primary studies conducted across multiple geographic regions and epidemic periods, encompasses the pediatric age spectrum from neonates through adolescents, and specifically integrates severe disease, neurological manifestations, perinatal transmission, intensive care requirements, vaccination evidence, and long-term outcomes. The updated search through August 11, 2026, enabled incorporation of recent pediatric neurological, vaccine, and longitudinal evidence [26,43,54,55,59–61]. Independent study selection, data extraction, and design-appropriate methodological appraisal further strengthened the review process. Several limitations must nevertheless be acknowledged. The pediatric evidence base remains dominated by observational studies, case series, and case reports, with relatively few large comparative cohorts and no robust controlled evidence for CHIKV-specific treatment [12,16,47–61]. Diagnostic criteria, definitions of severe disease, neurological classifications, clinical settings, and follow-up procedures varied substantially, precluding meaningful quantitative pooling of the principal outcomes [10,12,16]. Hospital-based studies may overrepresent severe phenotypes, whereas community cohorts may incompletely capture uncommon neurological or critical manifestations [10,12,22,49,50,57]. Potential participant overlap was another important limitation, particularly among publications derived from the historical maternal–neonatal and longitudinal cohorts conducted on Réunion Island [17,18,34,48,60]. These reports were retained when they contributed distinct outcomes or follow-up periods, but potentially overlapping participants were not treated as independent populations. Long-term studies were additionally limited by small samples, attrition, survivor bias, and heterogeneous neurodevelopmental assessment methods [34,48,54,55,58,60]. Finally, the absence of prospective protocol registration should be considered when interpreting the review, although eligibility criteria, dual-reviewer procedures, methodological appraisal, and the updated search strategy were explicitly defined and reported.

Conclusion

Pediatric chikungunya virus (CHIKV) infection encompasses a broad clinical spectrum, ranging from uncomplicated, self-limited febrile illness to severe neurological, cardiovascular, respiratory, and multisystem disease requiring intensive care. The evidence synthesized in this systematic review indicates that neonates and young infants particularly those with perinatally acquired infection and children with neurological or multiorgan involvement represent the populations at greatest risk of critical illness. Severe manifestations may include encephalitis, encephalopathy, seizures, hemodynamic instability, respiratory compromise, coagulopathy, and multiorgan dysfunction. Neurological involvement is an important determinant of both acute severity and long-term morbidity. Available longitudinal evidence indicates that survivors of severe perinatal or neonatal CHIKV infection may experience persistent neurological, cognitive, motor, behavioral, and neurodevelopmental abnormalities extending beyond infancy and, in some cohorts, into later childhood. These findings support structured neurological and developmental surveillance after severe pediatric infection, particularly following neonatal disease, encephalopathy, or seizures. Nevertheless, the magnitude and duration of this risk remain uncertain because the available longitudinal evidence is derived from relatively small and potentially overlapping cohorts with variable follow-up. Management remains predominantly supportive, as no CHIKV-specific antiviral therapy with established clinical efficacy in children has been demonstrated. Early recognition of severe disease, appropriate hydration and symptomatic treatment, close neurological and hemodynamic monitoring, and timely escalation to pediatric or neonatal intensive care and organ support remain fundamental. Corticosteroids and intravenous immunoglobulin have been described in the broader literature as adjunctive interventions for selected neurological or immune-mediated syndromes; however, pediatric comparative evidence is insufficient to establish their efficacy as CHIKV-specific therapies or support their routine use. Perinatal transmission remains one of the most consequential manifestations of pediatric CHIKV infection and underscores the importance of coordinated obstetric, neonatal, pediatric, and infectious diseases care when maternal infection occurs close to delivery. Prevention of mosquito exposure remains fundamental. Vaccination represents an evolving preventive strategy, including emerging evidence in adolescents; however, its application in pediatric populations must follow current product-specific age indications, regulatory authorizations, contraindications, and national or regional public health guidance. Future research should prioritize prospective multicenter pediatric cohorts, standardized definitions of severe and neurological disease, age-specific therapeutic studies, and long-term neurodevelopmental follow-up using validated assessment instruments. Rigorous evaluation of pediatric preventive strategies, including vaccine safety, immunogenicity, effectiveness, and duration of protection, is also required. Strengthening this pediatric-specific evidence base is essential to improve risk stratification, acute management, prevention, and long-term outcomes among children affected by CHIKV infection.

Author Contributions

Vicente M. Martinez Cardenas conceived and designed the study, developed the methodological framework, conducted the literature search, participated in study selection, data extraction, methodological appraisal, and qualitative synthesis, and drafted the manuscript.

Vivian R. Mena Miranda contributed to study conceptualization and methodology, independently participated in study selection, data extraction, and methodological appraisal, critically interpreted the pediatric intensive care, neurological, and neonatal evidence, and revised the manuscript.

Both authors reviewed and approved the final version of the manuscript and agree to be accountable for all aspects of the work.Both authors reviewed and approved the final version of the manuscript and agree to be accountable for all aspects of the work.

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Conflict of Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Ethics Statement

Not applicable. This study is a systematic review of previously published data and does not involve human participants, identifiable personal information, or interventions requiring ethical approval.

Data Availability Statement

The data supporting the findings of this systematic review were extracted from the published studies cited in the manuscript. The completed data-extraction framework and study-level methodological appraisal are available from the corresponding author upon reasonable request.

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Abbreviations: CHIKV, chikungunya virus; IVIG, intravenous immunoglobulin; NICU, neonatal intensive care unit; PAHO/IRIS, Pan American Health Organization Institutional Repository for Information Sharing; PICU, pediatric intensive care unit; WHO, World Health Organization.

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