

# Congenital Rubella Syndrome-a Case Report with Clinical Manifestation and Management Approach

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## Abstract

Congenital rubella syndrome (CRS) is an illness in infant resulting from maternal infection with rubella virus during pregnancy. Patients suffer from some complications included deafness, cataract, heart defects, mental retardation, bone alterations, liver and spleen damage. Purpose of this study is to create attention, early identification and keep special concern in management of such case. A 15 years old girl presented with dimness of vision since childhood. Her mother had a history of fever and skin rash during prenatal period. She had mental retardation, deafness, dumbness, thin stature, microcephaly. Unaided vision fixed and follows in both eyes. Anterior segments showed bilateral microphthalmos, nystagmus, microcornea, aphakia. Intraocular pressure was 40 mm of Hg in each eye. Color fundus photograph showed myopic crescent with tessellated fundus. Echocardiogram showed pulmonary stenosis. Ultrasonography whole abdomen revealed chronic hepatitis. LDH level was 380 units/L. She had hyperthyroidism. Her sensory neural hearing loss was detected by audiometry. She was referred to glaucoma clinic for raised ocular pressure; low vision clinic for visual rehabilitation; medicine specialist for cardiac problem, liver problem and hormonal imbalance. All presenting features revealed that it was a case of congenital rubella syndrome as the girl had deafness, cardiac problem and ocular abnormality which are triad of CRS. Early diagnosis, timely management and proper counseling to patient and guardian will consequently increase life quality of this patient. National awareness should be increased for full coverage of antenatal check up with MMR vaccination in all health care centers of developing countries.

## Keywords:

Rubella virus, Congenital Rubella Syndrome, deafness, cataract, microphthalmos, cardiac problem

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## Introduction

Congenital rubella syndrome (CRS) is an illness in infants that results from maternal infection with rubella virus during pregnancy. Rubella infection during early pregnancy leads to serious consequences—such as miscarriages, stillbirths, and a constellation of severe birth defects in

infants. The risk of congenital infection and defects is highest during the first 12 weeks of gestation and decreases thereafter; defects are rare after infection in the 20th week (or later) of gestation.<sup>[1-2]</sup> Common congenital defects of CRS include cataracts, congenital heart disease, hearing impairment, and developmental delay. Infants with CRS often present with more than one of these signs but may also present with a single defect, most commonly hearing impairment.

Rubella is a systemic virus infection. Congenital rubella syndrome (CRS) is a severe birth defect when infection occurs early in pregnancy. Rubella infection and CRS are now rare in the U.S. and in Europe due to widespread vaccination. However, autism rates have risen dramatically in recent decades to about 3% of children today. Rubella is a member of the togaviridae family, usually causing a benign systemic illness resembling a mild case of

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measles, and previously known as 'germane' (hence, 'German') measles<sup>[3]</sup>. The infection is characterized by rash, fever and lymphadenopathy. Up to 70% of infected adult women develop arthritis. If, however, infection occurs in the first weeks of pregnancy, up to 85% of neonates are born with a pattern of growth restriction and major birth defects known as congenital rubella syndrome (CRS). Up to 60% of women of childbearing age worldwide remain susceptible to rubella and the CRS. In poorer countries, CRS is a major cause of developmental anomalies, especially blindness and deafness<sup>[4]</sup>. Worldwide, about 100,000 infants are born annually with CRS<sup>[5,6]</sup>. Fetal damage associated with rubella tends to result only when infection occurs in the first 16 weeks of gestation. In general, the earlier the onset of infection, the more severe are the observed malformations<sup>[7]</sup>.



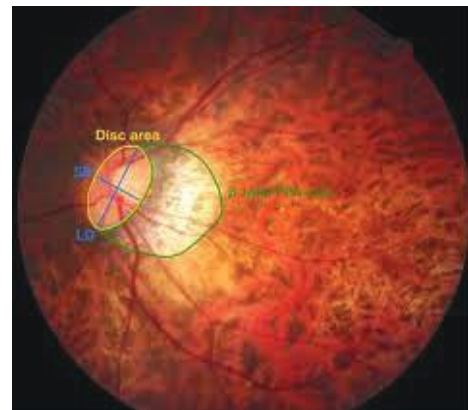
**Photograph 1:** Facial appearance showing microphthalmos, corneal opacity, microcornea

Infection-induced alterations in the hepatic metabolism of vitamin A (retinoids), causing mild liver dysfunction and the spillage of stored vitamin A compounds into the circulation in toxic concentrations, resulting in an endogenous form of hypervitaminosis A. Vitamin A is a known teratogen; initiation of the CRS in the early weeks of pregnancy is due to maternal liver dysfunction and exposure of the developing fetus to excessive vitamin A.

### Case report

An orphan girl of 15 years old presented in pediatric outpatient department with dimness of vision, photophobia, involuntary ocular motility. She was suffering with these problems since childhood. Her mother had a history of fever and skin rash during prenatal period. She had mental retardation, deafness, dumbness, thin stature,

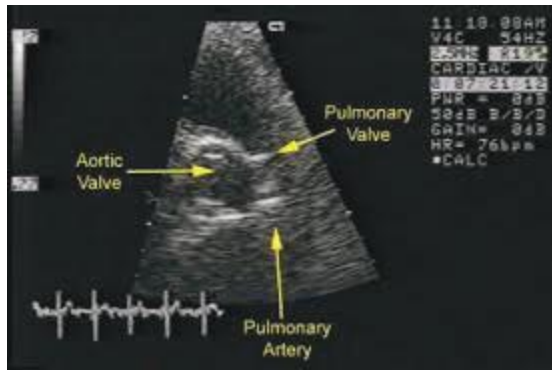
microcephaly on systemic examination. Her unaided vision was fixed and follows in both eyes. Anterior segment examination by slit lamp showed bilateral microphthalmos, corneal opacity, nystagmus, microcornea, iris atrophy and aphakia. Intraocular pressure measurement was 40 mm of Hg in each eye. Color fundus photograph showed myopic crescent with tessellated fundus, tilted disc in both eyes. Echocardiogram was suggested and it showed pulmonary stenosis. Ultrasonography whole abdomen revealed chronic hepatitis. LDH level was 380 units/L. She had hyperthyroidism. Her serum TSH level was  $<0.03$  mIU/L; Serum free T4 level is 4.2 ng/dl. She was sent to ENT specialist for auditory checkup. Her sensory neural hearing loss was detected by audiometry. She was referred to glaucoma clinic for raised ocular pressure; they prescribed antiglaucoma medication for her and advised for trabeculectomy after reducing intraocular pressure. For further management she was referred to medicine specialist for cardiac problem, liver problem and hormonal imbalance.



**Fig 1:** CFP showing myopic fundus with tilted disc



**Fig 2:** USG of abdomen reveals chronic Hepatitis



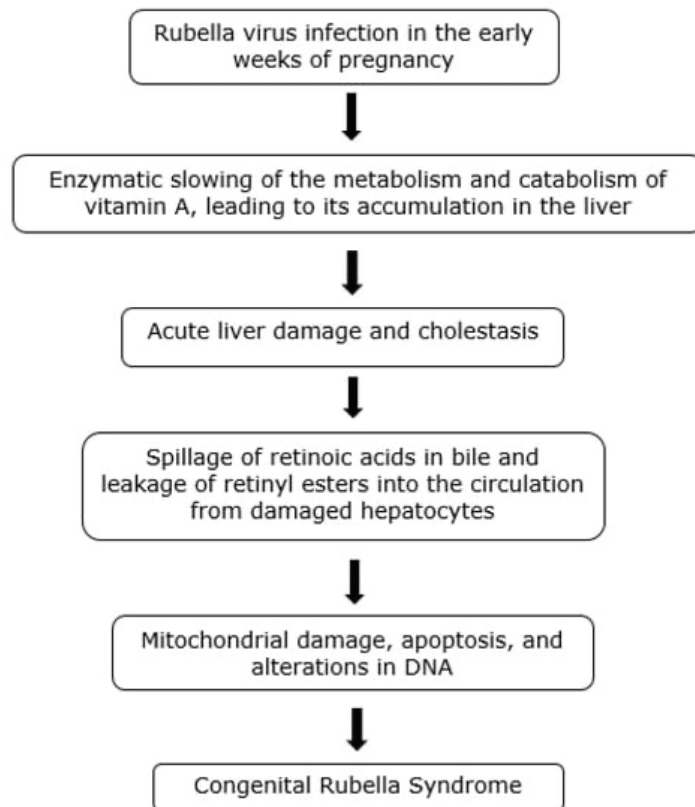
**Fig 3:** Echo cardiogram showing pulmonary stenosis

**Discussion**

Although rubella has been eliminated in the United States, it continues to be endemic in many parts of the world. It is estimated that more than 100,000 infants worldwide are born each year with CRS. In poorer countries, rubella and CRS remain common.<sup>[6]</sup>

Rubella infection is acquired by inhaling microorganisms exhaled, sneezed, or coughed by another infected individual. The virus infects cells in the upper respiratory tract, then spreads

throughout the vascular system and replicates in lymphoid tissue of the nasopharynx, leading to the infection of multiple organ systems, including the placenta in cases of infection occurring early in pregnancy<sup>[7]</sup>. Following respiratory transmission and replication of virus in the nasopharynx and regional lymph nodes, viremia occurs 5–7 days after exposure, spreading throughout the body and transplacentally, leading to fetal damage via destruction of cells and mitotic arrest<sup>[8]</sup>. The fetus is at highest risk of developmental abnormalities when infected during the first 16 weeks of gestation, particularly the first 8 to 10 weeks. Early in gestation, the virus is thought to establish a chronic intrauterine infection. Its effects include endothelial damage to blood vessels, direct cytolysis of cells, and disruption of cellular mitosis CRS-associated cardiovascular, central nervous system (CNS), hearing, and other systemic defects and growth restriction are attributed to direct damage to blood vessel walls and linings of the heart. Deafness, cardiovascular and neurological damage and retinopathy all appear when infection occurs in the first 16 weeks of gestation but are rare after that time.



**Fig 4:** Pathogenesis of congenital rubella syndrome

CRS has diverse manifestations affecting almost all organ systems including optic lens, cochlea and heart, the brain, lungs, liver, spleen, kidney, bone marrow, bones and endocrine organs are also affected in different degrees. The main defects result almost exclusively from rubella infection occurring in the first 16 weeks of gestation and include deafness, eye and cardiovascular defects.<sup>[9]</sup>

Signs and symptoms of rubella may be due to alterations in the hepatic metabolism of vitamin A (retinoids), precipitated by the acute phase of the infection. The infection causes mild liver dysfunction and the spillage of stored vitamin A compounds into the circulation, resulting in an endogenous form of hypervitaminosis A. Vitamin A is a known teratogen, it is suggested that rubella infection occurring in the early weeks of pregnancy causes CRS through maternal liver dysfunction and exposure of the developing fetus to excessive vitamin A. On this view, the multiple manifestations of CRS and associated autism represent endogenous forms of hypervitaminosis A. It is further proposed that regressive autism results primarily from post-natal influences of a liver-damaging nature and exposure to excess vitamin A, inducing CRS-like features as a function of vitamin A toxicity, but without the associated dysmorphogenesis.

Vascular defects, including necrotic damage to endothelial cells in the capillaries and larger vessels of the placenta and myocardium; impaired development of the septum; heart malformations, especially patent ductus arteriosus (PDA) and pulmonary artery stenosis, associated with findings of generalized fibromuscular proliferation; and occasional occlusion of the arterial intima of large and medium-sized arteries. Related vascular abnormalities included focal destruction of the walls of cerebral blood vessels, defects of the internal elastic lamina with proliferation of fibrous tissue, and endothelial proliferation with narrowing of the lumen.

Eye defects included opacities of the primary lens fibers, resulting in a characteristic central or nuclear cataract. In neonates, the nuclear portion of the lens was often necrotic. A characteristic

feature of rubella cataract was retention of nuclei in surviving lens fibers. The usually brief period of susceptibility to cataract was associated with the onset of maternal rash 12–43 days after fertilization. Damage to other ocular structures included focal necrosis of the pigment epithelium of the retina, necrosis of the ciliary body and iris, and microphthalmia. Compared to cataracts, the features of retinopathy and glaucoma occurred after infection over a much longer period (up to 117 days).

Sensorineural deafness associated with damage to the epithelium of the cochlear duct was the most common rubella-associated defect in surviving children.

Brain damage included mild to severe mental retardation associated with ischemia and variable microcephaly in about 25% of CRS patients. Many of the manifestations of CRS are present at birth but others are delayed, e.g., diabetes; thyroid disease; growth hormone deficiency; deafness; ocular damage (glaucoma, keratic precipitates, keratoconus, corneal hydrops, and absorption of the cataractous lens); vascular effects (including fibromuscular proliferation of the intima, arterial sclerosis, and hypertension, possibly secondary to renal disease, subretinal neovascularization), and PRP<sup>[10]</sup>

Many children showed a failure to thrive along with feeding difficulties. It has since been recognized that CRS includes ocular abnormalities, e.g., microphthalmia and retinopathy, as well as multiple systemic complications including the following:

- Bulging fontanelle and rash at birth;
- Fetal growth restriction (FGR) and low birth weight;
- Seizures;
- Hearing and cardiovascular defects (most commonly patent ductus arteriosus);
- Microcephaly;
- Psychomotor retardation;
- Behavioral and speech disorders;
- Thrombocytopenic purpura;
- Hepatitis;
- Hepatosplenomegaly;
- Bone lesions;



- Pneumonitis;
- Diabetes mellitus;
- Thyroid disorders;
- Progressive rubella panencephalitis

## Diagnosis

Diagnosis of congenital rubella syndrome is made based on clinical findings and laboratory criteria. Laboratory criteria include at least one of the following:

- Detection of the rubella virus via RT-PCR
- Detection of rubella-specific IgM antibody
- Detection of infant rubella-specific IgG antibody at higher levels (and persists for a longer time) than expected for passive maternal transmission
- Isolation of the rubella virus by nasal, blood, throat, urine, or cerebrospinal fluid specimens

Clinical definition is characterized by findings in the following categories:

- Group 1: Cataracts/congenital glaucoma, congenital heart disease (most commonly, patent ductus arteriosus or peripheral pulmonary artery stenosis), hearing impairment, pigmentary retinopathy
- Group 2: Purpura, hepato splenomegaly, jaundice, microcephaly, developmental delay, meningoencephalitis, radiolucent bone disease

A patient is classified into the following cases depending on their clinical and laboratory findings:

- Suspected: A patient that has one or more of the clinical findings listed above but does not meet the definition for probable or confirmed classification
- Probable: A patient that does not have laboratory confirmation of congenital rubella but has either two clinical findings from Group 1 as listed above OR one clinical finding from Group 1 and one clinical finding from Group 2 as listed above
- Confirmed: A patient with at least one laboratory finding and one clinical finding (from either group) as listed above
- Infection only: A patient with no clinical

findings as described above but meeting at least one confirmed laboratory criteria

## Prevention

Majority of the population is effective at preventing congenital rubella syndrome by vaccination. With the introduction of the rubella vaccine in 1969, the number of cases of rubella in the United States has decreased 99%. For women who plan to become pregnant, the MMR (measles mumps, rubella) vaccination is highly recommended; at least 28 days prior to conception. The vaccine should not be given to women who are already pregnant as it contains live viral particles. Other preventative actions can include the screening and vaccinations of high-risk personnel, such as medical and child care professions.

Infants with birth defects suspected to be caused by congenital rubella infection should be investigated thoroughly. Confirmed cases should be reported to the local or state health department to assess control of the virus and isolation of the infant should be maintained.

## Management

Infants with known rubella exposure during pregnancy or those with a confirmed or suspected infection should receive close follow-up and supportive care. Many infants can be born with multiple birth defects that require multidisciplinary management and interventions based on clinical manifestations. Often these infants will require extended period or life-long follow up with medical specialists.

## Ophthalmologic Care

Eye abnormalities including cataracts, infantile glaucoma and retinopathy are common in infants born with CRS. Infants should undergo eye examinations after birth and during early childhood. Cataract surgery (irrigation, aspiration followed by intraocular lens implantation) is recommended for management of congenital cataract. For management of congenital glaucoma trabeculotomy followed by antiglaucoma medication is indicated. Patients should undergo lifelong follow-up from a pediatric ophthalmologist for specialized care.

## Auditory Care

Many infants with CRS may be born with sensory neural deafness and thus should undergo a newborn hearing evaluation. Hearing loss may not be apparent at birth and thus requires close auditory follow up. Infants with confirmed hearing impairment may require hearing aids and may benefit from an early intervention program.

## Cardiac Care

Congenital cardiac anomalies including pulmonary artery stenosis and patent ductus arteriosus can be seen in infants with CRS. Infants should undergo cardiac evaluation soon after birth and those with confirmed cardiac lesions will require specialized care with a pediatric cardiologist for any interventions and follow-up care.

## Conclusions

Congenital rubella is a viral infection acquired from the mother during pregnancy. Multiple congenital anomalies can lead to fetal death. Diagnosis is by serology and viral culture. There is no specific treatment. Prevention is by routine vaccination. The national supervision still needs to be increased to capture more CRS cases in the community and early management to reduce morbidity. National awareness should be increased for full coverage of antenatal check up with MMR vaccination in all health care centers of developing countries.

**Conflict of interest:** There is no conflict of interest to declare.

## References

1. McLean H, Fiebelkorn A, Temte J, Wallace G. Prevention of measles, rubella, congenital rubella syndrome, and mumps, 2013. *MMWR* 2013;62:1–38 [PubMed] [Google Scholar]
2. Banatvala J, Peckham C, editors. *Rubella Viruses*. 1st ed. Oxford: Elsevier; 2007:1–79 p. [Google Scholar]
3. World Health Organization. Strategic plan for measles elimination and rubella and congenital rubella syndrome control in the South-East Asia Region 2014-2020. Available from: [http://apps.searo.who.int/PDS\\_DOCS/B5206.pdf](http://apps.searo.who.int/PDS_DOCS/B5206.pdf) [Google Scholar]
4. World Health Organization. Global measles and rubella strategic plan: 2012-2020. 2012. Available from: <http://apps.who.int/iris/bitstream/10665/44855/1/978924> [Google Scholar]
5. Kementerian Kesehatan Republik Indonesia. Pedoman surveilans CRS 2014. Jakarta 2014. [Google Scholar]
6. World Health Organization. Surveillance guidelines for measles, rubella, and congenital rubella syndrome in the WHO European region. 2012. Available from: [http://www.euro.who.int/data/assets/pdf\\_file/0018/79020](http://www.euro.who.int/data/assets/pdf_file/0018/79020) [Google Scholar]
7. Singh S, Bingwor F, Tayler-Smith K, et al. Congenital rubella syndrome in Fiji, 1995-2010. *J Trop Med*. 2013;2013. [PMC free article] [PubMed] [Google Scholar]
8. Wild NJ, Sheppard S, Smithells RW, et al. Onset and severity of hearingloss due to congenital rubella infection. *Arch Dis Child* 1999;64:1280–3. [PMC free article] [PubMed] [Google Scholar]
9. Ugnat AM, Grenier D, Thibodeau ML, Davis M. The Canadian Paediatric Surveillance Program: Celebrating 15 years of successful paediatric surveillance. *Paediatr Child Health (Oxford)* 2011;16:203–5. [PMC free article] [PubMed] [Google Scholar]
10. Kyaw-Zin-Thant Win-Mar-Oo, Thein-Thein-Myint, et al. Active surveillance for congenital rubella syndrome in Yangon, Myanmar. *Bull World Health Organ* 2006;022814:12–20. [PMC free article] [PubMed] [Google Scholar]