

Seroprevalance of Rubella in an Urban Infertility Clinic – Observations and Challenges Ahead

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ABSTRACT

Background: Rubella is a contagious viral illness that can be prevented by vaccination. Currently, vaccination is being offered to children and adolescents. Since an infection in pregnancy can have teratogenic effects, identification of susceptible women and vaccination before conception would be ideal.

Aims: The aim of this study is to estimate the deficiency in immunity against Rubella in women planning conception. **Settings and Design:** Retrospective data collected from all women who attended a private assisted reproduction center for evaluation of infertility or for pre-pregnancy counseling between January 2012 and October 2017. **Materials and Methods:** Women underwent measurement of the rubella-specific immunoglobulin G using enzyme-linked fluorescent assay. **Statistical Analysis:** Data between age groups were compared using the Chi-squared test. $P < 0.05$ was considered statistically significant. **Results:** Of the 1671 cases analyzed, 418 lacked sufficient immunity and therefore needed vaccination. **Conclusions:** One in four women was at risk of developing rubella during pregnancy. It is important to screen and vaccinate susceptible women to reduce the risk of congenital rubella syndrome.

KEYWORDS: India, prevalence, rubella, susceptibility, universal immunization program, vaccine

INTRODUCTION

Rubella or German measles is an acute contagious viral illness confined to humans and caused by the rubella virus, a single-stranded RNA virus of the Togaviridae family.^[1] It is of importance to the gynecologist because of the teratogenic effects that can result from rubella infection in pregnancy. Rubella infection in pregnancy, particularly during the first trimester of pregnancy, can lead to a 90% chance of the fetus having congenital rubella syndrome (CRS). Features of CRS include miscarriage; intrauterine fetal demise; and the birth of an infant with ophthalmic, auditory, cardiac, and craniofacial defects.^[2]

Approximately half of the babies born each year with CRS are from six developing countries – India, Indonesia, Nigeria, Pakistan, Democratic Republic of Congo, and Ethiopia.^[3] A review of the literature revealed the incidence of CRS to be 0.5–2.2/1000 live

births in developing countries during epidemics, which occurred every 4 to 7 years.^[4]

A vaccine to prevent rubella has been in existence for more than 40 years and has been recommended by the Indian Academy of Paediatrics.^[5] It has not yet been incorporated in the Indian national immunization schedule, though it is having a phased introduction in select states.^[6] Studies from India have shown close to a 100% immune response to vaccination.^[7–9] Economic data support the inclusion of the rubella vaccine in the immunization programs of both developing and developed countries.^[10] A systematic review of studies assessing the seroprevalence of rubella among Indian

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How to cite this article: Koshy AK, Varghese JG, Issac J. Seroprevalance of rubella in an urban infertility clinic – Observations and challenges ahead. J Hum Reprod Sci 2018;11:384-7.

Access this article online

Quick Response Code:



Website:
www.jhrsonline.org

DOI:
10.4103/jhrs.JHRS_16_18

females revealed that 10%–30% of adolescent girls and 12%–30% of women in the reproductive age group are susceptible to rubella infection.^[2]

Vaccination to rubella in India has been primarily through the measles mumps rubella (MMR) vaccination, which is not part of the national immunization program and has been mainly administered by private practitioners. However, since 2017, measles-rubella (MR) vaccine is being introduced by the Government of India through a wide age range MR vaccination campaign, targeting children in the age group of 9 months to 15 years. This campaign will be followed by replacement of the measles vaccine in the national immunization program by the MR vaccine.^[11]

However, to reduce the incidence of CRS, it is crucial to not only attain high levels of vaccination coverage against rubella among children but also among those in the reproductive age group. This approach will effectively reduce the total viral circulation in the community. A vaccination coverage of over 80% must be maintained to avoid the risk of increasing the incidence of CRS, which would happen if poor vaccine coverage reduced viral circulation in the population enough to shift rubella susceptibility from children to young mothers.^[12]

It is therefore helpful to estimate the deficiency in immunity against Rubella among those in the reproductive age group. Couples meeting a gynecologist for treatment of infertility or for pre-conception counseling provide a unique opportunity to assess immunity toward rubella. This can be done by measurement of rubella-specific immunoglobulin G (IgG). Susceptible women can be advised vaccination to prevent infection in pregnancy. The World Health Organization (WHO) advises that patients receiving rubella vaccination avoid conception for 1 month.^[13]

Rubella-specific IgM is used in the diagnosis of active infection. However, it may be present a year or more after natural infection, vaccination, and after asymptomatic re-infection.^[14] Therefore, its presence should not be a contraindication to attempting conception.

MATERIALS AND METHODS

Retrospective data were collected from January 2012 to October 2017 of all women attending a private assisted reproduction center in an urban area for evaluation of infertility or for pre-pregnancy counseling. Ethical approval was obtained from the Institutional Ethics Committee of the hospital. All women had undergone measurement of the rubella-specific IgG using enzyme-linked fluorescent assay (ELFA)

technique using VIDAS (Biomerieux India Pvt., Ltd.). Values <10 IU/mL were considered negative, between 10 and 14.9 IU/mL were considered equivocal, and equal to or more than 15 IU/mL were considered positive. Seronegative women were advised rubella vaccination and advised against conception for 1 month. Data were analyzed using statistical package for social sciences version 19. Comparison of data between age groups was performed using the Chi-squared test. $P < 0.05$ was considered statistically significant.

RESULTS

A total of 1671 cases were analyzed. The mean age of the women was 28.75 ± 5 years. 323 women had a low titer indicating a lack of immunity to rubella. 95 samples had an equivocal report. A total of 418 women, which translates to 25% of the studied population, lacked sufficient immunity and therefore needed vaccination. Figure 1 illustrates the rubella IgG antibody levels of the studied patients. Table 1 shows the age-wise distribution of patients and their immune status. Comparison of immunity levels using Chi-squared test showed that there was no significant difference between the percentage of susceptible women in the different age groups studied ($P = 0.054$).

DISCUSSION

Several studies have assessed the susceptibility of adolescent girls and women of reproductive age group to rubella infection in different population groups and settings. There are no large-scale pan-India population studies. Most of the data at present are based on the review of multiple studies on smaller but diverse population groups. Dewan and Gupta published a systematic review of studies on the burden of CRS in India.^[2] They concluded that though different techniques have been used to assess immunity, all studies point to a significant subpopulation which needs vaccination.

Susceptibility to rubella in the adolescent age group has been mainly studied in school- and hospital-based

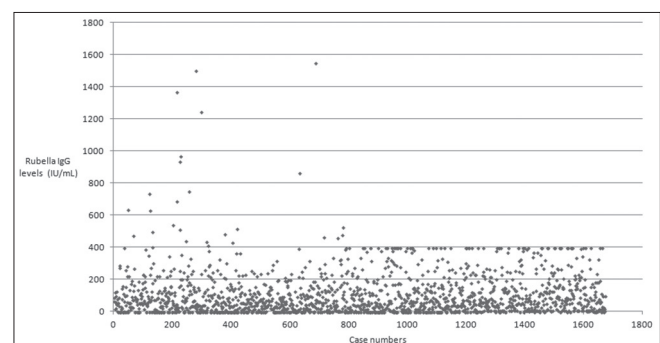


Figure 1: Rubella immunoglobulin G levels

Table 1: Rubella immunity by age

Age group	Immune (%)	Not immune (%)	Gray zone (%)	Needs vaccination (%)
<20	18 (54.55)	11 (33.33)	4 (12.12)	15 (45.45)
21-25	306 (74.27)	82 (19.90)	24 (5.83)	106 (25.72)
26-30	528 (73.54)	142 (19.78)	48 (6.69)	190 (26.46)
31-35	265 (77.49)	63 (18.42)	14 (4.09)	77 (22.51)
36-40	103 (83.06)	16 (12.90)	5 (4.03)	21 (16.93)
>40	33 (78.57)	9 (21.43)	0 (0.00)	9 (21.42)

Chi-squared test, $P=0.054$

settings. In a large study conducted on 1,329 female adolescents in 12 districts of Maharashtra state in India, 23.6% of girls were not immune to rubella.^[7] A study of 275 girls aged 11–18 years in two public schools from Jammu showed that 90 (32.7%) were seronegative for rubella IgG antibodies.^[8] In a community-based study from five districts of rural Tamil Nadu, 13.5% of 148 girls were seronegative for rubella.^[15] Hospital-based studies from Amritsar^[16] and Delhi^[17] revealed that 36% and 10% of adolescent girls were susceptible to rubella infection. In general, the urban population had a higher immune status than that of the rural population.^[7,16]

A similar vulnerability has been seen in studies performed in women of the reproductive age group.^[9,18-22] In a study performed in Vellore among 770 women attending the gynecology departments, 12.5% of women aged 18 or more lacked immunity toward rubella.^[18] Of the 1000 female health personnel tested for rubella IgG antibodies from three eye hospitals in Tamil Nadu, 15% were seronegative for rubella.^[19] In a hospital-based study from Thiruvananthapuram on 485 pregnant women, 34.3% of were not immune.^[20] Two studies of pregnant women from Delhi showed the prevalence of seronegative women to be 12.8%^[21] and 14.6%.^[22]

We need to look at the present study in the backdrop of the study location – Kerala is a state with the highest human development index in India with high levels of immunization uptake.^[23] MMR vaccine has been widely administered by doctors in the private sector, although the uptake is less compared to that of the vaccines in the universal immunization program.^[24] Our results show that one in four women of childbearing age needs rubella vaccination at this time to prevent CRS. This high percentage of susceptible women in a state with a fairly good MMR vaccine coverage is a matter of concern.

The WHO has elaborated on strategies to eliminate rubella.^[25] The present strategy adopted in India is similar to the WHO “catch up campaign” – which involves vaccinating children between the age of 9 months and 14 years. This is likely to ensure elimination of

the disease in 10–20 years. A better option would be the WHO “speed up campaign,” which will also need vaccinating older children, adolescents, and adults of both sexes. This is likely to eliminate the disease within 10 years but will be logistically and financially more difficult.

Since the newly introduced MR vaccine only targets a younger age group and not adults, it will not be effective against CRS in the immediate future.^[25] Until then, we need to actively screen women planning pregnancies and vaccinate them. This needs to be continued until we reach a stage of “disease elimination.”

Screening opportunities for lack of immunity to rubella include pre-conception visits, women coming for evaluation for subfertility, and during antenatal care. In our experience, the response to such screening has been positive. However, such screening is seldom performed by gynecologists in India at present, and a change in this practice would seem a step in the right direction.

CONCLUSION

Rubella and CRS can be prevented by vaccination. The findings of this study indicate that there are a significant number of women in the reproductive age group who are vulnerable to rubella. The current vaccination strategies are likely to take some years to reduce the risk of rubella infection in pregnancy. It is therefore imperative for gynecologists and fertility specialists to routinely screen and vaccinate susceptible women planning for pregnancy.

Acknowledgment

The authors would like to thank Dr. Rajeev Jayadevan for his valuable inputs in the preparation of this manuscript.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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