



Seroprevalence Of Rubella Antibody Titres Amongst School Going Children

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ABSTRACT

Rubella, caused by the rubella virus, poses a significant risk to pregnant women, leading to congenital rubella syndrome (CRS) in infants. Despite being a self-limiting disease, its consequences during pregnancy can be severe. Rubella vaccination has been crucial in reducing its prevalence. However, inadequate vaccination coverage poses challenges, especially in developing countries like India. A cross-sectional observational study was conducted among 105 school-going girls aged 7-15 years in Chennai. Blood samples were collected to assess rubella IgG antibody titres using ELISA. Children with documented primary rubella vaccination were included, while those with chronic illnesses or undocumented immunizations were excluded. Of the participants, 80% had protective rubella IgG antibody titres (>10 IU/ml), while 20% had titres below the protective level. Majority received two doses of rubella vaccine (54.3%), while 45.7% received a single dose. Adolescents aged 14-15 years showed the highest proportion (85.7%) of inadequate antibody levels. There was a significant decrease in protective antibody titres with increasing age ($p < 0.01$). The study highlights a seroprevalence of 80% for protective rubella antibodies among school-going girls. However, a substantial proportion, especially adolescents, had inadequate antibody levels. This underscores the need for additional rubella vaccination, possibly through the inclusion of the MMR vaccine in the immunization schedule, to enhance population immunity and prevent CRS.

Keywords: Rubella, seroprevalence, antibody titres, vaccination, congenital rubella syndrome, school-going children.

INTRODUCTION:

Rubella disease is caused by rubella virus belonging to the family *Togaviridae* (1). Rubella occurs worldwide and being a mild self-limiting disease; it is of little concern as such. However, consequences are dreadful if women become infected during the early months of their pregnancy. Rubella virus is highly teratogenic and may lead to abortion or intrauterine foetal death. The surviving foetuses may develop congenital rubella syndrome (CRS) which includes mental retardation, deafness, cataract, congenital heart defects, microcephaly, and hepatitis. According to the World Health Organization, every year 100,000 children are born with CRS globally." CRS rates are highest in the African and South-East Asian regions where vaccine coverage is lowest and the WHO recommends that all countries that have not yet introduced a rubella vaccine should consider doing so using existing, well-established measles immunisation programmes (2). The WHO Strategic Advisory Group of Experts on Immunization (SAGE) recommends an increased focus on improving national immunisation systems in general to better control rubella (2). As has been reported in Europe, suboptimal coverage levels in childhood (<95%) can lead to a prolonged inter-epidemic period and to a paradoxical shift of disease incidence towards older age groups, including women of childbearing age (3). After the introduction of Rubella vaccine in 1969, Rubella vaccination emerged as the most effective public health measure against congenital rubella infection (4). In India, 50% of children acquire rubella antibodies by the age of 5 years and

80 to 90% become immune by the age of 15. Studies from India and abroad have found that 10 in childbearing age are susceptible to rubella and between 6 to 12% of babies are born with congenital malformations or with serological evidence of rubella (5). The measles, mumps, and rubella (MMR) vaccine was available in India since 2000, but only recently, i.e., in 2017, the Rubella-containing vaccine was introduced in the National Immunization Schedule (6). It, therefore, is imperative that the current Rubella vaccination is insufficient, and the virus may still be circulating among the population, which poses a threat to pregnant women and the foetus. Hence the present study was carried out with the objective to find out the seroprevalence of rubella antibody titres after primary immunization in school going children.

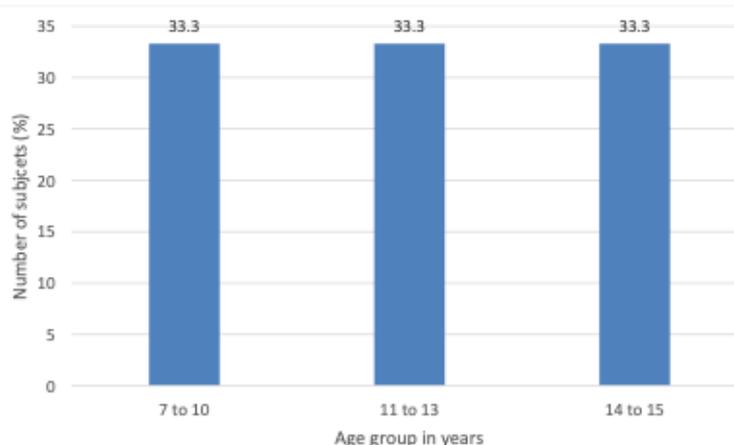
METHODOLOGY:

This is a cross sectional observational study conducted in the OPD at Department of Paediatrics, Saveetha Medical college and Hospital, Chennai. 105 girls were included in the study and segregated into three groups – 7 to 10 years, 11 to 13 years and 14 to 15 years.

The study included 1. Female children aged between 7-15 years coming to paediatrics outpatient department for vaccination or any other minor illness (URTI, follow up patients, siblings of the patients) who received at least 1 dose of documented primary rubella vaccination and 2. Those willing to participate in the study with due written consent.

The following were excluded from the study 1. Current illness requiring admission to inpatient ward 2. Undocumented immunization 3. Children on immunosuppressive therapies. 4. Children suffering from chronic diseases 5. Children who will come for follow up to OPD within 2 weeks of recovery 6. Children /Mothers who had possible rubella infection previously (Fever, rash, neck swelling, arthritis).

Figure 1: Bar diagram showing Distribution according to age group



From the children coming to the outpatient department two ml of intravenous blood was drawn and the serum from the collected sample was separated immediately and stored at -20°C and the pooled sample was tested for IgG antibodies in batches by ELISA. The titre was considered “protective” if the antibody levels were greater than 10 IU/ml.

Figure 2: Seroprevalence of rubella

		Frequency	Percent
IgG protective antibody titre	< 10	21	20.0
	> 10	84	80.0
	Total	105	100.0

Statistical analysis:

Data was collected by using a structure proforma. Data entered in MS excel sheet and analysed by using SPSS 24.0 version IBM USA. Qualitative data was expressed in terms of proportions. Quantitative data was expressed in terms of Mean and Standard deviation. Association between two qualitative variables was seen by using Chi square/ Fischer’s exact test. Comparison of mean and SD between two groups was done by using unpaired t test to assess whether the mean difference between groups is significant or not. Descriptive statistics

of each variable was presented in terms of Mean, standard deviation, standard error of mean. A p value of <0.05 was considered as statistically significant whereas a p value <0.001 was considered as highly significant.

Figure 3: Pie diagram showing Distribution according to doses of Rubella

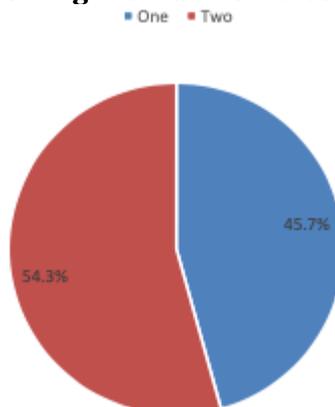


Figure 4: Bar diagram showing Seroprevalence of rubella and its distribution according to age group

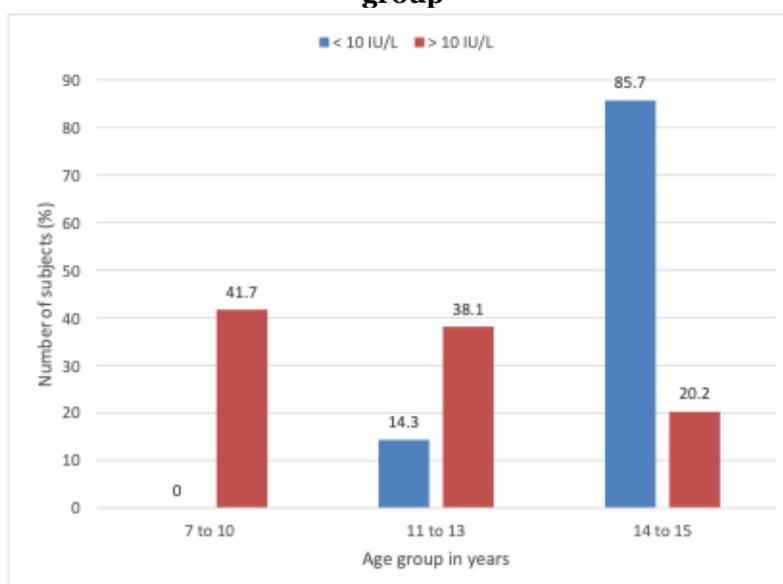


Figure 5: IgG protective antibody titre according to age group

		N	Mean titre	SD	F	p	Inference
Age group in years	7 to 10	34	29.79	5.01	44.22	0.0001 (<0.01)	Highly significant
	11 to 13	24	24.87	8.60			
	14 to 15	47	15.50	7.16			
	Total	105	22.27	9.37			

RESULTS:

105 girls were included in the study and segregated into three groups – 7 to 10 years, 11 to 13 years and 14 to 15 years (Fig 1). 15 of the 105 girls (14.3%) had received optional vaccines. None of the children included in the study had had rubella in the past or any history of progressive neurological deficit or immunosuppressive disorder. None of the children had received IVIg in the past. 25 children had been hospitalized recently (23.8%). All the children were noted to have a BCG scar.

Assessment of IgG protective antibody titre revealed that 21(20%) children had titre less than 10 IU and remaining 84 (80%) had titre more than 10 IU (Fig 2). Seroprevalence of protective antibody titre in our study was 80% and in 20% it was below protective levels in our study. Majority of the children had taken two doses of rubella i.e. 57(54.3%) and remaining 48 i.e. 45.7% had taken a single dose of rubella vaccine (Fig 3).

Out of 21 children with low levels of IgG protective antibody titre (<10 IU/L), majority were from 14-15 years of age group i.e. 18(85.7%) followed by 3 children from 11-13 years age group i.e. 14.3%.

Out of 84 children with IgG protective antibody titre (>10 IU/L), majority were from 7-10 years age group i.e. 35 (41.7%), followed by 32(38.1%) from 11-13 years of age group and 17 children from 14-15 years age group i.e. 20.2%.

Low levels of protective IgG antibody titre were seen in 85.7% of children from 14-15 years age group as against 20.2% children with protective titre from same age group. This difference in the proportion of children between two groups was found statistically significant ($p < 0.05$)

Low levels of protective IgG antibody titre were also seen in 14.3% of children from 11-13 years age group as against 38.1% children with protective titre from same age group. This difference in the proportion of children between two groups was found statistically significant ($p < 0.05$)

Mean IgG protective antibody titre from 7 to 10 years of age group was 29.79 ± 5.01 IU/L, 11 to 12 age group was 24.87 ± 8.60 IU/L and 13 to 14 years age group was 15.50 ± 7.16 IU/L. When we compared the protective IgG antibody titre between three different age groups, the difference in the titre was found to be statistically significant ($p < 0.01$). It means the protective antibody titre was gradually decreasing as age increases.

DISCUSSION:

Rubella is a contagious viral infection that is mostly seen in children under 15 years of age and young adults. Rubella is a vaccine-preventable viral infection that has no specific treatment. The infection is usually self-limiting but may result in serious complications in the new-born babies born to women infected with Rubella virus in their early pregnancy. Vaccination/immunization appears to be the only way to prevent infection, especially among pregnant women. Also, the vaccination among children will be instrumental in the elimination of the Rubella virus from the general population, thereby eliminating the probability of infection to the susceptible population, like pregnant women. The Rubella vaccine was not incorporated in the National Immunization Schedule (India) until recently. Although the MMR vaccine was available in India since 2010, it was not a part of the immunization program at birth (7). Studies have also noted that the MMR immunization status among children was well below 50%. The Indian government, therefore, had included the Rubella vaccine in the National Immunization Program from 2017 (8).

Seroprevalence of protective antibody titre:

Assessment of IgG protective antibody titres revealed that 21(20%) children had titres less than 10 IU and remaining 84 (80%) had titre more than 10 IU. Seroprevalence of protective antibody titre in our study was 80% and in 20% it was below protective levels in our study. The prevalence of Rubella-specific IgG antibodies was found to be 68.3% among non-vaccinated girls in the age group of 13-15 years as noted by a study from Kerala, South India. The same study had observed that the seropositive girls had unprotective Rubella-specific IgG antibody titres (9). This makes them potential carriers of infection to the fetuses during pregnancy and the development of congenital Rubella syndrome (CRS).

A seroprevalence rate of 67.3% was noted among girls in the age group of 11-18 years as reported by a study from Jammu and Kashmir, North India (10). The seroprevalence of Rubella specific IgG antibodies appear to vary significantly with geographic locations, age, socioeconomic status, and the standards of living as evidenced by the reports from New Delhi, also a North Indian state with a 90% seroprevalence (11).

A seroprevalence of more than 90%, both in pregnant and non-pregnant women was observed in a study from Nigeria (12). A study from Turkey, which screened school going girls within the age range of 12-18 years and pregnant women in the age range of 26-35 years found a seroprevalence of 92.5%, and 100%, respectively, for Rubella-specific IgG antibodies by using a microparticle enzyme immunoassay (13). This study, which was done among the non-vaccinated population, showed no relationship of socioeconomic status with Rubella seropositivity.

A post-vaccination survey among women in the age range of 12-42 years from Iran showed a 96% prevalence of Rubella-specific protective IgG antibodies (14). A study from Zambia, which evaluated the seroprevalence of Rubella-specific IgG antibodies among female blood donors, noted seropositivity of 91.9% (15).

An evaluation of the presence of protective Rubella-specific IgG antibodies in pregnant women in Canada revealed that 87.6% had protective antibodies (>10 IU/mL), and 2.3% showed antibody titers <5 IU/mL (seronegative). This study found a positive

relationship of seronegativity with educational qualifications where the university graduates had comparatively lower seronegativity rates (1.6%) as compared to other women in schools and colleges (3.1%) (16).

The World Health Organization (WHO) aims to improve the seropositivity rates of Rubella-specific IgG antibodies to 95% and limit the seronegativity rates to not >5% among pregnant women globally by the year 2020 (17).

A recent meta-analysis of the global prevalence of seronegativity of Rubella-specific IgG antibodies in women of child-bearing age (WCBA) that included five different WHO regions (Europe, Africa, America, Middle-East, and South-East Asia) revealed that all the studies from South-East Asia showed a seronegativity of >10% (18). A study of the seroprevalence of Rubella-specific IgG antibodies among healthy pregnant women in China revealed that 83.3% of women had protective antibodies (19). In a recent study from Cameroon, which evaluated the seroprevalence of Rubella-specific IgG antibodies among pregnant women found 94.4% seroprevalence. This study had hypothesized that the increased seroprevalence in the absence of adequate immunization could be attributed to the circulating wild strain of the Rubella virus (20).

A seroprevalence of 50% was recently reported from Kerala, South India. This study recruited 1671 non-vaccinated girls in the age range of 13-15 years and evaluated the Rubella-specific IgG antibody titres. The study revealed that among the seropositive girls, 50% had protective antibodies, 12% had an equivocal antibody titre, and 38% had low titres of antibodies (21).

In a meta-analysis of the seroprevalence of Rubella-specific IgG antibodies among women in Bangladesh showed a seropositivity range of 14 to 53% (seronegativity of 47% to 86%) (22).

A recent study from Pakistan, which included pregnant women, showed a seroprevalence of 16% and 2.5% to Rubella-specific IgG and IgM antibodies, respectively (23).

In a large-scale study from Nepal, which included more than 2000 women of childbearing age, a 90.8% seroprevalence was noted against Rubella-specific IgG antibodies (24). In a population-based cross-sectional study reported from Tanzania, an economically constrained underdeveloped country, it was noted that the seroprevalence rates of anti-Rubella IgG antibodies were <5% (25).

Study by Gutierrez et al (26) in Mexican women were seropositive and the figure increased with age. They also found that it was 82.5% in the higher socioeconomic group and 77% in the lower socioeconomic group. These contradictory results of rubella immune status with rest of the socio-economic status in the western countries and in our study can be explained on the basis of wider availability, affordability, acceptability and greater knowledge of rubella vaccine in the West.

CONCLUSION:

- Total 105 children between the age of 7-15 years in our study. We planned to take the following samples in each age group: Age group 7-10 years – 35, age group 11-13 years – 35, age group 14- 15 years – 35.
- Optional vaccines were opted by 15 children i.e. 14.3%
- No single child has history of rubella in the past
- No single child has history of h/o progressive neurological deficit
- No single child has history of h/o immunosuppressive disorder
- No single child has history of h/o treatment with IVIG in the past 9 months
- No single child has history of h/o treatment with IVIG in the past 9 months
- History of blood transfusion was present in the past one year in 5 children i.e. 4.8%
- History of recent hospitalisation was seen in 25 children i.e. 23.8%
- BCG scar was present in all the children i.e. 100%
- Assessment of IgG protective antibody titre revealed that 21(20%) children had titre less than 10 IU and remaining 84 (80%) had titre more than 10 IU.
- Seroprevalence of protective antibody titre in our study was 80% and in 20% it was below protective levels in our study.
- Majority of the children took two doses of rubella i.e. 57(54.3%) and remaining 48 i.e 45.7% took single doses of rubella
- Out of 21 children with low levels of IgG protective antibody titre (<10 IU/L), majority were from 14-15 years of age group i.e. 18(85.7%) followed by 3 children from 11-13 years age group i.e. 14.3%.
- Out of 84 children with IgG protective antibody titre (>10 IU/L), majority were from 7-10 years age group i.e. 35 (41.7%), followed by 32(38.1%) from 11-13 years of age group and 17 children from 14-15 years age group i.e. 20.2%.
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- Seroprevalence of protective antibody titre in our study was 80% and in remaining 20% it was below protective levels. Majority of the children with inadequate antibody levels were in the adolescent age group which is similar to the other studies done. Our study shows that an extra dose of rubella is needed in the form of MMR in adolescent age group. Hence we suggest the inclusion of MMR vaccine in the immunization schedule.

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