International Journal of Scientific Advances
ISSN: 2708-7972
Volume: 6 | Issue: 6 | Nov – Dec 2025 Available Online: www.ijscia.com
DOI: 10.51542/ijscia.v6i6.10

Ocular Abnormalities in Congenital Rubella Syndrome: A Literature Review

Aisyah Rahmah Salsabila[1], Dwiyanti Puspitasari[2*], Indri Wahyuni[3], Rozalina Loebis[3]

[1]Medical Program, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia

[2]Department of Pediatric, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia

[3]Department of Ophthalmology, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia

E-mail: aisyah.rahmah.salsabila-2022@fk.unair.ac.id; dwiyanti-p@fk.unair.ac.id; indri-w@fk.unair.ac.id; rozalina-l@fk.unair.ac.id

*Corresponding author details: Dwiyanti Puspitasari; dwiyanti-p@fk.unair.ac.id

ABSTRACT

This literature review examines the epidemiology, clinical profile, diagnosis, and management of Congenital Rubella Syndrome (CRS), focusing on endemic regions. Despite global success in reducing cases to 32,000 by 2019, severe disparities persist, particularly in Southeast Asia. Indonesia reported 229 cases in 2021, constituting 57% of the total regional burden, highlighting critical immunization gaps. The clinical findings confirmed the CRS triad, with hearing impairment being the most prevalent sequela. Management is strictly preventative, as no curative treatment exists. Diagnosis relies on serological confirmation and early screening, given the high rate of diagnosis in the month age group. This review advocates for aggressive RCV campaigns for women of childbearing age, coupled with urgent neonatal screening protocols for auditory and ocular defects to ensure timely surgical and rehabilitative intervention, mitigating the lifelong developmental costs of the syndrome.

Keywords: congenital rubella syndrome; CRS; rubella; ocular abnormalities

INTRODUCTION

The most critical consequence of maternal rubella infection is Congenital Rubella Syndrome (CRS), a constellation of severe developmental anomalies resulting from transplacental viral transmission, particularly when the mother contracts the virus during the first trimester of pregnancy. CRS is defined by a spectrum of defects traditionally grouped into major and minor categories. The major defects, which are responsible for the most significant lifelong morbidity, involve the auditory, cardiac, and ocular systems. This classic triad comprises sensorineural hearing impairment, specific congenital heart defects, and serious ocular abnormalities [1]. While minor defects as purpura, splenomegaly, and microcephaly may present, the severity of the major anomalies underscores the urgent clinical necessity of preventing maternal infection.

Despite the availability of highly effective Rubella-containing Vaccines (RCV), the global burden of CRS remains high and unevenly distributed, highlighting critical gaps in immunization and surveillance programs. Epidemiological data consistently reveal significant geographic disparities, with regions of suboptimal vaccination coverage, notably in Africa and the Eastern Mediterranean, bearing the highest incidence estimated at thousands of cases annually. Furthermore, local institutional data from areas like Indonesia documented hearing impairment in over half, 55.4% of recorded CRS cases.

The high, heterogeneous burden of CRS necessitates current comparative analysis beyond mere incidence statistics. Therefore, this literature review aims to synthesize the current global evidence to comprehensively delineate the regional epidemiological patterns and provide a comparative analysis of the specific clinical manifestations of CRS.

METHODS

This study was conducted as a focused Narrative Literature Review aimed at synthesizing current evidence regarding the global epidemiology, clinical profile, and management strategies for Congenital Rubella Syndrome (CRS).

RESULT

The structured literature review confirmed a significant global reduction in CRS cases (down to an estimated 32,000 in 2019); however, this success is overshadowed by pronounced regional disparities. Indonesia was identified as a critical focus area, reporting 229 cases in 2021, which constituted 57% of the total cases in the WHO SEARO region (2). Local studies further emphasized the urgency, showing a high proportion of suspected cases presenting in the month age group in Surabaya (3,4). Clinically, the analysis consistently reinforced hearing impairment as the most prevalent sequela, with ocular defects (cataracts and glaucoma) demanding time-sensitive surgical intervention (e.g., cataracts optimally managed between 4 to 10 weeks of age). The collective findings underscore that since no curative treatment exists, management relies solely on primary prevention (RCV vaccination) and rigorous secondary prevention, emphasizing the need for early neonatal screening protocols to facilitate timely surgical management.

CONGENITAL RUBELLA SYNDROME

Definition and Epidemiology of CRS

Rubella, or German measles, is an infection caused by a positive-stranded RNA virus of the Togaviridae family. The virus spreads via droplets, leading to systemic infection. While generally mild, the infection is critical when acquired by pregnant women, particularly during the first trimester. This maternal infection frequently leads to severe complications, including miscarriage, fetal demise, or Congenital Rubella Syndrome (CRS), defined by a constellation of severe defects. The highest risk of severe fetal damage occurs within the first 12 weeks of gestation, diminishing rapidly after the 20th week [1,5]. CRS is characterized by the classic triad: hearing impairment, congenital heart defects, and ocular abnormalities.

The urgency is acute in Southeast Asia; Indonesia reported 229 cases in 2021, accounting for 57% of the total cases in the region. WHO SEARO region [2]. Local studies in Surabaya (RSUD Dr. Soetomo) reported 145 clinically confirmed CRS cases from 346 suspects, with the majority of suspected cases occurring in the <1-month age group [3,4]. Further analysis of this cohort indicated that the most frequent defect was hearing impairment. This significant local disease burden, combined with the fluctuating national incidence in Indonesia and the early age of diagnosis, necessitates a focused review.

Risk Factor, Diagnosis, and Therapy of CRS

Understanding the risk factors contributing to Congenital Rubella Syndrome (CRS) is crucial for primary prevention. The key risk factors include lack of Rubella vaccination, travel to endemic regions, exposure to infected individuals, and underlying immune deficiency [6]. CRS pathogenesis hinges critically on the timing of maternal infection; the highest risk of severe fetal anomalies occurs during the first 12 weeks of gestation, highlighting that protection strategies must exclusively target the susceptible population of women of childbearing age (WOCBA) before conception. The resulting clinical profile is characterized by the classic triad auditory, cardiac, and ocular anomalies with local data often establishing hearing impairment as the most frequent and persistent sequela.

The definitive diagnosis of CRS is multi-faceted, requiring careful anamnesis, specific physical examination, and serological confirmation, as outlined by the WHO criteria [7]. Clinical identification includes physical signs such as microcephaly, ocular abnormalities (glaucoma), and cardiac defects (e.g., PDA, marked by murmurs) [8]. Diagnosis relies on a classification system differentiating between suspected CRS (one major manifestation) and clinical CRS (two major or one major and one minor manifestation). Serological testing is the cornerstone for confirmation: positive Rubella IgM is required for infants aged <6 months, while older infants necessitate positive IgM/IgG results. The presence of IgG antibodies is indicative of protective immunity, guiding the evaluation of maternal susceptibility.

As no specific curative treatment exists for established CRS, prevention is the paramount management strategy. Primary prevention is achieved through the prioritization of Rubella vaccination, which is essential for infants, adolescents, and WOCBA [5]. The vaccine is typically delivered as a combined Measles-Mumps-Rubella (MMR) vaccine, with standard schedules recommending a primary dose followed by a booster dose to ensure sustained immunity [8]. Aligning with the 2011 WHO recommendation to integrate RCV into national immunization programs, the success of this primary prevention hinges on achieving and maintaining high vaccination coverage to break the chain of maternal transmission.

Beyond primary vaccination, secondary prevention and rehabilitative management are crucial for minimizing long-term morbidity in affected infants. Given that local studies demonstrate a high proportion of cases are diagnosed in the <1-month age group [3,4], early intervention is feasible and vital. This necessitates the urgent establishment of standardized neonatal screening protocols for auditory and ocular defects in high-burden centers. Prompt identification of anomalies allows for timely surgical intervention (e.g., cataracts, cardiac defects) and rehabilitation (e.g., hearing aids), thereby improving developmental outcomes and reducing the substantial lifelong burden of the syndrome.

CONGENITAL CATARACT

Definition and Epidemiology of Congenital Cataract

Congenital cataract, defined as opacity of the lens reducing light transmission to the retina, is a major global cause of reversible visual impairment and blindness [9]. Its significance within the context of CRS is paramount, as maternal Rubella infection during the first trimester is consistently cited as the most frequent infectious cause associated with complex congenital anomalies [10].

The global incidence of congenital cataracts is substantial, estimated at between 20,000 to 40,000 cases annually [11]. Regional data emphasize this burden; Indonesia, for example, shares a significant prevalence, estimated at 0.6% per 10,000 births, falling within the 1.7–14.7 cases per 10,000 births reported across Asia [9]. Furthermore, visual impairment due to congenital cataract remains the leading cause of childhood blindness. This high prevalence underscores the urgent need for robust Rubella immunization programs, as prevention remains the only means to mitigate this severe and costly outcome of CRS.

Risk Factor, Diagnosis, and Therapy of Cataract Congenita

The discussion of CRS management must incorporate the specialized management of congenital cataracts, a leading cause of treatable childhood blindness globally. While intrauterine infection, notably by the Rubella virus during the first trimester, is a key risk factor for congenital cataracts associated with CRS [9,10], other factors include autosomal dominant genetic inheritance (and less commonly, recessive or X-linked), metabolic disorders, diabetes, and trauma [12].

Diagnosis relies on timely ocular screening, ideally performed in infants aged 0 to 4 months. The definitive diagnostic procedure begins with a detailed anamnesis, followed by physical examination of the eye, crucially including the red reflex screening using a direct ophthalmoscope in a dimmed room [13].

Management is bifurcated: non-surgical therapy (using spectacles and pupil dilation) is reserved for incomplete or peripheral cataracts (<3 mm opacity), whereas surgery is indicated for opacities obstructing the red reflex or exceeding 3 mm. The timing of surgical intervention is critical: the optimal age for unilateral congenital cataract surgery is 4–6 weeks, while bilateral cataracts are optimally addressed at 8–10 weeks to prevent vision-depriving amblyopia, highlighting the urgency of early detection [13].

CONGENITAL GLAUCOMA

Definition and Epidemiology of Congenital Glaucoma

Congenital glaucoma is a rare, inherited developmental anomaly occurring at birth, fundamentally characterized by abnormally high intraocular pressure (IOP) [14]. This elevation in IOP stems from a developmental abnormality in the trabecular meshwork and the anterior chamber angle. The underlying pathophysiology involves impaired aqueous humor outflow, often conceptualized by Barkan's theory, which proposes an imperforate membrane hindering fluid drainage [14]. Congenital glaucoma is a significant ocular disorder that contributes to total blindness, and its presence can be a key component of complex syndromes, including Congenital Rubella Syndrome (CRS).

While rare, it manifests across diverse countries and ethnic groups. Epidemiological data show considerable variation in incidence rates globally. In Western countries, such as Ireland, the United Kingdom, and the United States, the incidence of PCG ranges from 1 per 10,000 to 1 per 20,000 live births [15]. Other sources report an overall prevalence of approximately 1:10,000 live births [16]. This persistent, albeit low, incidence underscores the need for early and accurate diagnostic screening, as timely intervention is crucial for mitigating the irreversible vision loss associated with chronic high intraocular pressure in infancy.

Risk Factor, Diagnosis, and Therapy of Congenital Glaucoma

The etiology of congenital glaucoma is largely defined by genetic inheritance, predominantly following an autosomal recessive pattern with incomplete penetrance ranging from 40% to 100% [17]. Five specific gene loci (GLC3A through GLC3E) have been implicated, with mutations in CYP1B1 often linked to the autosomal recessive form (Schuster, 2020). Beyond genetics, high myopia and a family history of glaucoma serve as significant risk factors. Given that the single modifiable risk factor is elevated intraocular pressure (IOP), the entire therapeutic approach is focused on maintaining IOP within a healthy range.

Definitive diagnosis of congenital glaucoma requires a comprehensive pediatric ophthalmological examination. Primary assessment involves funduscopic examination to evaluate the optic disc and retinal nerve fiber layer for glaucomatous changes, such as neuroretinal rim loss, optic nerve head enlargement, or nerve fiber layer thinning. Advanced imaging, like Optical Coherence Tomography (OCT), can provide objective morphometric measurements of the optic nerve. Crucially, a confirmed diagnosis often necessitates IOP measurement performed under general anesthesia or sedation [17].

Since congenital glaucoma is an irreversible condition, treatment aims to control the disease progression and prevent subsequent vision loss, rather than achieving a total cure [14]. Early detection remains the cornerstone of prevention, minimizing the risk of permanent blindness. Management varies based on the patient's age and disease severity at presentation, but treatment for PCG is primarily surgical [14]. Common surgical procedures include trabeculectomy, often supplemented by antifibrotic agents like mitomycin-C or 5-fluorouracil, or the placement of glaucoma drainage devices. The goal of these interventions is to improve aqueous outflow and stabilize IOP, thereby preserving the optic nerve and visual function [14]. A successful long-term outcome is highly dependent on achieving early diagnosis and executing timely, appropriate surgical management.

PIGMENTARY RETINOPATHY

Definition and Epidemiology of Pigmentary Retinopathy

Another distinct ocular manifestation of Congenital Rubella Syndrome (CRS) is Salt and Pepper Pigmentary Retinopathy. This specific condition is characterized by granular changes and pigment alteration across the macula and peripheral retina, presenting as small areas of hypo- and hyperpigmentation [18]. The resulting salt and pepper pattern on the fundus is considered a hallmark sign of Rubella infection. While generally non-progressive and benign, and typically not affecting central visual function, complications such as the development of choroidal neovascularization in the macular area can rarely occur [18].

Data specific to the prevalence of this particular pattern are scarce; however, one study reported this salt and pepper retinal degeneration pattern in 93 patients examined [19], highlighting its unique but uncommon presentation within the full spectrum of CRS defects.

Risk Factor, Diagnosis, and Therapy of Pigmentary Retinopathy

The development of Salt and Pepper Pigmentary Retinopathy is attributed not only to congenital pathogens like the Rubella virus but also to complex underlying factors. Key risk factors include immunization and vaccination status, coupled with a history of maternal infection during pregnancy [20]. Non-infectious contributors, such as metabolic abnormalities and retinal vascular disturbances, can also damage the retinal pigment epithelium. Furthermore, the use of certain drugs with known retinal toxicity, including chloroquine, hydroxychloroquine, and thioridazine, is associated with the development of this pigmentary pattern [20].

Diagnosis requires a thorough ophthalmological evaluation, beginning with visual acuity and contrast sensitivity assessment. Advanced techniques are vital: Fundus Autofluorescence (FAF) is noninvasively sensitive for detecting retinal pigment epithelial disruption caused by Rubella, while Electroretinogram (ERG) assesses the severity based on retinal function. Optical Coherence Tomography (OCT) and its angiography variant (OCTA) help determine the condition and vascular changes, and specialized tools like AOSLO (Adaptive Optics Scanning Laser Ophthalmoscopy) evaluate photoreceptor damage [21].

Currently, there is no specific drug or therapy that can fully cure Salt and Pepper Pigmentary Retinopathy [22]. Consequently, the management strategy is purely preventative and focused on stabilization. Given that the condition is often a sequela of Congenital Rubella Syndrome, the most effective preventative measure is MMR vaccination to ensure lifelong immunity, thereby preventing Rubella infection during pregnancy and eliminating the risk of congenital transmission [22]. For diagnosed cases, management shifts to continuous monitoring for complications. Fluorescein Angiography (FA) is utilized to detect serious, albeit rare, complications such as choroidal neovascularization. Overall, preventing the initial viral infection through high vaccination coverage offers the only reliable method for mitigating this distinct retinal damage.

CONCLUSIONS

This review confirms that despite significant success in reducing global incidence, Congenital Rubella Syndrome (CRS) remains a serious public health burden driven by persistent regional vaccination gaps, particularly in the Southeast Asian context. The clinical synthesis established that the hearing impairment is the most frequent and long-lasting sequela among the classic triad of defects. Crucially, as no specific curative treatment exists, and considering the early diagnosis often seen in high-burden cohorts, future strategies must prioritize multi-level intervention. We advocate for strengthening primary prevention through aggressive Rubella-containing Vaccine (RCV) catch-up campaigns for women of childbearing age, coupled with the urgent implementation of standardized neonatal screening protocols for auditory and ocular defects. Timely detection is essential to ensure swift surgical and rehabilitative management, thereby mitigating the substantial lifelong developmental burden associated with the syndrome.

ACKNOWLEDGMENT

The authors wish to express their deepest gratitude to all researchers and institutions whose published work provided the foundational evidence for this literature review. We gratefully acknowledge the significant contributions made by authors who conducted critical epidemiological and clinical studies on Congenital Rubella Syndrome, particularly those focusing on the Southeast Asian region.

REFERENCES

[1] Shukla, S. and Maraqa, N.F. (2023). Congenital Rubella. [online] PubMed. Available at: https://www.ncbi.nlm.nih.gov/books/NBK507879/.

[2] Masfufah, S. and Syarif, S. (2023). Factors Related to the Incidence of Congenital Rubella Syndrome (CRS) in Indonesia. Poltekita : Jurnal Ilmu Kesehatan. Available at: https://doi.org/10.33860/jik.v16i4.1627.

[3] Purnami, N., Rachmadhan, H.F., Moon, I.S., and Sudaryo, M.K. (2023). A Study Prevalence of Congenital Rubella Syndrome Cases Before and After Rubella Vaccination Campaign. Indian Journal of Otolaryngology and Head and Neck Surgery. Available at: https://doi.org/10.1007/s12070-023-03882-3.

[4] Paramita, D.V. and Purnami, N. (2020). Profile of congenital rubella syndrome in Soetomo General Hospital Surabaya, Indonesia. Infectious Disease Reports. Available at: https://doi.org/10.4081/idr.2020.8718.

[5] Lanzieri, T. (2020). Surveillance of Vaccine-Preventable Disease Chapter 15: Congenital Rubella Syndrome. Available at: https://www.cdc.gov/vaccines/pubs/surv-manual/chpt15-crs.html.

[6] Leonor, M.C. and Mendez, M.D. (2022). Rubella. [online] PubMed. Available at: https://pubmed.ncbi.nlm.nih.gov/32644466/.

[7] World Health Organization. (2018). Rubella. Available at: https://www.who.int/news-room/fact-sheets/detail/rubella.

[8] Fitriany, J., Husna, Y., Ilmu, B. and Anak, K. (2018). SINDROM RUBELLA KONGENITAL. Journal Averrous, 4(1). Available at: https://ojs.unimal.ac.id/averrous/article/view/808.

[9] Tariq, M.A., Uddin, Q.S., Ahmed, B., Sheikh, S., Ali, U. and Mohiuddin, A. (2022). Prevalence of Pediatric Cataract in Asia: A Systematic Review and Meta-Analysis. Journal of Current Ophthalmology, [online] 34(2), pp.148–159. https://doi.org/10.4103/joco.joco_339_21.

[10] Imelda, E. and Putri Hermaya (2022). Tatalaksana katarak kongenital dengan sangkaan Congenital Rubella Syndrome. Jurnal Kedokteran Syiah Kuala, [online] 22(1). https://jurnal.usk.ac.id/JKS/article/view/23180/16014.

[11] Bell, S.J. (2020). Congenital cataract: a guide to genetic and clinical management. Available at: https://doi.org/10.1177/2633004020938061.

[12] Nalbandyan, M., Papadopoulos, E.A., Leckman-Westin, E., and Browne, M.L. (2021). Nongenetic risk factors for infantile cataracts: Systematic review of observational studies. Birth Defects Research. Available at: https://doi.org/10.1002/bdr2.1904.

[13] Taba, J.A.P. (2021). Katarak Kongenital: Skrining dan Diagnosis. Cermin Dunia Kedokteran, 48(7), pp.399–405. Available at: https://doi.org/10.55175/cdk.v48i7.95.

[14] Kaur, K. and Gurnani, B. (2023). Primary Congenital Glaucoma. Available at: https://pubmed.ncbi.nlm.nih.gov/34662067/.

[15] Badawi, A.H., Al-Muhaylib, A.A., Al Owaifeer, A.M., Al-Essa, R.S. and Al-Shahwan, S.A. (2019). Primary congenital glaucoma: An updated review. Saudi Journal of Ophthalmology, [online] 33(4), pp.382–388. Available at: https://doi.org/10.1016/j.sjopt.2019.10.002.

[16] Gunawan, P. I., Komaratih, E., Nurwasis, Etika, R., Harianto, A., & Saharso, D. (2018). Rare Case Of Primary Congenital Glaucoma With Hypoplasia Corpus Callosum. Journal of Ayub Medical College, Abbottabad : JAMC, 30(2), 286–288. Available at: http://orcid.org/0000-0003-3199-2826.

[17] Schuster, A.K., Erb, C., M. Hoffmann, E., Dietlein, T. and Pfeiffer, N. (2020). The Diagnosis and Treatment of Glaucoma. Deutsches Ärzteblatt International, 117(13), pp.225–234. https://doi.org/10.3238/arztebl.2020.0225.

[18] Khurana, R.N. and Sadda, S.R. (2006). Salt-and-Pepper Retinopathy of Rubella. New England Journal of Medicine, 355(5), pp.499–499. https://doi.org/10.1056/nejmicm040780.

[19] Irma, J., Sovani, I., Wahyu, M. and Karfiati, F. (2017). Clinical Research Manifestasi Okular dan Non Okular Sindrom Rubella Kongenital Pada Penderita Katarak Kongenital. Available at: https://doi.org/10.19166/med.v6i3.1148.

[20] American Academy of Ophthalmology. (2011). Hydroxychloroquine-Induced Retinal Toxicity. https://www.aao.org/eyenet/article/hydroxychloroquine-induced-retinal-toxicity.

[21] Goldberg, N., Chou, J., Moore, A. and Tsang, S. (2009). Autofluorescence Imaging in Rubella Retinopathy. Ocular Immunology and Inflammation, [online] 17(6), pp.400–402. https://doi.org/10.3109/09273940903118634.

[22] Jain, R. and Daigavane, S. (2024). Ophthalmology Section Salt and Pepper Pigmentary Retinopathy in Congenital Rubella Syndrome: A Case Report. Journal of Clinical and Diagnostic Research, [online] 18(6), pp.1-02. https://doi.org/10.7860/JCDR/2024/67103.19506.