Epidemiology, Burden, and Public Health Impact of Rubella Infection and Congenital Rubella Syndrome: A Systematic Review

Muhammad S. Fahad[1,6], Alhaji A. Aliyu[2], Andrew N. Reigns[3], Ifezulike Adaobi Maureen[4], Aminu Usman Gusau[5], Khalifah Abubakar[6], Darlington Chukwuma Ugwu[4,6]

[1] School of Public Health, University of Port Harcourt, Port Harcourt, Nigeria

[2] Department of Community Medicine, Ahmadu Bello University, Zaria, Nigeria

[3] Department of Geography, Federal Polytechnic Ugep, Cross River State, Nigeria

[4] Africa Leadership in Vaccine Expertise (ALIVE), University of the Witwatersrand, Johannesburg, South Africa

[5] Global Health and Infectious Disease Control Institute, Nasarawa State University, Keffi, Nasarawa, Nigeria.

[6] Nigeria Centre for Disease Control and Prevention (NCDC), Abuja, Nigeria

DOI: https://doi.org/10.51244/IJRSI.2026.1308000064

Received: 19 August 2026; Accepted: 24 August 2026; Published: 02 September 2026

ABSTRACT

Rubella is a vaccine-preventable viral infection that remains a significant public health concern because of its association with congenital rubella syndrome (CRS), a leading cause of preventable congenital disability worldwide. This systematic review aimed to synthesize the available evidence on the epidemiology, disease burden, clinical manifestations, and public health impact of rubella infection and CRS.

A systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020) guidelines. A total of 293 records were identified through database searching. Following duplicate removal, screening, and eligibility assessment, 15 studies published between 2014 and 2021 met the inclusion criteria and were included in the review. Data were extracted on study characteristics, study populations, diagnostic approaches, epidemiological findings, clinical manifestations of CRS, and public health outcomes.

The included studies comprised seroprevalence investigations, outbreak studies, surveillance reports, cohort studies, case series, and case reports. The evidence demonstrated ongoing rubella transmission in both endemic and outbreak settings, with susceptibility persisting among pregnant women and other vulnerable populations. School-based outbreak investigations highlighted the contribution of inadequate vaccination coverage to sustained transmission, while serological studies revealed variations in population immunity. Congenital rubella syndrome was associated with congenital heart disease, cataracts, retinopathy, hearing impairment, developmental delay, and neurodevelopmental disorders. Most of the available evidence was derived from descriptive observational studies, highlighting the need for additional large-scale epidemiological investigations.

Rubella infection and CRS continue to impose substantial health and social burdens despite advances in vaccination programmes. Strengthening immunization coverage, enhancing surveillance systems, expanding laboratory diagnostic capacity, and supporting robust epidemiological research are essential for reducing disease burden and advancing rubella elimination efforts.

Keywords: Rubella; Congenital Rubella Syndrome; Epidemiology; Disease Burden; Public Health; Systematic Review

INTRODUCTION

Rubella is an acute vaccine-preventable viral infection that is generally mild or asymptomatic in children and adults but remains an important public health concern because of its consequences during pregnancy. Transmission occurs primarily through respiratory droplets. When infection occurs during early pregnancy, particularly during the first trimester, transplacental transmission may result in miscarriage, stillbirth, fetal death, or congenital rubella syndrome (CRS)(1,2). CRS is characterized by a spectrum of congenital abnormalities, including sensorineural hearing loss, cataracts and other ocular defects, congenital heart disease, developmental delay, and neurological impairment(1,3).

The introduction of rubella-containing vaccines (RCVs) has substantially altered the global epidemiology of rubella and CRS. Countries that have achieved and maintained high vaccination coverage have experienced marked reductions in rubella transmission and CRS, and some regions have achieved elimination of endemic rubella(4,5). Nevertheless, rubella transmission persists in settings where vaccine introduction has been delayed or population-level coverage remains inadequate. Global surveillance data also demonstrate substantial geographical variation in rubella incidence and vaccination coverage, highlighting persistent inequalities in disease control(4).

Population immunity is particularly important for women of reproductive age because susceptibility during pregnancy creates the risk of congenital infection. Seroprevalence studies have demonstrated considerable variation in immunity across populations and settings. Studies among pregnant women and children have identified susceptible population subgroups despite evidence of widespread previous exposure or vaccination(6,7). Rubella outbreaks may consequently occur where immunity gaps accumulate, particularly in schools and other settings characterized by close interpersonal contact(8). Imported infections may also threaten settings in which endemic transmission has been interrupted, emphasizing the importance of sustained laboratory-supported surveillance(9).

Beyond transmission, the principal burden of rubella arises from CRS and its potentially lifelong consequences. Affected children may experience multiple sensory, cardiovascular, ophthalmological, neurological, and developmental impairments, often requiring prolonged medical, rehabilitative, educational, and social support(3,10). Consequently, preventing maternal rubella infection through effective vaccination programmes and maintaining robust surveillance remain central components of CRS prevention and rubella elimination(1,4).

Although numerous studies have investigated rubella seroprevalence, outbreaks, surveillance, CRS manifestations, and vaccination-related public health interventions, the evidence is distributed across diverse populations, geographical settings, and study designs. Differences in diagnostic approaches, population characteristics, surveillance capacity, and reported outcomes complicate direct comparison across studies and may limit a comprehensive understanding of the epidemiology and burden of rubella and CRS. Consolidating this evidence is important for identifying persistent immunity gaps, strengthening surveillance and immunization strategies, and defining priorities for future research.

The aim of this systematic review was to synthesize current evidence on the epidemiology, burden, clinical manifestations, and public health impact of rubella infection and congenital rubella syndrome across different populations and settings.

Main Objective

The main objective of this systematic review was to synthesize available evidence on the epidemiology, burden, and public health impact of rubella infection and congenital rubella syndrome.

Specific Objectives

- To describe the prevalence, seroprevalence, incidence, transmission patterns, and geographical distribution of rubella infection across different populations and settings.

- To assess the burden of congenital rubella syndrome, including its clinical manifestations, complications, and long-term outcomes.
- To evaluate the public health impact of vaccination programmes, surveillance systems, and outbreak response strategies on rubella control and CRS prevention.
- To identify gaps in the current evidence base and highlight priorities for future research, surveillance, and rubella elimination efforts.

METHODOLOGY

Study design and reporting framework

This study employed a systematic review design to synthesize available evidence on the epidemiology, burden, clinical manifestations, and public health impact of rubella infection and congenital rubella syndrome (CRS). The review was conducted and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020) guidelines(11).

The review protocol was registered with the International Prospective Register of Systematic Reviews (PROSPERO) under registration number CRD420261430579.

Inclusion and exclusion criteria

Eligibility criteria were predefined using a Population–Outcome–Study Design framework(12).

Inclusion criteria: Studies were eligible if they: reported epidemiological data on rubella infection or congenital rubella syndrome; examined prevalence, seroprevalence, incidence, outbreaks, transmission patterns, surveillance findings, disease burden, or public health interventions;

included children, adolescents, adults, pregnant women, women of reproductive age, travellers, school populations, or patients with CRS; used laboratory confirmation, surveillance data, or clinical diagnostic criteria;employed observational study designs, including cross-sectional studies, cohort studies, outbreak investigations, surveillance studies, case series, or case reports; and were published in English.

Exclusion criteria: Studies were excluded if they were: review articles, editorials, commentaries, or conference abstracts lacking primary data animal studies; laboratory-only studies without epidemiological or clinical outcomes; vaccine immunogenicity studies without epidemiological findings; or studies lacking sufficient outcome data.

Information sources

A comprehensive literature search was conducted across PubMed/MEDLINE, Embase, Web of Science, Scopus, and African Journals Online (AJOL). Databases were searched from inception to 23 February 2026. The initial search was conducted between 5 and 20 February 2026, followed by a final search update on 23 February 2026. Grey literature was sought from World Health Organization publications, UNICEF reports, institutional repositories, dissertations, theses, Google Scholar, and other relevant sources. Reference lists of included studies and relevant review articles were also manually screened to identify additional eligible publications

Search strategy

The search strategy combined Medical Subject Headings (MeSH) and free-text keywords related to rubella infection, CRS, epidemiology, disease burden, and public health. Principal search terms included “Rubella,” “Rubella virus,” “German measles,” “Congenital Rubella Syndrome,” “CRS,” “epidemiology,” “prevalence,” “seroprevalence,” “incidence,” “outbreak,” “surveillance,” “disease burden,” and “public health.”

Boolean operators AND and OR were used to combine terms. An example of the PubMed search strategy was:

("Rubella" OR "Rubella virus" OR "German measles") AND ("Congenital Rubella Syndrome" OR CRS) AND (epidemiology OR prevalence OR seroprevalence OR incidence OR outbreak OR surveillance OR "disease burden" OR "public health")

The PubMed strategy was adapted for the indexing systems and search functions of the other databases.

Study selection

All records identified through database and supplementary searches were imported into reference management software and duplicates were removed. Screening was conducted in two stages.

First, titles and abstracts were independently screened by two reviewers against the predefined eligibility criteria. Second, full texts of potentially eligible articles were retrieved and independently assessed by the same reviewers. Reasons for exclusion at the full-text stage were documented.

Disagreements regarding eligibility were resolved through discussion and consensus. Where consensus could not be reached, a third reviewer was consulted. The study-selection process was documented using a PRISMA 2020 flow diagram(11).

Data extraction

A standardized data extraction form was developed and piloted using a subset of the included studies(12). Data extracted included author and year of publication, country and geographical region, study design and setting, study population and sample size, participant characteristics, diagnostic methods, prevalence and seroprevalence, incidence, outbreaks and transmission patterns, clinical manifestations and complications of CRS, surveillance findings, vaccination status, outbreak response, key findings, and study limitations.

Extracted data were reviewed for completeness and consistency before synthesis, and discrepancies were resolved through discussion and consensus.

Methodological quality assessment

The methodological quality of included studies was evaluated using the appropriate Joanna Briggs Institute (JBI) Critical Appraisal Checklists, selected according to study design(12). Assessment considered domains relevant to each design, including participant selection, measurement methods, outcome assessment, potential bias, confounding where applicable, and completeness of reporting.

Data synthesis

Because of substantial heterogeneity in study designs, populations, geographical settings, diagnostic methods, and reported outcomes, quantitative meta-analysis was not considered appropriate. Findings were therefore synthesized using a structured narrative approach(12,13). Studies were organized around four principal themes: epidemiology of rubella infection; burden and clinical manifestations of CRS; diagnostic approaches; and public health impact. Findings were compared across studies to identify common patterns, geographical variations, inconsistencies, evidence gaps, and implications for public health practice and future research. Descriptive tables and thematic summaries were used to present the synthesized evidence

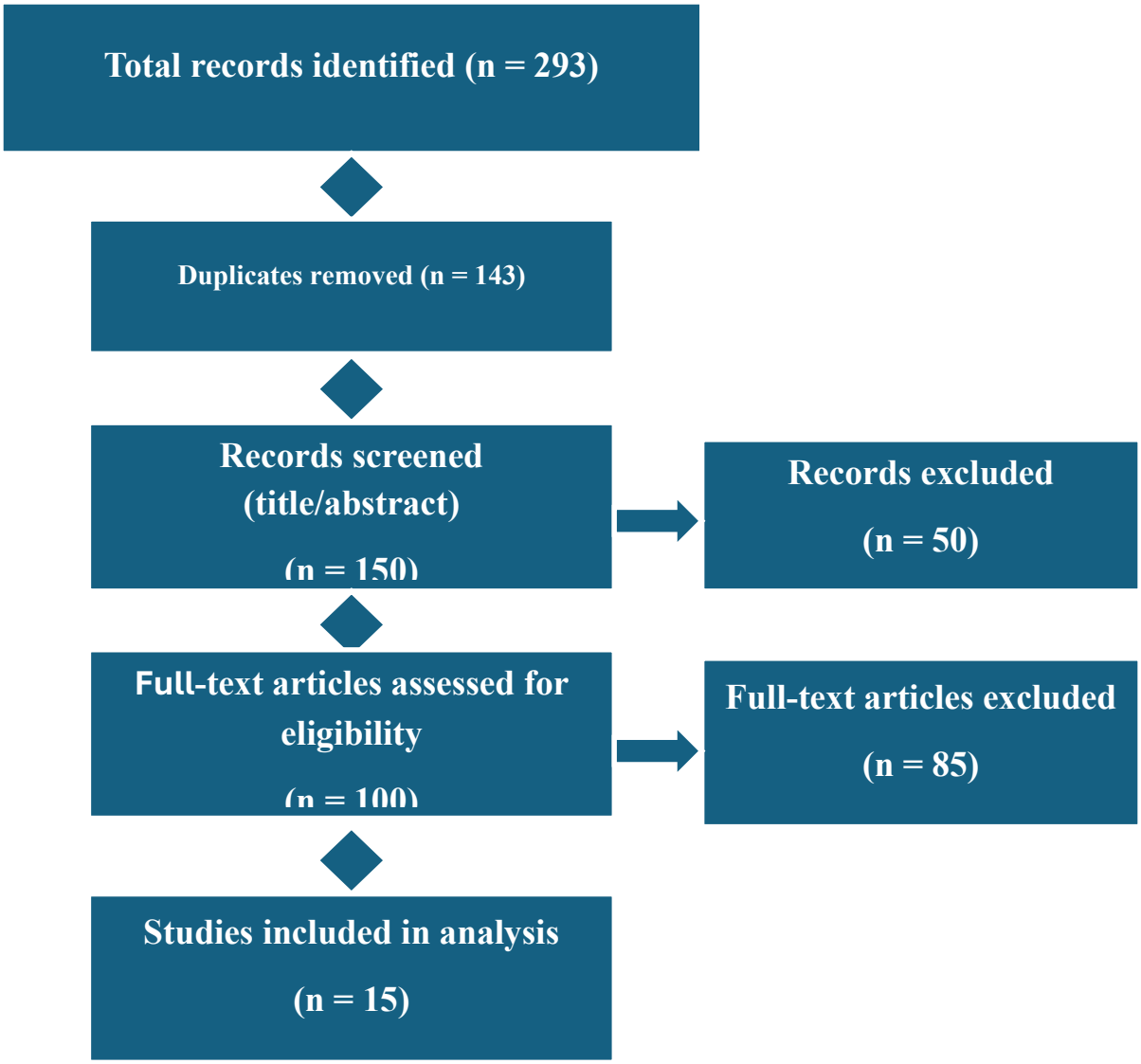
RESULTS

Study selection

A total of 293 records were identified through electronic database and supplementary searches. Following removal of 143 duplicate records, 150 unique records underwent title and abstract screening. Of these, 50 were excluded for not meeting the predefined eligibility criteria, leaving 100 full-text articles for eligibility assessment. Following full-text review, 85 articles were excluded because of failure to meet the eligibility

criteria, insufficient epidemiological or clinical outcome data, ineligible publication type, duplicate publication, or lack of relevance to the review objectives. Ultimately, 15 studies met the inclusion criteria and were included in the systematic review. The study-selection process is presented in

Figure 1: PRISMA 2020 Flow Diagram of Study Selection Process



Characteristics of included studies

The 15 included studies were published between 2014 and 2021 and represented geographical settings across Africa, Asia, Europe, and North America. The evidence base comprised three cross-sectional studies, one cohort study, one outbreak investigation, two surveillance studies, and eight case reports.

Study populations included pregnant women and women of reproductive age, infants and children with CRS, school-aged children, international travellers, and community-based populations. Sample sizes varied substantially, ranging from individual clinical case reports to population-based, surveillance, and outbreak studies involving several hundred or more participants.

Diagnostic approaches also varied. Serological studies predominantly used rubella-specific immunoglobulin M (IgM) and immunoglobulin G (IgG) testing, including enzyme-linked immunosorbent assays (ELISA)(6,7). Molecular techniques, including reverse-transcription polymerase chain reaction and viral genotyping, were employed in outbreak and surveillance investigations(8,9). Clinical assessment combined with laboratory confirmation was used in several CRS investigations(10,14), while histopathological examination was reported in a clinical investigation of congenital rubella(15).

The characteristics and principal findings of the included studies are summarized in Table I.

Table 1. Characteristics of the Included Studies (n = 15)

Author (Year)	Country/Setting	Study Design	Study Population	Diagnostic/Study Focus	Main Findings
Matalia & Shirke (2016)	Not specified	Case report/clinical image	Patient with congenital rubella	Clinical manifestations of congenital rubella syndrome (CRS)	Reported clinical features of congenital rubella syndrome.
Bypareddy et al. (2016)	Not specified	Case report/clinical image	Patient with rubella cataract and retinopathy	Ocular manifestations of CRS	Described rubella-associated cataract and retinopathy in a patient with CRS.
Gupta et al. (2021)	India (tertiary hospital, Northern India)	Cross-sectional observational study	80 infants (<6 months) with structural congenital heart disease and their mothers	Congenital rubella infection among infants with congenital heart disease	CRS prevalence was 8.75% (7/80). Maternal IgG seronegativity was 12.5%. Cataract, splenomegaly, and microcephaly were common findings.
Chan, MacFadden & Leis (2016)	Returned traveller	Case report	Returned traveller	Imported rubella infection	Documented rubella infection in an international traveller, highlighting the risk of disease importation.
Chang et al. (2017)	China (Guangzhou middle school)	Outbreak investigation	1,621 students	School-based rubella outbreak	Identified 162 outbreak cases, including 24 laboratory-confirmed and 138 epidemiologically linked cases. Outbreak-response immunization substantially increased vaccine coverage and reduced transmission.
Kanbayashi et al. (2018)	Japan/Indonesia	Molecular surveillance / Case report	Two travellers returning to Japan	Rubella virus genotyping	Detected Rubella virus genotype 1E lineage 2, demonstrating international transmission.
Ahuja et al. (2015)	Not specified	Case report	Patient with CRS	Dental manifestations of CRS	Reported characteristic dental abnormalities associated with congenital rubella syndrome.

Pitts et al. (2014)	New Jersey, USA	Case report / Public health investigation	Child with CRS	CRS surveillance and public health investigation	Reported CRS in a child born to a woman without recognised risk factors, emphasizing continued surveillance even in elimination settings.
Hutton et al. (2014)	Houston, USA	Prospective descriptive study	298 rubella-nonimmune pregnant women	Rubella exposure during pregnancy	Nineteen women seroconverted during pregnancy, corresponding to an exposure incidence of 6.38**%**.
Ajij, Nangia & Dubey (2014)	India	Case report	Newborn with CRS	Clinical manifestations of CRS	Reported blueberry muffin lesions, congenital heart disease, and metaphysitis in a newborn with CRS.
Singh et al. (2017)	India	Case report	Preterm female infant with CRS	Clinical burden of CRS	Reported low birth weight, hepatosplenomegaly, atrial septal defect, patent ductus arteriosus, bilateral cataracts, and laboratory-confirmed rubella infection.
Toizumi et al. (2017)	Vietnam	Cohort follow-up study	41 children with CRS (21 followed longitudinally)	Long-term outcomes of CRS	Reported 14 deaths, frequent hearing impairment, ophthalmological abnormalities, developmental delay, and suspected autism spectrum disorder among survivors.
Tamirat, Hussen & Shimelis (2017)	Hawassa, Ethiopia	Hospital-based cross-sectional study	422 pregnant women attending antenatal clinics	Rubella seroprevalence	Rubella IgG seroprevalence was 86.3%, IgM positivity was 2.1%, and 13.7% of women remained susceptible to infection.
Lazar et al. (2016)	Fatal CRS cases	Autopsy/pathology case series	Three fatal CRS cases	Distribution of rubella antigen	Demonstrated widespread rubella antigen distribution across multiple tissues in fatal congenital rubella syndrome.
Chotta et al. (2017)	Kilimanjaro, Tanzania	Population-based cross-sectional study	Children aged 0–36 months	Rubella seroprevalence before vaccine introduction	Overall rubella seroprevalence was 1.8%, indicating low natural immunity before introduction of rubella vaccination.

Epidemiology of rubella infection

The included studies demonstrated continued rubella virus transmission in both endemic and non-endemic settings. Three studies investigated rubella seroprevalence or susceptibility in different populations.

Among pregnant women in Ethiopia, rubella IgG seroprevalence was 86.3%, while 2.1% were positive for rubella-specific IgM antibodies, indicating recent infection. Importantly, 13.7% of the pregnant women remained susceptible to rubella infection(6).

In Tanzania, a population-based study conducted before the introduction of rubella-containing vaccine reported a seroprevalence of 1.8% among children aged 0–36 months, indicating low naturally acquired immunity in this population(7). A prospective study involving 298 rubella-nonimmune pregnant women in the United States documented seroconversion in 19 women during pregnancy, corresponding to an exposure incidence of 6.38%(16).

Outbreak investigations provided further evidence of transmission within susceptible populations. A school-based outbreak in Guangzhou, China, identified 162 rubella cases, comprising 24 laboratory-confirmed cases and 138 epidemiologically linked cases. Incomplete vaccination coverage contributed to transmission, while outbreak-response immunization substantially increased vaccine uptake and helped interrupt transmission(8).

International transmission was also documented. Molecular surveillance of travellers returning to Japan identified rubella virus genotype 1E lineage 2, demonstrating the role of international travel in cross-border transmission(9). A separate report of rubella in a returned traveller further illustrated the continuing risk of imported infection in settings where endemic transmission had been controlled(17).

Collectively, the included studies showed substantial geographical variation in rubella epidemiology. Settings with immunity gaps experienced susceptible populations and localized outbreaks, whereas countries with established immunization programmes primarily reported imported infections and relied on surveillance for rapid case identification.

Burden and clinical manifestations of congenital rubella syndrome

CRS was associated with a broad spectrum of cardiovascular, ophthalmological, auditory, neurological, and developmental abnormalities. Congenital heart disease was reported in six studies, making it one of the most frequently documented manifestations.

A cross-sectional study among infants with structural congenital heart disease in Northern India identified laboratory-confirmed congenital rubella infection in 8.75% (7/80) of participants. Reported abnormalities included congenital cardiac defects, cataract, splenomegaly, and microcephaly(18).

Several clinical reports also documented congenital heart defects and multisystem manifestations of CRS(14,15, 17–21).

Ocular abnormalities were prominent. Cataracts were reported in five studies, while rubella retinopathy was reported in two. Clinical reports described congenital cataracts and characteristic retinal changes(15,19), while longitudinal evidence demonstrated persistent visual impairment among affected children(10).

Hearing impairment was reported in four studies, developmental delay in two, and neurological manifestations in three. Long-term follow-up identified developmental delay, impaired cognitive function, and suspected autism spectrum disorder in some children with CRS. Hearing impairment was also associated with speech and language difficulties(10).

Additional manifestations included hepatosplenomegaly, microcephaly, low birth weight, thrombocytopenia, metaphysitis, dental abnormalities, and characteristic “blueberry muffin” skin lesions(18–21).

Mortality was reported in two studies. In the longitudinal cohort from Vietnam, 14 deaths occurred among children with CRS during follow-up(10). Mortality was also documented in another clinical report(22). Survivors frequently experienced multiple coexisting disabilities requiring long-term medical, rehabilitation, developmental, and educational support.

Public health impact

The included studies highlighted vaccination coverage, surveillance, outbreak response, molecular epidemiology, and CRS prevention as major public health considerations.

Seroprevalence findings demonstrated persistent immunity gaps among vulnerable populations. In Ethiopia, 13.7% of pregnant women lacked protective rubella immunity, while 2.1% had evidence of recent infection(6). Similarly, the 1.8% seroprevalence among Tanzanian children before vaccine introduction demonstrated limited naturally acquired immunity and a large susceptible population(7).

The school outbreak in China demonstrated the importance of rapid public health intervention. Case identification, exclusion of infected students, enhanced surveillance, and outbreak-response immunization were associated with increased vaccine coverage and interruption of transmission(8).

Surveillance studies demonstrated that countries approaching or achieving elimination remained vulnerable to imported infections. Laboratory confirmation, molecular surveillance, and viral genotyping enabled identification of imported infections and circulating viral lineages and supported monitoring of transmission pathways(9,17). CRS generated substantial longer-term healthcare needs. Children with CRS frequently required multidisciplinary care because of coexisting cardiac, visual, auditory, neurological, and developmental impairments(10, 18–21).

Overall, the findings emphasized the importance of maintaining high routine immunization coverage, protecting susceptible women before pregnancy, strengthening laboratory-supported surveillance, ensuring timely outbreak investigation and response, and monitoring imported infections.

Methodological quality of included studies

Methodological quality assessed using the appropriate Joanna Briggs Institute critical appraisal checklists ranged from moderate to high. Cross-sectional studies generally had clearly defined populations, appropriate measurement methods, and suitable statistical analyses, although reporting of potential confounding and selection bias was limited in some studies.

The cohort study was rated as high quality, with appropriate follow-up and clearly defined outcomes, although its relatively small sample and loss to follow-up may have affected the precision of its estimates. The outbreak investigation was of moderate-to-high methodological quality, while the two surveillance studies were rated moderate. The eight case reports generally provided adequate descriptions of patient characteristics, clinical presentation, diagnostic procedures, interventions, and outcomes and were rated moderate to high. Nevertheless, their descriptive designs inherently limited generalizability.

Overall, the methodological quality of the included evidence was considered sufficient to address the review objectives, although interpretation was constrained by the predominance of observational studies and case reports and by geographical and methodological heterogeneity.

DISCUSSION

Principal findings

This systematic review synthesized evidence from 15 studies examining the epidemiology, burden, and public health impact of rubella infection and congenital rubella syndrome (CRS) across diverse geographical settings. The evidence demonstrated substantial variation in rubella epidemiology, with persistent susceptibility among vulnerable populations, localized outbreaks associated with immunity gaps, and imported infections in settings

where endemic transmission had been controlled. The review further demonstrated that CRS remains associated with substantial multisystem morbidity, including congenital heart disease, cataracts, hearing impairment, neurological abnormalities, developmental delay, and other long-term complications.

The findings also emphasize the central role of vaccination and surveillance in determining rubella transmission patterns. Settings with suboptimal population immunity continued to demonstrate susceptible populations and localized transmission(6–8), whereas studies from countries with established immunization programmes highlighted imported infections and the importance of continued surveillance(9,17). These findings reinforce the need to maintain high and equitable vaccination coverage alongside effective laboratory-supported surveillance.

Epidemiology and population susceptibility

Considerable variation in population immunity was observed across the included studies. Among pregnant women in Ethiopia, rubella IgG seroprevalence was 86.3%; however, 13.7% remained susceptible to infection and 2.1% had evidence of recent infection(6). This finding is particularly important because susceptibility among women of reproductive age creates an opportunity for primary rubella infection during pregnancy and subsequent congenital infection.

In contrast, the Tanzanian population-based study reported a seroprevalence of only 1.8% among children aged 0–36 months before introduction of rubella-containing vaccine(7). The difference between the Ethiopian and Tanzanian findings should not be interpreted as a direct comparison of disease prevalence because the studies involved different age groups, populations, and vaccination contexts. Rather, the findings demonstrate the heterogeneity of population immunity across settings. The observed geographical variation may reflect differences in vaccination coverage and policies, previous rubella virus circulation, population demographics, and surveillance capacity across settings(4).

Evidence from the school-based outbreak in China further demonstrated the epidemiological consequences of immunity gaps. The outbreak involved 162 cases, including 24 laboratory-confirmed and 138 epidemiologically linked cases(8). The subsequent implementation of outbreak-response immunization increased vaccine uptake and contributed to interruption of transmission. This suggests that high overall vaccination coverage alone may not be sufficient if susceptible individuals remain clustered within particular communities or institutions.

The review also identified international travel as an important consideration for rubella control. Molecular surveillance among travellers returning to Japan identified rubella virus genotype 1E lineage 2 (9), while another imported infection was documented in a returned traveller(17). These findings indicate that interruption of endemic transmission does not eliminate the possibility of virus reintroduction and reinforce the importance of continued case-based and laboratory-supported surveillance in elimination settings.

Burden and clinical manifestations of CRS

The clinical findings demonstrate the multisystem nature of CRS. Congenital heart disease was the most frequently reported manifestation, occurring in six included studies, followed by cataracts in five studies and hearing impairment in four. Neurological manifestations and hepatosplenomegaly were each reported in three studies, while developmental delay and rubella retinopathy were each reported in two.

Cardiovascular abnormalities were documented across several clinical studies (15,18–21)

supporting congenital heart disease as a prominent manifestation of CRS. Gupta et al. (18) identified laboratory-confirmed congenital rubella infection in 8.75% of infants investigated for structural congenital heart disease. However, because much of the evidence arose from clinical case reports and selected patient populations, these findings should be interpreted as demonstrating the spectrum of CRS manifestations rather than estimating their population prevalence.

Ophthalmological complications were also prominent. Cataracts were documented across five studies(10,15,18–20), while rubella retinopathy was reported by Bypareddy et al. (15) and Matalia and Shirke (19). The longitudinal evidence further demonstrated that visual abnormalities may persist into childhood (10).

Hearing impairment was reported in four studies (10,15, 19,23), and represents an important long-term consequence because auditory deficits may subsequently affect speech, language development, education, and social functioning. Developmental delay and neurological manifestations were also identified, with longitudinal follow-up documenting impaired development and suspected autism spectrum disorder among some survivors (10).

The review additionally identified hepatosplenomegaly, microcephaly, low birth weight, thrombocytopenia, metaphysitis, blueberry-muffin lesions, and dental abnormalities(18,20,21,23). Mortality was documented in two studies(10,22), including 14 deaths in the Vietnamese longitudinal cohort(10). Survivors frequently experienced multiple coexisting disabilities requiring multidisciplinary and long-term healthcare. These findings demonstrate that the burden of CRS extends beyond the acute neonatal period and can have enduring consequences for affected children, families, healthcare systems, and social support services.

Vaccination, surveillance and public health implications

Vaccination emerged as a central theme across the evidence. The persistence of susceptible pregnant women in Ethiopia(6) and low natural immunity among young children in Tanzania before vaccine introduction(7) illustrate how immunity gaps can maintain the conditions necessary for rubella transmission and CRS occurrence.

The findings also demonstrate that effective rubella control requires more than routine vaccination alone. During the school outbreak in China, rapid identification of cases, exclusion of infected students, enhanced surveillance, and outbreak-response immunization contributed to interruption of transmission(8).

Laboratory-supported surveillance is particularly important in settings approaching or maintaining elimination. Molecular confirmation and genotyping in the surveillance studies enabled identification of imported infections and transmission pathways(9,17). Consequently, sustained surveillance remains necessary even where endemic transmission has been interrupted.

The findings have particular implications for women of reproductive age. Prevention of maternal infection remains fundamental to preventing CRS. Public-health programmes should therefore aim to maintain high childhood vaccination coverage while also addressing susceptible women before pregnancy in accordance with national immunization policies. CRS surveillance should complement rubella surveillance because monitoring congenital outcomes provides additional information on the consequences of gaps in population immunity.

Strengths and limitations

A major strength of this review was its broad consideration of epidemiological, clinical, and public-health evidence rather than focusing exclusively on a single outcome such as seroprevalence. The review included evidence from Africa, Asia, Europe, and North America and considered populations ranging from pregnant women and young children to school populations, travellers, and children affected by CRS. Methodological quality was assessed using study-design-specific JBI critical appraisal checklists, with overall quality ranging from moderate to high.

Several limitations must nevertheless be considered. First, the evidence base comprised only 15 studies, limiting the breadth of evidence available for synthesis. Second, eight studies were case reports, while only three were cross-sectional studies, one was a cohort study, one was an outbreak investigation, and two were surveillance studies. The predominance of case reports limits generalizability and prevents reliable estimation of the population frequency of many CRS manifestations.

Third, substantial heterogeneity existed in study populations, geographical settings, diagnostic approaches, study designs, and reported outcomes. Quantitative meta-analysis was therefore considered inappropriate, and the evidence was synthesized narratively. This limits the ability to generate a single pooled estimate of rubella prevalence or CRS burden.

Fourth, evidence from some low- and middle-income countries where rubella remains an important public-health concern was limited. Differences in surveillance systems, vaccination policies, diagnostic capacity, and reporting practices across countries may also have influenced the observed epidemiological and clinical findings.

These limitations mean that the review findings should be interpreted as a synthesis of the patterns, clinical spectrum, and public-health implications represented by the available studies, rather than as precise global estimates of rubella or CRS burden.

Implications for policy and future research

The findings support strengthening routine rubella immunization and addressing immunity gaps among susceptible populations, particularly women of reproductive age. Laboratory-supported surveillance should be maintained or strengthened to facilitate early case detection, confirmation, outbreak investigation, molecular characterization where feasible, and identification of imported infections. Infants suspected of having CRS should receive appropriate multidisciplinary assessment and long-term follow-up because of the potential for cardiovascular, ophthalmological, auditory, neurological, and developmental complications. These priorities are consistent with the findings of the present review and reinforce the need for integrated vaccination, surveillance, and long-term clinical management strategies.

Future research should prioritize large population-based epidemiological studies, particularly in underrepresented low- and middle-income settings. Prospective cohort studies are also needed to characterize the long-term health, developmental, educational, and social consequences of CRS. Further evaluations of vaccination strategies, surveillance systems, and outbreak-response interventions would strengthen the evidence available for policy decisions and rubella elimination programmes.

International collaboration also remains important because rubella can cross national borders through travel and population movement. Information sharing, coordinated surveillance, laboratory capacity, equitable access to vaccination, and timely outbreak response are therefore relevant components of sustained rubella control and elimination.

FUTURE DIRECTIONS

Future research on rubella infection and congenital rubella syndrome should prioritize large-scale, population-based epidemiological studies, particularly in low- and middle-income countries where surveillance and diagnostic capacity may be limited. The predominance of case reports among the studies included in this review highlights the need for more robust observational and longitudinal studies capable of generating representative estimates of rubella transmission, population susceptibility, and CRS burden.

Prospective seroprevalence and surveillance studies are needed to identify immunity gaps, particularly among women of reproductive age and other susceptible populations. Greater standardization of rubella and CRS case definitions, diagnostic methods, and outcome reporting would also improve comparability across studies and facilitate future quantitative synthesis.

Long-term cohort studies should examine the clinical, developmental, educational, and social outcomes of children affected by CRS. Such studies are particularly important for understanding the long-term consequences of hearing impairment, visual abnormalities, congenital heart disease, neurological complications, and developmental disorders identified in this review.

Future research should also evaluate the effectiveness of vaccination strategies, laboratory-supported surveillance systems, outbreak-response interventions, and molecular epidemiological approaches. Evidence from such studies could strengthen programme planning and support national, regional, and global efforts toward sustained rubella and CRS elimination.

CONCLUSION

This systematic review demonstrates that rubella infection and congenital rubella syndrome remain important public health concerns despite the availability of effective vaccination. Evidence from the 15 included studies showed substantial geographical variation in rubella epidemiology, persistent susceptibility among vulnerable populations, localized outbreaks associated with immunity gaps, and imported infections in settings where endemic transmission had been controlled.

CRS was associated with substantial multisystem morbidity, particularly congenital heart disease, cataracts, hearing impairment, neurological abnormalities, and developmental delay. The occurrence of multiple coexisting disabilities and mortality among affected children demonstrates that the consequences of maternal rubella infection can extend well beyond infancy and impose long-term healthcare and social burdens.

Sustained progress toward rubella and CRS elimination therefore requires high and equitable vaccination coverage, protection of susceptible women of reproductive age, strengthened laboratory-supported surveillance, timely outbreak detection and response, and continued monitoring of CRS. More robust population-based and longitudinal research is also required to address existing evidence gaps and provide stronger epidemiological evidence for public health decision-making.

REFERENCES

1. WHO (2023) Rubella [Internet]. Available from: https://www.who.int/news-room/fact-sheets/detail/rubella
2. Papka NY, Okoro CC, Anani E, Raji MA, Chinawa JM. Congenital rubella syndrome and its protean manifestation in Nigeria. Egypt Pediatr Assoc Gaz. 2024 Nov 25;72(1):97. doi:10.1186/s43054-024-00337-4
3. Simons EA, Reef SE, Cooper LZ, Zimmerman L, Thompson KM. Systematic Review of the Manifestations of Congenital Rubella Syndrome in Infants and Characterization of Disability-Adjusted Life Years (DALYs). Risk Anal. 2016 Jul;36(7):1332–56. doi:10.1111/risa.12263
4. Patel MK, Antoni S, Danovaro-Holliday MC, Desai S, Gacic-Dobo M, Nedelec Y, et al. The epidemiology of rubella, 2007–18: an ecological analysis of surveillance data. Lancet Glob Health. 2020 Nov;8(11):e1399–407. doi:10.1016/S2214-109X(20)30320-X
5. Vynnycky E, Adams EJ, Cutts FT, Reef SE, Navar AM, Simons E, et al. Using Seroprevalence and Immunisation Coverage Data to Estimate the Global Burden of Congenital Rubella Syndrome, 1996-2010: A Systematic Review. Trotter CL, editor. PLOS ONE. 2016 Mar 10;11(3):e0149160. doi:10.1371/journal.pone.0149160
6. Tamirat B, Hussen S, Shimelis T. Rubella virus infection and associated factors among pregnant women attending the antenatal care clinics of public hospitals in Hawassa City, Southern Ethiopia: a cross-sectional study. BMJ Open. 2017 Oct;7(10):e016824. doi:10.1136/bmjopen-2017-016824
7. Chotta NAS, Mgongo M, Uriyo JG, Msuya SE, Stray-Pedersen B, Stray-Pedersen A. Rubella sero-prevalence among children in Kilimanjaro region: a community based study prior to the introduction of rubella vaccine in Tanzania. Ital J Pediatr. 2017 Dec;43(1):63. doi:10.1186/s13052-017-0379-3
8. Chang C, Ma H, Liang W, Hu P, Mo X, An Z, et al. Rubella outbreak and outbreak management in a school setting, China, 2014. Hum Vaccines Immunother. 2017 Apr 3;13(4):772–5. doi:10.1080/21645515.2016.1252494
9. Kanbayashi D, Kurata T, Nishino Y, Orii F, Takii Y, Kinoshita M, et al. Rubella Virus Genotype 1E in Travelers Returning to Japan from Indonesia, 2017. Emerg Infect Dis. 2018 Sep;24(9):1763–5. doi:10.3201/eid2409.180621

10. Toizumi M, Nguyen GTH, Motomura H, Nguyen TH, Pham E, Kaneko K ichi, et al. Sensory defects and developmental delay among children with congenital rubella syndrome. Sci Rep. 2017 Apr 13;7(1):46483. doi:10.1038/srep46483
11. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021 Mar 29;n71. doi:10.1136/bmj.n71
12. Aromataris E, Lockwood C, Porritt K, Pilla B, Jordan Z, editors. JBI Manual for Evidence Synthesis [Internet]. JBI; 2024 [cited 2026 Jul 13]. Available from: https://jbi-global-wiki.refined.site/space/MANUAL doi:10.46658/JBIMES-24-01
13. Popay J, Roberts H, Sowden A, Petticrew M, Arai L, Rodgers M, et al. Guidance on the conduct of narrative synthesis in systematic reviews: A product from the ESRC Methods Programme [Internet]. Lancaster University; 2006 [cited 2026 Jul 13]. Available from: https://www.researchgate.net/doi/10.13140/2.1.1018.4643 doi:10.13140/2.1.1018.4643
14. Pitts SI, Wallace GS, Montana B, Handschur EF, Meislich D, Sampson AC, et al. Congenital Rubella Syndrome in Child of Woman without Known Risk Factors, New Jersey, USA. Emerg Infect Dis. 2014 Feb;20(2):307–9. doi:10.3201/eid2002.131233
15. Bypareddy R, Chawla R, Azad SV, Khokhar S. Rubella cataract and retinopathy. BMJ Case Rep. 2016 Jun 10;2016:bcr2016216112. doi:10.1136/bcr-2016-216112
16. Hutton J, Rowan P, Greisinger A, Mouzoon M. Rubella monitoring in pregnancy as a means for evaluating a possible reemergence of rubella. Am J Obstet Gynecol. 2014 Nov;211(5):534.e1-534.e4. doi:10.1016/j.ajog.2014.05.046
17. Chan T, MacFadden DR, Leis JA. Rubella in a returned traveller. Can Med Assoc J. 2016 Mar 15;188(5):363–6. doi:10.1503/cmaj.150574
18. Gupta S, Verma S, Dash N, Goel M, Rawat A, Singh MP, et al. Congenital Rubella: A Salient Cause of Congenital Heart Defects in Infants. J Trop Pediatr. 2021 May 17;67(2):fmab044. doi:10.1093/tropej/fmab044
19. Matalia J, Shirke S. Congenital Rubella. N Engl J Med. 2016 Oct 13;375(15):1468–1468. doi:10.1056/NEJMicm1501815
20. Singh A, Narula S, Kareem H, Devasia T. An infant with congenital rubella syndrome in developing India. BMJ Case Rep. 2017 Nov 28;2017:bcr-2017-221665. doi:10.1136/bcr-2017-221665
21. Ajij M. Congenital Rubella Syndrome with Blueberry Muffin Lesions and Extensive Metaphysitis. J Clin Diagn Res. 2014. doi:10.7860/JCDR/2014/10271.5293
22. Lazar M, Perelygina L, Martines R, Greer P, Paddock CD, Peltecu G, et al. Immunolocalization and Distribution of Rubella Antigen in Fatal Congenital Rubella Syndrome. EBioMedicine. 2016 Jan;3:86–92. doi:10.1016/j.ebiom.2015.11.050
23. Ahuja R, Shigli AL, Thakur G, Jain U. Dental manifestations of congenital rubella syndrome. BMJ Case Rep. 2015 Feb 26;2015:bcr2015209382. doi:10.1136/bcr-2015-209382