CASE REPORT

An infant with congenital rubella syndrome in developing India

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SUMMARY

Congenital rubella syndrome (CRS), caused by rubella virus infection during pregnancy, remains a public health concern in developing countries. Three to five per cent of all suspected CRS cases in India have been proven to be a rubella infection. Only about 45%–60% of pregnant women and infants in India receive the rubella vaccination. We present a case of a preterm female infant who tested positive for the rubella virus. The baby was born with low birth weight and, on examination, showed pallor and hepatosplenomegaly. She was detected to have an ostium secundum atrial septal defect (ASD) and a large patent ductus arteriosus (PDA) on echocardiography. On ophthalmic examination, she was diagnosed with bilateral cataract. She was treated with diuretics, and she underwent surgical correction for PDA. With this case we intend to present the literature, clinical manifestations and management of CRS. We will also focus on prevention, vaccination and disease burden in India.

CASE PRESENTATION

We present a 34-week late preterm female child who was born to a 29-year-old primi mother delivered by an emergency lower segment caesarean section due to the intrauterine growth retardation of the baby. The conception was a spontaneous one. The mother had received immunisation for tetanus and was on iron, calcium and folic acid prophylaxis during the pregnancy. A blood sample

was tested for TORCH (TOxoplasmosis, Rubella, Cytomegalovirus and Herpes simplex) profile by PCR technique at the 10th week of pregnancy, which was negative. There was no history of any high blood pressure reading during the pregnancy. An anomaly scan was done at 21 weeks of gestation, which showed a small-length intrauterine fetus with a biparietal diameter of 37 mm, which lies below the 2.5 percentile and no other abnormalities. Antenatal ultrasound was done at 33 weeks, which revealed all parameters below the fifth percentile with an effective fetal weight of 1 kg.

The birth weight of the baby was 1165 g, length was 37 cm, and the head circumference was 26.5 cm and remains below the fifth percentile. On examination, the child had pallor and hepatosplenomegaly. Mild subcostal retractions were present bilaterally, and there were no added breath sounds. S1 and S2 were heard, and apex beat was present in the fourth intercostal space, medial to the midclavicular line. A pan systolic murmur of grade 3 was heard. Blood investigations revealed thrombocytopenia (64 000/ μ L of blood). Ophthalmic evaluation revealed bilateral cataract in the eyes. Chest X-ray showed cardiomegaly and osteopenic ribs ([figure 1](#)).

Various differentials causing such manifestations include infections, neoplasia and genetically acquired syndromes. Since an infectious cause was suspected, a TORCH serology was done by PCR technique in blood sample, which was positive for rubella infection in the neonate.

Echocardiography showed an ostium secundum atrial septal defect (ASD) of 6 mm, a significant patent ductus arteriosus (PDA) of 4 mm and moderate pulmonary hypertension (PAH). Left ventricular function was normal. Neurosonogram was normal. Speech and hearing evaluation was performed, and it was found to be normal. Infant apraxia was assessed by evaluating oral motor function for lack of babbling and cooing and signs of dysarthria. Hearing evaluation was done by the auditory brainstem response method. Hence, all the positive findings and serology done confirmed congenital rubella syndrome (CRS) in this case.

The baby was initially started on antibiotics: a combination of piperacillin and tazobactam 50 mg/kg/day along with amikacin 7.5 mg/kg for every 12 hours intravenously for 5 days. Furosemide 4 mg/kg for every 12 hours orally was started for symptomatic relief. The course of ibuprofen was given until PDA closure. PDA was closed by performing a double ligation surgery after 3 months of birth under standard antibiotic prophylaxis. The infant

Figure 1 Chest X-ray showing cardiomegaly and osteopenic ribs.

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was advised to be continued on diuretics, and sildenafil was given for PAH for 4 weeks. Cataract was left untreated as it was small and covering only the peripheral portions of the lenses bilaterally. The patient is currently on follow-up and is clinically fine; PAH has subsided.

GLOBAL HEALTH PROBLEM LIST

1. Prevalence and diagnosis of CRS in the general population,
2. Morbidity and mortality due congenital rubella infection,
3. Economic burden of disease,
4. Vaccination in pregnant women and infants against rubella,
5. Prevention of rubella infection in pregnant women,
6. Role of governments in prevention and vaccination.

GLOBAL HEALTH PROBLEM ANALYSIS

Prevalence and diagnosis of CRS in the general population

CRS refers to the array of clinical manifestations resulting from rubella virus infection during pregnancy. Rubella virus belongs to *Rubivirus* genus of the family *Togaviridae*. Rubella is a benign communicable exanthematous disease. An estimated 238 000 children are born worldwide with CRS each year, with a majority of them in the developing countries. The prevalence of rubella immunity in India is 55% in pregnant women during the first 3 months of pregnancy, and nearly 45% of women are susceptible to CRS.¹ Twenty-eight per cent of non-pregnant women in their reproductive age have suspected rubella infection, and 50%–85% among those suspected were seropositive.^{2–4} The exact epidemiology or actual burden of CRS has not yet been assessed in the Indian population. Most of the epidemiological studies have been done in tertiary care hospitals. The prevalence and incidence have not yet been estimated in the general population. Due to lack of national surveys and registries on CRS, epidemiological data are not available.⁵ The only community-based study was done in the state of Tamil Nadu from 2002 to 2004 and more than 50 000 children under the age of 5 with hearing impairments, mental retardation and developmental delays were assessed. Among the study population, 2.3% of the children had probable CRS, and only 0.58% had clinically confirmed CRS.⁶ In another study at a tertiary care centre in Delhi, 10% of babies suspected to have intrauterine infection had positive rubella IgM.⁷ In India, 3%–5% of all suspected CRS cases are confirmed to have rubella infection. The prevalence of CRS in infants with congenital anomalies is 15%–55%. Reporting and adequate surveillance are lacking even at the international level: during the endemic year 2009, only 165 CRS cases were reported by 183 member states of the WHO.

Morbidity and mortality due to CRS

The risk of fetal infection is very high (>80%) if the mother is infected within 0–12 weeks of gestation. The fetal risk is negligible if the soon-to-be mother contracts rubella before the last menstrual period prior to gestation. The risk of fetal infection is high if the maternal infection occurs in the third trimester.⁸

The major complications of rubella occur when a pregnant woman contracts the virus in the early weeks of gestation. The virus is capable of causing congenital defects, abortions and stillbirths. Rubella infection is progressive even after birth until it is eradicated from the body.

Manifestations of CRS include cataract, congenital glaucoma, congenital heart disease, microcephaly, deafness and mental retardation. Thrombocytopenia purpura, hepatosplenomegaly with jaundice and bone defects may also be present. The fetal defects observed in CRS are likely secondary to vasculitis resulting in

tissue necrosis without inflammation. Another possible mechanism is direct viral damage of infected cells.⁹

PDA, ventricular septal defect, ASD, PAH and pulmonary stenosis are the common cardiac manifestation of CRS. The most common cardiovascular lesion is PDA associated with infection 11–48 days after fertilisation. Mental retardation, deafness, microcephaly and postinfection encephalitis are the major neurological complications seen in infants with CRS.

A multicenter study in Delhi by Manjunath and Balaya assessed 272 infants with complaints of mental retardation, congenital cardiac defects, hearing impairments, neonatal hepatitis and congenital cataract. Babies and mothers were tested for rubella infection by the haemagglutination test. Among all, 90% of mothers and 64.3% of infants were seropositive for rubella infection.¹⁰

Between 2000 and 2008, Chandy *et al* reviewed 646 infants and reported 9.4% of clinically proven CRS cases. Among the confirmed cases congenital cataract, cardiac defects, neonatal hepatitis, deafness and developmental delay were the clinical manifestations.²

Mental retardation has been identified in 15% and 28% of rubella-infected infants in two studies done by Ballal and Shivananda¹¹ and Chaturvedi *et al*,¹² respectively. Chaturvedi *et al* described the prevalence of congenital heart disease in infants: PDA, septal defects with or without Eisenmenger's physiology and pulmonary stenosis were noted, alone or in combination, in 33% of patients with confirmed rubella infection.¹²

Toizumi *et al* described 38 CRS infants, among whom PDA (72%) and thrombocytopenia (76%) were the most common manifestations. Pulmonary hypertension (PH)-associated mortality in cases of PDA was about 37%. Cataract was found in only 13% of CRS infants in this study.¹³

Direct viral damage to the septa of the heart may be the cause of the increased incidence of septal defects.^{9 14}

Mortality from rubella virus infection is not well documented internationally; national data on mortality too is lacking.

Economic burden of disease

Caring for a child with CRS is costly in developed and developing countries. The government provides free vaccination, but the burden of illness has an influence on the annual budget.¹⁵ The estimated budget for the elimination of measles–rubella and control of CRS, as per the WHO strategic plan, for India is US\$4.5 billion. This budget will be used for outbreak response immunisation, supplementary immunisation activities and surveillance of measles–rubella for the period of 7 years from 2014 to 2020. This is more than 50% of the total proposed cost for Southeast Asia. This budget also includes the cost of CRS surveillance, research, technical support and communication. Diagnosis, immunisation and treatment of CRS complications are expensive.¹⁶

As per the 'global strategic plan to reduce measles and rubella 2012–2020', World Health Assembly was committed to reducing rubella and measles deaths by 95% by 2015 as compared to 2000. By 2010, the CRS-related deaths had decreased by 74%.¹⁷

Vaccination in pregnant women and infants against rubella

Data on the national and international immunisation coverage for rubella-containing vaccine (RCV) or measles, mumps and rubella (MMR) vaccine is inadequate. Few regional studies are available from India regarding the status of RCV or MMR immunisation in infants and adolescents. Vaccination status is around

45%–60% in Indian pregnant women and infants against rubella infection. The MMR coverage in Delhi, Chandigarh and Goa was reported to be 42%, 30% and 5%, respectively.^{18–20} Vaccination coverage data of RCVs is not available in India. Sharma *et al* reported that re-vaccination rubella immunity was 76% in 1359 Indian female children tested in 13 districts of Maharashtra state. After giving R-vac vaccine, 99.7% children developed antibodies to rubella.²¹ Studies on immunogenicity of MMR vaccine showed average 95% seroprevalence in children aged between 1 and 10 years in India after 5-year follow-up. The children were vaccinated between 12 and 24 months of age.^{22–24} Seroprevalence among adolescents and children are nicely achieved with fast seroconversion, whereas in pregnant women and infants, it did not achieve a good seroprevalence status due to slow seroconversion. Immunisation should be provided for all mentioned age groups according to WHO programme to prevent this high prevalence condition (CRS).²⁵

Prevention of rubella infection in pregnant women

Active childhood immunisation is not the only step to prevent or eliminate congenital rubella infection, but identification and vaccination of suspected childbearing women is necessary. The pregnant and non-pregnant women of reproductive age, who have no evidence of previous rubella vaccination, should be screened for rubella infection. Suspected pregnant cases should receive MR vaccine postpartum and non-pregnant should be immunised before pregnancy. National guidelines should be implemented for screening of non-pregnant women before pregnancy and infants after birth. As we have discussed in vaccination section, India has achieved only 40%–60% vaccination status in pregnant women and children against rubella infection. Surveillance of CRS cases is a vital step in prevention and elimination of the disease. Every healthcare centre should start a registry for CRS cases, which will be monitored by the national health department. Continuous universal infant vaccination is important to prevent the circulation of the virus. Identifying suitable candidates for vaccination and immunity is recommended for all healthcare professionals, students from other countries and non-pregnant immigrants.^{15 26}

Pregnant and non-pregnant girls at reproductive age should be careful about transmission modes of measles–rubella virus. Checking rubella immunity should be a part of preconception counselling. Awareness should be created among women of reproductive age group regarding the disease and its severe outcomes. However the universal screening for rubella virus infection is controversial and debatable as it increases anxiety level in pregnant women. Awareness about ‘the disease and associated complications in babies’ can encourage the pregnant woman for testing. TORCH is verified for rubella profile testing in infants and pregnant mothers; it can be done by using blood and tissue culture. In some cases, TORCH serology could be negative during pregnancy, but can turn positive in infant immediately after birth.

Role of governments in prevention and vaccination

High immunisation coverage, as well as high-quality surveillance of rubella, is required to eliminate the disease. The government has a significant role in prevention and protection of any kind of infection at the national level. The union health ministry of India launched the vaccination campaign against measles–rubella (MR) in five states including Karnataka, Pondicherry, Goa, Tamil Nadu and Lakshadweep on 5 February 2017. The campaign will cover nearly 36 million children in these states, but the campaign has a

target of 410 million children (largest ever in any campaign) of age between 9 months and 15 years all over the country. The MR vaccine will regularly be given replacing previous two doses of measles vaccine at 9–12 months of age and 16–24 months of age. MR vaccine will be provided free of cost all over the country at secondary schools, healthcare centres and outreach centres. The union health ministry has involved various non-government organisations in its drive to achieve the target successfully.

Patient's perspective

‘Screening of all suspected pregnant women and infants is necessary to prevent infection and further clinical manifestations. Lack of awareness and vaccination in rural areas increase the risk of this kind of infections.’ (Mother of infant)

Learning points

- ▶ All pregnant women and non-pregnant women of reproductive age should be screened for rubella infection if they have not been vaccinated previously.
- ▶ All pregnant women and infants should be immunised with the measles–rubella vaccine.
- ▶ All the suspected and confirmed congenital rubella syndrome cases should be reported to National database or registry.
- ▶ Female immigrants should be screened and should be counselled regarding rubella infection.

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REFERENCES

- 1 Vijayalakshmi P, Kakkar G, Samprathi A, *et al*. Ocular manifestations of congenital rubella syndrome in a developing country. *Indian J of Ophthalmology* 2002;50:307–11.
- 2 Chandy S, Abraham AM, Jana AK, *et al*. Congenital rubella syndrome and rubella in Vellore, South India. *Epidemiol Infect* 2011;139:962–6.
- 3 Singla N, Jindal N, Aggarwal A. The seroepidemiology of Rubella in Amritsar (Punjab). *Indian J Med Microbiol* 2004;22:61–3.
- 4 Yadav S, Wadhwa V, Chakravarti A. Prevalence of rubella antibody in school going girls. *Indian Pediatr* 2001;38:280–3.
- 5 Banatvala JE, Brown DW. Rubella. *Lancet* 2004;363:1127–37.
- 6 Vijayalakshmi P, Rajasundari TA, Prasad NM, *et al*. Prevalence of eye signs in congenital rubella syndrome in South India: a role for population screening. *Br J Ophthalmol* 2007;91:1467–70.
- 7 Deorari A, Broor S, Maitreyi RS, *et al*. Incidence, clinical spectrum, and outcome of intrauterine infections in neonates. *J Trop Pediatr* 2000;46:155–60.
- 8 Robert-Gnansia E. Congenital Rubella Syndrome. *Orphanet Encyclopedia* 2004;1–2.
- 9 Webster WS. Teratogen update: congenital rubella. *Teratology* 1998;58:13–23.
- 10 Manjunath N, Balaya S. Serological study on congenital rubella in Delhi. *Indian J Med Res* 1984;79:716–21.
- 11 Ballal M, Shivananda PG. Prevalence of rubella virus in suspected cases of congenital infections. *Indian J Pediatr* 1997;64:231–5.
- 12 Chaturvedi UC, Tripathi BN, Mathur A, *et al*. Role of rubella in congenital malformations in India. *J Hyg* 1976;76:33–40.
- 13 Tozumi M, Motomura H, Vo HM, *et al*. Mortality associated with pulmonary hypertension in congenital rubella syndrome. *Pediatrics* 2014;134:e519–26.

- 14 Way RC. Cardiovascular defects and the rubella syndrome. *Can Med Assoc J* 1967;97:1329–34.
- 15 Integrated Management of Pregnancy and Childbirth. *Prevention of congenital rubella syndrome (CRS) Standards for Maternal and Neonatal Care*: WHO, 2017. http://www.who.int/reproductivehealth/publications/maternal_perinatal_health/prevention_crs.pdf?ua=1 (cited 25 June 2017).
- 16 World Health Organization. *Strategic plan for measles elimination and Rubella and congenital Rubella syndrome control in the South-East Asia region 2014–2020*. New Delhi: World Health House. http://www.searo.who.int/entity/immunization/documents/sear_mr_strategic_plan_2014_2020.pdf (cited 25 Jun 2017).
- 17 World Health Organization. *Global measles and rubella strategic plan: 2012–2020*: World Health Organization. <http://www.measlesrubellainitiative.org/wpcontent/uploads/2013/06/Measles-Rubella-Strategic-Plan.pdf> (cited 9 aug 2017).
- 18 Chhabra P, Nair P, Gupta A, et al. Immunization in urbanized villages of Delhi. *Indian J Pediatr* 2007;74:131–4.
- 19 Puri S, Bhatia V, Singh A, et al. Uptake of newer vaccines in Chandigarh. *Indian J Pediatr* 2007;74:47–50.
- 20 Dalal A, Silveira MP. Immunization status of children in Goa. *Indian Pediatr* 2005;42:401–2.
- 21 Sharma HJ, Padbidri VS, Kapre SV, et al. Seroprevalence of rubella and immunogenicity following rubella vaccination in adolescent girls in India. *J Infect Dev Ctries* 2011;5:74–81.
- 22 Gomber S, Arora SK, Das S, et al. Immune response to second dose of MMR vaccine in Indian children. *Indian J Med Res* 2011;134:302–6.
- 23 Raut SK, Kulkarni PS, Phadke MA, et al. Persistence of antibodies induced by measles-mumps-rubella vaccine in children in India. *Clin Vaccine Immunol* 2007;14:1370–1.
- 24 Yadav S, Thukral R, Chakarvarti A. Comparative evaluation of measles, mumps & rubella vaccine at 9 & 15 months of age. *Indian J Med Res* 2003;118:183–6.
- 25 Dewan P, Gupta P. Burden of congenital rubella syndrome (CRS) in India: a systematic review. *Indian Pediatr* 2012;49:377–99.
- 26 Anon. Prevention of congenital rubella syndrome. *Paediatr Child Health* 2007;12:795–7.

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