

Congenital Rubella Syndrome among Hospitalised Infants in South India - A Long Way to Go

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ABSTRACT

BACKGROUND

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 congenital rubella syndrome. The exact epidemiology or actual burden of congenital rubella syndrome has not yet been assessed in the Indian population. In the run up to the target of controlling congenital rubella by 2020, there is added impetus to document congenital rubella syndrome cases, its clinical characteristics, interventions needed and psychosocial problems of infants and their parents, admitted with laboratory confirmed congenital rubella syndrome.

METHODS

A retrospective study based on hospital records was conducted between January 2016 and December 2017. Clinically confirmed cases not satisfying laboratory criteria for congenital rubella syndrome were excluded. In-depth interviews of mothers were conducted.

RESULTS

16 infants with a positive IgM rubella antibody were included. Microcephaly was observed in 9 (56 %) babies. Ophthalmological manifestations were present in 12 (75 %) babies; of whom 9 (75 %) had cataract. Glaucoma occurred in 3 (18 %) babies and 2 (12.5 %) had salt and pepper retinopathy. Hearing impairment was detected in 8 (50 %) babies. Congenital heart disease was present in 15 (93.7 %) infants. Surgical interventions including cataract surgery, patent ductus arteriosus ligation and cochlear implantation were necessary in 14 babies.

CONCLUSIONS

Congenital rubella syndrome is still a significant problem and urgent measures are needed to increase immunisation coverage of the target population. Affected families endure a heavy physical and psychosocial burden, which should be addressed simultaneously.

KEYWORDS

Congenital Rubella Syndrome, Rubella Vaccination, Cataracts

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BACKGROUND

Congenital rubella syndrome refers to an 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 238000 children are born worldwide with congenital rubella syndrome 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 congenital rubella syndrome.¹ Twenty-eight percent of non-pregnant women in their reproductive age have suspected rubella infection, and 50 % – 85 % among those suspected were seropositive.^{2,3,4}

The exact epidemiology or actual burden of congenital rubella syndrome 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 congenital rubella syndrome, epidemiological data is not available.⁵ The disastrous consequences of rubella infection in early pregnancy including miscarriages, stillbirths and congenital rubella syndrome could well be consigned to history very soon. In the run up to the target for control of congenital rubella by 2020, there is added impetus to document the current situation in parts of the world where transmission still occurs. The fact that infants with congenital rubella syndrome are potential sources of infection should be considered. 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. The fetal defects observed in congenital rubella syndrome are likely secondary to vasculitis resulting in tissue necrosis without inflammation. Another possible mechanism is direct viral damage of infected cells.⁶

Direct viral damage to the septa of the heart may be the cause of the increased incidence of septal defects.^{6,7} Rubella and congenital rubella syndrome elimination is defined by the WHO as the absence of endemic virus transmission in a defined geographical area for > 12 months and the absence of congenital rubella syndrome cases associated with endemic transmission in the presence of a well-performing surveillance system. Rubella and congenital rubella syndrome control are defined as a 95 % reduction as compared with the 2008 baseline, nationally and for the region.⁸

The objectives of the present study were to delineate the clinical characteristics of infants admitted with laboratory confirmed congenital rubella syndrome, to document the interventions undertaken for affected children and to understand psychosocial problems in the mothers of affected children.

METHODS

A retrospective study was conducted among infants with clinically confirmed congenital rubella syndrome admitted in the Neonatal ICU, Paediatric ICU and wards of the Institute of Maternal and Child Health, Calicut between January 2016 and December 2017. The study was approved by the institutional ethics committee (No. GMCKKD / RP 2018 / IEC / 89). Clinically confirmed cases not satisfying laboratory criteria for inclusion were excluded. Data was entered in a structured proforma and analysed using SPSS software. (SPSS Version 20). In-depth interviews have conducted by purposive sampling for four mothers after obtaining written consent.

Case Definitions ^{8,9}

Clinically Confirmed Congenital Rubella Syndrome CRS Case

An infant in whom a qualified physician detects at least two of the complications listed in (a) below or one in (a) and one in (b): (a) cataract (s), congenital glaucoma, congenital heart disease, loss of hearing, pigmentary retinopathy. (b) Purpura, splenomegaly, microcephaly, mental retardation, meningoencephalitis, radiolucent bone disease, jaundice that begins within 24 hours after birth.

Laboratory Confirmed Congenital Rubella Syndrome Case

An infant with clinically-confirmed congenital rubella syndrome CRS who has a positive blood test for rubella-specific IgM (100 % of such infants are positive at the age of 0 - 5 months; 60 % are positive at 6 - 11 months).

RESULTS

There were seventeen infants with clinically confirmed congenital rubella syndrome. Among them, 16 infants were included in the study since laboratory confirmation was obtained with a positive test for IgM rubella antibody by enzyme linked fluorescent assay (ELFA). There were 7 (43 %) males and 9 (56 %) females. The male: female ratio was 1: 1.28. The Percentage of babies born preterm was 50 % and 15 (93 %) babies were small for gestational age. The mean birth weight was 1.77 Kg (Table 1). Mortality occurred in 4 (25 %) babies. Surgical interventions were necessary in 14 babies (Table 3).

Gender	Male	7 (43.7 %)
	Female	9 (56.3 %)
Gestation	Term	8 (50 %)
	Preterm	8 (50 %)
Birth weight	SGA	15 (93.7 %)
	AGA	1 (6.3 %)
Fever with rash in mother	Yes	10 (62.5 %)
	No	6 (37.5 %)

Table 1. Background Characteristics of Subjects

Ophthalmological manifestations were present in 12 (75 %) babies; of whom 9 (75 %) had cataracts, which were unilateral in 3 (25 %) babies. Glaucoma was in 3 (18 %) babies and 1 (6.3 %) had salt and pepper retinopathy.

Cataract surgery was done for 8 (50 %) babies. Hearing impairment was detected in 8 (50 %) babies. (Table 2)

	Hearing Impairment	8 (50 %)
Cardiac	PDA	13 (81 %)
	ASD	7 (43 %)
	Pulmonary stenosis	2 (12.5 %)
Ocular	Cataract	9 (56 %)
	Glaucoma	3 (18 %)
	Retinopathy	2 (12.5 %)
	Rash	1 (6.3 %)
	Bony changes	2 (12.5 %)
	Hepatosplenomegaly	8 (50 %)
	Developmental delay	5 (31.3 %)
	Microcephaly	9 (56 %)
	Seizures	2 (12.5 %)
	Neonatal hyperbilirubinemia	8 (50 %)
	Thrombocytopenia	5 (31.3 %)
	Hypothyroidism	1 (6.3 %)

Table 2. Clinical Characteristics of Subjects

Congenital heart disease was present in 15 (93.7 %) infants and apart from patent ductus arteriosus, atrial septal defect and pulmonary stenosis, also included ventricular septal defects, tricuspid regurgitation and mitral regurgitation. Ligation of patent ductus arteriosus (PDA) was performed in 3 (18.7 %) babies and device closure was done for 3 (18.7 %) babies. Radiolucencies of long bones were found to be present in 2 (12.5 %) infants. Microcephaly was observed in 9 (56 %) babies and hearing impairment was detected in 8 (50 %) babies. Rash was observed in 1 (6.3 %) baby in the neonatal period. Hepatosplenomegaly was present in 8 (50 %) children. Neonatal hyperbilirubinemia occurred in 8 (50 %) babies.

Interventions	Number of Children
PDA closure	6 (37 %)
Cataract surgery	8 (50 %)
Auditory	6 (37 %)
Hearing aid	4 (25 %)
Cochlear implant	2 (12 %)
Cardiac and auditory	2 (12 %)
Cardiac and ocular	3 (18 %)
Ocular and auditory	5 (31 %)
Cardiac, ocular and auditory	1 (6 %)

Table 3. Interventions Required

Thrombocytopenia was detected in 5 (31 %) babies. Radiolucencies of long bones were found to be present in 2 (12.5 %) infants. Mortality occurred in 4 (25 %). Some of the relevant statements given by the 4 mothers have been reproduced verbatim.

1. 'My husband opposed doing cataract surgery and stayed away from home for a few months after the operation. Now the doctors have advised a cochlear implant'.
2. 'It is very difficult to make the child wear spectacles and hearing aids at the same time'.
3. 'We never felt guilty about not giving our child the rubella vaccine. No one in our locality is aware of it'.
4. 'My brother used to say that I should have stopped with one child. I do my best and find solace in prayers'.

All mothers were unaware of rubella or 'congenital rubella syndrome' and none of them had heard of the rubella vaccine.

DISCUSSION

The prevalence and incidence of congenital rubella syndrome has not yet been estimated in the general population in India due to lack of national surveys and registries.^{10,2} Although reporting and surveillance are poor even at the international level, it is estimated that there are more than 100,000 infants born with congenital rubella syndrome each year.^{11,12} India has achieved only 40 % – 60 % immunisation coverage with rubella vaccine in pregnant women and children. There were 16 children with confirmed congenital rubella syndrome in our study. The data assumes significance since the elimination of rubella and congenital rubella syndrome is being targeted. Cataract was the major ocular complication in the study. Cataracts among children have a high sensitivity for detecting congenital rubella syndrome in India and are the only clinical eye finding that has a high enough sensitivity and specificity to be useful as a screening tool for congenital rubella syndrome.¹³ 4.6 - 10 % of paediatric cataracts in India are due to congenital rubella syndrome.^{14,15} In our study, 9 patients (56 %) had cataract, 8 (50 %) requiring intervention. Among published reports from India, cataract due to congenital rubella syndrome was estimated to be 21 %¹⁶ and 8 %.¹⁷

Among congenital heart disease in PDA being the major anomaly. 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.^{18,19} Among 6 (37 %) babies having hearing issues, cochlear implantation was done in 2 babies. Other babies were managed on hearing aids.

Rout et al. found perinatal rubella as a significant aetiological factor for deafness amongst the 38 factors evaluated in a retrospective study reviewing records of 1000 children < 15 years with deafness.²⁰ The disastrous effects of congenital rubella syndrome have been reported to continue during later life and result in progressive sensory, motor and behavioural abnormalities like autism and hearing impairment. Development of short stature, endocrine abnormalities like diabetes mellitus and thyroid dysfunction, progressive rubella pan encephalopathy, glaucoma and immunological deficiency have also been described.²¹

A multi-centre 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.²² Congenital rubella syndrome is not only an important cause of morbidity, but is also responsible for infant mortality, which is now easily preventable. Mortality from rubella virus infection is not well documented internationally; national data on mortality too is lacking⁵. In our study, 25 % of babies did not survive; most deaths were due to bronchopneumonia in association with congenital heart disease. Thus, preventing maternal rubella is of paramount importance if the sustainable development goals are to be brought within reach.

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 measles-rubella (MR) vaccine postpartum and non-pregnant should be immunised before pregnancy.⁵

Integrated surveillance of rubella and measles plays a crucial role in prevention and elimination of the disease. The estimated budget for the elimination of measles-rubella and control of congenital rubella syndrome, as per the WHO strategic plan, for India is US \$ 4.5 billion.^{8,5}

Elimination of rubella is possible as humans are the only reservoirs and vaccine efficacy is high.²³ Although the available rubella containing vaccines are safe and highly effective with a seroconversion rate of more than 95 %, awareness among mothers remains poor, even in a highly literate state like Kerala. Thus, there is a need for high awareness campaign among the public. Since a single dose of the RA 27 / 3 vaccine results in lifelong immunity, and has demonstrated efficacy by eliminating rubella and congenital rubella syndrome from the western hemisphere countries, it is hoped that the success can be replicated in India and the rest of Southeast Asia.

The WHO goal of attainment of rubella control seems far beyond reach by the year 2020. Caring for a child with congenital rubella syndrome entails a huge social and economic burden in developing countries. Caring for a child with congenital rubella syndrome is costly in developed and developing countries. The government provides free vaccination, but the burden of illness has an influence on the annual budget.²² The estimated budget for the elimination of measles-rubella and control of congenital rubella syndrome, 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 congenital rubella syndrome surveillance, research, technical support and communication. Diagnosis, immunisation and treatment of congenital rubella syndrome complications are expensive.⁸ The necessity for immediate interventions in the neonatal period and early infancy imposes a huge burden on the family, especially the mother, both physically and psychologically, and often results in financial difficulties for the family. There were several babies who required multiple interventions. During one to one interview, we came to know that apart from urgent measures for prevention, it is imperative to provide psychosocial support to affected families. We found that none of the mothers were neither aware of congenital rubella syndrome nor aware of the importance of taking the rubella vaccine in the antenatal period. This emphasises the importance of improved awareness and universal immunisation of childbearing women with no evidence of previous rubella vaccination. Even in a literate state like Kerala, awareness of mothers

regarding rubella vaccine remains poor, and calls for newer and more innovative strategies to make a difference, empowering them to take decisions for their own health and for their children's health as well.

CONCLUSIONS

There remains a lot to be done to realise the goal of elimination of congenital rubella syndrome and affected families endure a heavy physical and psychosocial burden, which should be addressed simultaneously.

Data sharing statement provided by the authors is available with the full text of this article at jebmh.com.

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