

Original Article

Frequency of Patent Ductus Arteriosus in Children with Congenital Rubella Syndrome — A Study in a Tertiary Care Hospital

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ABSTRACT

Introduction: Congenital Rubella Syndrome (CRS) has long been characterized by the triad of deafness, cataracts, and cardiovascular malformations (CVMs). The frequency of Patent Ductus Arteriosus (PDA) in children with Congenital Rubella Syndrome (CRS) is a critical topic in pediatric cardiology and infectious disease research. **Aim of the study:** This study aimed to assess the frequency of Patent Ductus Arteriosus (PDA) among children with Congenital Rubella Syndrome (CRS). **Methods and Materials:** This cross-sectional observational study was conducted at the Department of Pediatric Cardiology, Combined Military Hospital (CMH), Dhaka, Bangladesh, from June 2020 to June 2021. A purposive sampling technique was adopted. A total of 50 cases with CRS were selected as the study population. Data were collected and processed, and subsequent analysis and reporting were conducted using MS Office tools. **Result:** Among the total participants, 98% were IgG-positive and 48% were IgM-

positive. Out of the 50 study patients, seven cases (14.0%) were diagnosed with pure PDA (Patent Ductus Arteriosus) without any other associated abnormalities. The remaining patients exhibited various combinations of PDA and other cardiac abnormalities. Specifically, thirteen patients (26.0%) were found to have normal cardiac anatomy without any significant abnormalities. **Conclusion:** Among children with suspected congenital rubella syndrome (CRS), cardiovascular malformations are common. Patent Ductus Arteriosus was found in more than two-thirds of children with congenital heart disease,

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either occurring in isolation or combination with other congenital heart diseases.

Keywords: *Rubella, Patent Ductus Arteriosus, IgG, IgM, Congenital Rubella Syndrome*

INTRODUCTION

Rubella, often referred to as German measles, typically manifests as a mild illness characterized by symptoms like fever and rash. However, the significant public health concern associated with rubella is its teratogenic effects, particularly when an individual contracts a rubella infection during the early stages of pregnancy. When the fetus is exposed to rubella, it can lead to fetal death or the birth of an infant with severe congenital birth defects ^[1]. Globally, it is estimated that between 100,000 to 238,000 children are born each year with Congenital Rubella Syndrome (CRS), with the majority of cases occurring in developing countries ^[2]. In Bangladesh, a study conducted in Dhaka during 1994-1995 focused on 120 children with disabilities as a result of CRS. Among the children in the study, 25 of them (20.83%) were found to be seropositive for rubella-specific antibodies ^[3]. Notably, it was observed that 40% of mothers with seropositive children had a clinical history suggesting rubella infection during the 1st trimester of their pregnancy, while 12% had such a history during the 2nd trimester ^[3]. The risk of severe congenital defects is closely linked to the stage of gestation at the time of maternal infection. Maternal infection during the 1st 8 weeks of gestation is associated with the most severe and extensive defects. The risk for congenital defects is estimated at 90% when maternal infection occurs before 11 weeks of gestation, 33% at 11-12 weeks, 11% at 13-14 weeks, and 24% at 15-16 weeks. Defects occurring after 16 weeks of gestation are rare, even if fetal infection takes place ^[4]. In early literature, the incidence of heart defects varied widely. Children born with congenital rubella defects were found to have heart disease in 30% to 90% of cases, with an average

estimate of around 50% ^[5]. The most common congenital heart disease (CHD) observed in Congenital Rubella Syndrome (CRS) is Patent Ductus Arteriosus (PDA), which can manifest as an isolated condition or co-occur with an Atrial Septal Defect (ASD), Ventricular Septal Defect (VSD), or pulmonary stenosis. The incidence of PDAs in CRS patients is reported to range from 60% to 100% in current knowledge ^[6]. Similar findings were reported in a study where 85.7% of CRS patients presented with either an isolated PDA or in combination with either an ASD or a VSD ^[7]. However, in another study conducted in Ghana, more patients were found to have pulmonary stenosis ^[8]. Additionally, other cardiac abnormalities, such as peripheral arterial stenosis and myocardial abnormalities, have been documented. Valve abnormalities reported include valvular pulmonic stenosis, poly-valvular dysplasia, and valvular aortic stenosis ^[9]. A diagnosis of Congenital Rubella Syndrome (CRS) in infants is made based on the presence of clinically compatible manifestations. CRS cases are often diagnosed well after birth, as the clinical symptoms may not become evident immediately. Consequently, there is no specific time limit for diagnosing and reporting CRS cases ^[10]. In recent times, the majority of congenital heart diseases (CHD) in CRS patients can be effectively managed through surgical procedures or percutaneous cardiac catheter-based treatments, which have shown positive outcomes. Furthermore, advancements in intensive care units and peri-operative care have significantly reduced the morbidity and mortality associated with cardiac surgery or intervention for CHD ^[11]. The objective of this study is to determine the prevalence of Patent Ductus Arteriosus in CRS patients at CMH Dhaka and compare

these findings with those of previously reported studies.

OBJECTIVE

General Objective

- To find out the frequency of patent ductus arteriosus in children with congenital rubella syndrome.

Specific Objectives

- To identify PDA among children with Congenital Rubella Syndrome.
- To see the sociodemographic picture of the respondents.
- To know the maternal details of the study population.
- To assess the distribution of the respondents according to the Serological test.
- To compare the position of PDA among all CHD in CRS.

METHODS & MATERIAL

The cross-sectional observational study was carried out at the Department of Pediatric Cardiology in the Combined Military Hospital (CMH) in Dhaka, Bangladesh. The study was conducted from June 2020 to June 2021. A purposive sampling technique was employed, and the study population consisted of 50 cases diagnosed with Congenital Rubella Syndrome (CRS), chosen based on specific inclusion and exclusion criteria. Ethical clearance was obtained from the Ethical Committee of CMH to conduct the study. Informed written consent was taken from parents/guardians, and all documents were preserved confidentially.

Inclusion Criteria:

- Children up to 18 years of age.
- All confirmed cases of congenital rubella syndrome were diagnosed clinically and serologically.
- Guardians of the patients who had given consent to participate in the study.

Exclusion Criteria:

- Children with CRS who had a history of administration of indomethacin or surgical procedure.
- Other syndromes with some similarity to congenital rubella syndrome like microcephaly due to neural tube defects, and cataracts due to metabolic diseases.
- Guardians of the patients who did not give consent to participate in the study.

The study subjects were confirmed by clinical examination and laboratory investigations, such as rubella-specific IgM and IgG, X-ray chest, Colour Doppler Echocardiography, and ocular as well as hearing assessment. Data collection was done in a semi-structured questionnaire and by interviewing the selected patients. A descriptive analysis was done in this study. Data collection, processing, analysis, and reporting were carried out using Microsoft Office tools.

RESULTS

Among the study subjects, 30.0% were between 1 to 2 years of age, 36.0% were aged 2 to 3 years, 20.0% were in the 3 to 4 years age group, and 14.0% were between 4-5 years of age. Out of the 50 patients, 58.0% were male, and 42.0% were female. In terms of socioeconomic status, most of the children came from families with a low socioeconomic status, accounting for 76.0% of the cases. Only 4.0% of the children were from upper-middle-class families. Feeding difficulties were observed in 82% of the cases, while 98% experienced repeated respiratory tract infections. A significant portion of the participants, 78%, faced challenges in gaining weight. Bluish discoloration of nails and lips was noted in 6% of cases, whereas visual impairment affected 68% and hearing impairment affected 32% of the participants. Furthermore, 54% exhibited delayed milestones in

development. In this study, 49 (98.0%) participants were found to have high titers for rubella-specific IgG, and 24 (48.0%) cases were positive for rubella-specific IgM. Among the mothers of the 50 study patients, most of them were within the age group of 21-30 years. None of them had undergone serology testing for rubella infection, and none had received vaccination against rubella. Among the 50 study patients, seven (14.0%) cases were found to have isolated PDA, while others had associated abnormalities with PDA and additional findings. Thirteen (26.0%) patients had normal cardiac anatomy.

Table I: Sociodemographic status of participants (N=50)

Characteristics	n	%
Age group (year)		
1-2	15	30.0
2-3	18	36.0
3-4	10	20.0
4-5	7	14.0
Gender		
Male	29	58.0
Female	21	42.0
Socioeconomic status		
Poor	38	76.0
Lower middle class	10	20.0
Upper middle class	2	24.0
Affluent	0	0.0

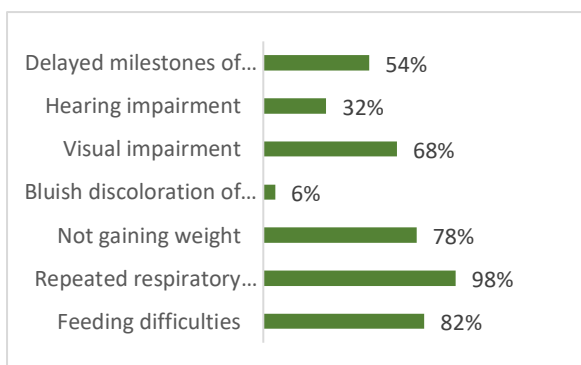


Figure 1: Distribution of presenting problems

Table II: Serological test results

Serology	n	%
IgG persistence beyond 6 months	49	98.0
IgM	24	48.0

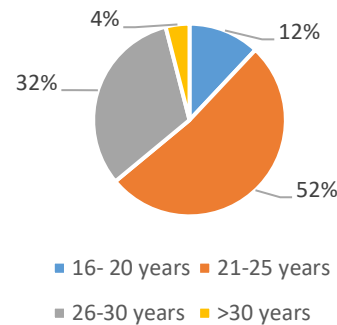


Figure 2: Maternal age distribution (N=50)

Table III: Frequency of Patent Ductus Arteriosus

Types	N	%
Patent ductus arteriosus (PDA)	7	14.0
PDA and PS	12	24.0
ASD, PDA and PS	2	4.0
PDA and VSD	3	6.0
PDA and ASD	5	10.0
Pulmonary stenosis (PS)	7	14.0
PDA and CoA	1	02.0
Normal cardiac anatomy	13	26.0

ASD; Atrial septal defect, VSD: Ventricular septal defect, CoA: Coarctation of aorta

DISCUSSION

The study revealed that the majority of patients aged 2-3 years (36.0%) and were male (58.0%) [10]. Patients under two years of age often received early diagnoses and were referred to pediatricians for cardiac screening before cataract surgery. Notably, cardiac abnormalities frequently occur in children infected during the first 8 weeks of gestation. A separate study conducted by Nazme NI et al. in a tertiary care hospital found that among 40 children, 53% of cases were in the 0-6 months age group. The mean age was 6.6 months

(± 5.7), with 68% of cases being male [12]. The male predominance in the present CRS study is in line with the findings of a study conducted by Fatema NN et al. [6]. This study also revealed an association between CRS and low socioeconomic status, similar to a study by Nazme NI et al. where 62% of patients belonged to poor socioeconomic backgrounds [12]. Regarding serology for Rubella infection, this study found that IgM was positive in about half of the patients, while IgG was positive in nearly all patients, consistent with serological findings in a study by Fatema et al. [10]. In terms of presenting problems, the majority of patients in this study had repeated respiratory tract infections (98%) and feeding difficulties (82%), which aligns with the findings of Mawson AR et al. [13]. Reviewing prospectively ascertained CRS cases revealed that congenital heart defects were noted in approximately half of the patients. In our study, the most common congenital heart defect (CHD) was a Patent Ductus Arteriosus (PDA), occurring either in isolation in about one-fifth of the study population or in combination with other cardiac anomalies like Atrial Septal Defect (ASD), Ventricular Septal Defect (VSD), or pulmonary stenosis, among others, in more than half of the patients. Current knowledge indicates the incidence of PDAs in CRS patients ranges from half to almost all patients [14,15]. Similar observations were made in our study, where nearly all patients with CHD had PDA. However, a study in Myanmar reported that Ventricular Septal Defect (VSD) was the most common cardiac defect, while in Ghana, more patients were found to have pulmonary stenosis [13]. In a study by Toizumi M. et al., cardiac defects were found in 99% of cases, cataracts in 72%, and hearing impairment in 7% [16-17]. Cardiac abnormalities in CRS are infrequent, like peripheral arterial stenosis, myocardial issues, and valve problems, including pulmonic stenosis, poly-valvular dysplasia, and aortic stenosis. Given the

>50% frequency of cardiovascular abnormalities, thorough cardiac examinations are essential for all suspected CRS cases, involving auscultation, palpation, and blood pressure checks. Murmurs may not indicate the full issue, so an echocardiography consultation is recommended if detected. Alternatively, prospective baseline echocardiography for suspected CRS patients could be considered. Patients with CRS and congenital heart defects are managed medically and surgically in the same manner as non-CRS patients [18-20].

Limitations of the study

The study has notable limitations. These encompass a small sample size, potentially reducing generalizability and effect detection. It's a single-center study, which may restrict data diversity. Interpretation should be cautious, considering applicability beyond this population or over time.

CONCLUSION

In patients with Congenital Rubella Syndrome, congenital heart disease is a prevalent condition, affecting more than two-thirds of the individuals. The most frequently observed cardiovascular abnormality in this context is Patent Ductus Arteriosus, which can occur either in isolation or in combination with other abnormalities. This underscores the importance of early diagnosis and intervention in managing Congenital Rubella Syndrome and its associated cardiac complications.

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Conflict of interest: None declared

Ethical approval: The study was approved by the institutional ethics committee

RECOMMENDATIONS

Because of a high incidence of congenital heart defects in CRS (>50%) and difficulty in recognizing heart defects by physical

examination alone, all infants and children with CRS should have at least an echocardiogram before discharge from the hospital. If the child is symptomatic, immediate pediatric cardiology consultation should be provided. Moreover, further studies should be conducted involving a large sample size and multiple centers.

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