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Congenital Rubella Infections among the Pregnant Women at a Tertiary Care Hospital in Karachi, Pakistan

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Authors' contributions

This work was carried out in collaboration among all authors. Author MS designed the study, wrote the protocol and wrote the first draft of the manuscript. Author SB performed the statistical analysis. Authors UI and SI managed the analyses of the study. Authors MS and UI managed the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

Introduction: Rubella virus is an important human pathogen that causes an acute and contagious disease known as rubella and also, causes congenital rubella syndrome more commonly occur during the first trimester of pregnancy. The incidence of CRS varies in different populations and the highest burden found in developing countries where rubella vaccination is not included in their national immunization programs. Therefore, the aim of this study was to determine the burden of CRS-related birth defects and its incidence in the pre-vaccine era in Karachi Pakistan.
Objective: The aim of the study to determine the rate of congenital rubella infection among the pregnant women at a Tertiary Care Hospital.
Methods: The retrospective descriptive cross sectional study was conducted in different departments of Dr Ruth PFAU Civil Hospital Karachi, including Eye OPD and Pediatric units from Jan 2016 till December 2019. The medical records of clinically suspected infants or confirmed

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cases were reviewed. The confirmed cases were positive for maternal IgM rubella antibodies and tested by ELISA (Enzyme Linked immunosorbant assay) where as the rubella IgM antibodies in suspected infants were lost to follow. Inclusion criteria were infants admitted less than or equal to 1 year of age with history of either congenital cataract, congenital glaucoma, pigmented retinopathy, congenital heart defects like (patent ductus arteriosus, periphery pulmonary stenosis, ventricular septal defects), hearing impairment, deafness or microcephaly were included in the study.

Results: Out of total 142 infants that were admitted in the hospital during 4 years period from 2016 to 2019 only 7 (4.93%) infants were diagnosed as confirmed cases of congenital rubella infection where as 14 (9.86%) infants were found to be clinically suspected. The ocular manifestation were more common among 6 infants which presented with cataract (85.7%) and 2 infants presented with pigmented retinopathy (28.6%). Besides this other manifestations like developmental delay were seen in only 2 patients DD (28.6%) and 3 infants presented with congenital heart diseases CHD (42.9%). The combinations of clinical features of congenital heart defect with cataract and developmental delay were seen in only 1 infant whereas cataract with pigmented retinopathy and developmental delay was seen in 1 infant and 2 infants presented with combination of congenital heart defects and cataracts.

Conclusion: Our study reported the rate of congenital rubella infection was 4.93% in a four years study period. Therefore, with a rising trend in congenital rubella infections in the last past years there is a need to built strong surveillance system and to introduce a childhood immunization in the national immunization program to eliminate the Rubella infection.

Keywords: Congenital Heart Diseases (CHD); Enzyme Linked Immuno Sorbent Assay (ELISA); Pigmented Retinopathy (PR); Developmental Delay (DD).

1. INTRODUCTION

Rubella RNA enveloped virus classified as Rubivirus in the family Togaviridae a highly contagious viral illness also known as German measles, a mild disease in most cases characterized by maculopapular rash, lymphadenopathy, and fever. The rubella virus causes fetal malformation that occurs during the first trimester of pregnancy. In 1969 Rubella was a common disease in the United States before the introduction of Rubella vaccine but was eliminated in 2004 [1].

Rubella infection possess a global public health concern as ongoing transmission in many parts of world and half of the patients developed subclinical manifestation and causes miscarriage, congenital rubella syndrome as well as fetal death during pregnancy. The infectivity period of Rubella virus is 8 days before the illness and 8 days after the onset of rash [2]. Congenital rubella defects occurs during the first 12 weeks of gestation that is up to 85% of the neonate becomes infected with this virus, 50% of the neonate become infected during the first 13 to 16 week of pregnancy whereas only 25% of the infection occurs during the second trimester of pregnancy [3,4]. Therefore rubella infection should be screened in the early phase of gestation by Rubella IgM titers in mothers [5].

The treatment options depends at the onset of infection, if the infection occur before the 18 weeks of gestation, the fetus is at the highest risk and therefore termination of the pregnancy are the only option where as if the infection occur after 18 week of gestation the fetus is at low risk and the pregnancy could be continued by ultrasound monitoring and neonatal physical examination and rubella IgG titers. The infected children with congenital rubella syndrome are contagious at least up to one year of age. Infected children should be isolated and hand hygiene practices should be adhering in order to prevent spread of transmission to others [6,7,8].

Furthermore, in non industrial countries more than 100,000 cases of Congenital rubella infections reported where as from entire globe 40% of Congenital rubella infections under 5 years of age with mortality rate up to 36% has been reported [9,10]. In other countries like India, the seropositive cases of rubella are 7% IgM and 94% IgG [11], whereas study in Bangladesh reported the quantitative analysis of rubella IgM (1.74%) and 68.87% IgG positive [12]. The seroprevalence data in Pakistan showed that 3% were IgM positive and 34% were IgG positive [13]. Since there is limited data is available related to rubella infection in pregnant women [14] and therefore the objective of our study was to conduct surveillance in the Tertiary care Hospital to rule out the number of rubella

infections in infants that are prevalent in Pakistan and to predict the extent of increasing infections among pregnant women.

2. MATERIALS AND METHODS

The retrospective descriptive cross sectional study was conducted in different departments of Dr Ruth PFAU Civil Hospital Karachi, including Eye OPD and Pediatric units from Jan 2016 till December 2019. The Medical records of clinically suspected infants or confirmed cases whose maternal IgM rubella antibodies positive were reviewed. Inclusion criteria were infants admitted less than or equal to 1 year of age with history of congenital cataract, congenital glaucoma, pigmented retinopathy, congenital heart defects like (patent ductus arteriosus, periphery pulmonary stenosis, ventricular septal defects), hearing impairment or deafness, microcephaly were taken. Data was analyzed by using Chi-square test. Probability of $p < 0.05$ was considered statistically significant.

3. RESULTS

Out of total 142 infants that were admitted in the hospital during 4 years period from 2016 to 2019 only 7 (4.93%) infants were diagnosed as confirmed cases of congenital rubella infection where as 14 (9.86%) infants were found to be clinically suspected. The ocular manifestation were more common among 6 infants which presented with cataract (85.7%) and 2 infants presented with pigmented retinopathy (28.6 %.). Besides this other manifestations like developmental delay were seen in only 2 patients DD (28.6%) and 3 infants presented with congenital heart diseases CHD (42.9%).The combinations of clinical features of congenital heart defect with cataract and developmental delay were seen in only 1 infant whereas cataract with pigmented retinopathy and developmental delay was seen in 1 infant and 2 infants presented with combination of congenital heart defects and cataracts.

4. DISCUSSION

In 2019 Pakistan reported seropositivity rate of rubella virus was IgM 2.5% and IgG 16% in pregnant women [14].Congenital rubella syndrome include the serious birth defects like congenital heart defects (patent ductus arteriosus, atrial septal defect, ventricular septal defect, peripheral pulmonary artery stenosis), auditory defects (sensorineural hearing impairment), ophthalmologic defects (cataract, microphthalmos, chorioretinitis pigmented retinopathy), neurological defect (cerebral calcifications, microcephaly, mental retardation, meningoencephalitis, behavioral disorders), hematological disturbances (thrombocytopenia, petechial purpura, hemolytic anemia, blue berry muffin rash), delayed onset of insulin dependent diabetes mellitus, thyroid disease, neonatal manifestations like low birth weight, hepatospleenomegaly and "celery stalking" of long bone metaphyses [3,4]. Rubella infection in pregnant lady can cause the substantial number of the reproductive losses in pregnant women [15].

Table 1. Shows the percentage of congenital disorder in infants

Laboratory confirmation of rubella infection (IgM positive) in infants

	Suspected		Positive	
	No of infants	%	No of infants	%
Total number of cases out of 142	14	9.8%	7	4.9%
CHD	0	0%	3	42.9%
Hearing impairmen/deafness	1	7.1%	0	0%
Bilateral congenital cataract	8	57.1%	6	85.7%
Pigmentary Unilateral	5	35.7%	1	14.3%
Retinopathy Bilateral	0	0%	1	14.3%
Microcephaly	1	7.1%	0	0%
Developmental delay	14	100%	2	28.6%
Hepato-spleenomegaly	0	0%	0	0%
Meningoencephalitis	3	21.4%	0	0%
Juandice (<24hrs)	6	42.9%	1	14.3%
Congenital glucoma	0	0%	0	0%

N# represents number of cases of infants

The multi-factorial pathogenesis of rubella virus which include the non inflammatory necrosis of chorionic epithelial and endothelial cells, inhibition of intra cellular actin assembly by rubella virus which causes inhibition of mitosis, restriction of development of precursor cells and up regulation of cytokines, and interferon in infected cells which could contribute to congenital defects. Rubella virus has also been isolated from the lens aspirate of children with congenital cataract for several years. However in few infants the virus continues to spread in nasopharyngeal secretions and urine for a year or more [3,4].

Rubella infection should be evaluated in the first trimester of pregnancy and the confirmed rubella case is diagnosed by positive Rubella IgM titers. Prenatal diagnosis is done by the molecular detection at the genomic level by detecting the viral genome in the amniotic fluid, chorionic villous biopsies and in fetal blood .However the postnatal diagnosis is based on the detection of rubella virus in the nasopharyngeal swabs, oral fluid and in urine or increasing rubella IgG titer over the first year of life, however it is difficult to diagnose the congenital rubella syndrome in older children. The postnatal confirmation of congenital rubella is essential despite the absence of clinical manifestation in order to prevent the long term ocular and neurological complications [5,16].

A study in Japan in 2018 showed that the prevalence of congenital rubella infection was 9.5% [17]. Where as our study showed 4.9% of CRS in the three years period with estimated 7 confirmed cases of congenital rubella syndrome. Another study conducted in 2004 in Brazil which showed 11 cases of congenital rubella infections [18]. Previous studies from USA reported a rapid decline in 2004 from 2001 after the vast childhood vaccination program [19]. Our study reported 3 patients (42.9%) with congenital heart diseases (CHD), pigmented retinopathy (28.6 %.) developmental delay (28.6%), cataract (85.7%) in infants born to Rubella IgM positive mothers. One of the studies conducted in 1993 at USA showed 60% of patients with pigmented retinopathy in which 57% presented with bilateral retinopathy and only 3% with unilateral manifestation [20]. In 2011 outbreak at Vietnam reported 41 cases of congenital rubella cases which were associated with developmental difficulties and sensory dysfunction [21].

5. CONCLUSION

Our study reported the rate of congenital rubella infection was 4.93% in a four years study period. Therefore, with a rising trend in congenital rubella infections in the last past years there is a need to built strong surveillance system and to introduce a childhood immunization in the national immunization program to eliminate the Rubella infection.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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