

# Seroprevalence of Rubella in a Subfertility Clinic of a Semi Urban Tertiary Care Private Hospital of Eastern India

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## ABSTRACT

**Introduction:** Primary maternal rubella virus infection during the first trimester of pregnancy carries a high risk for development of congenital rubella syndrome. According to the estimate of World Health Organization, worldwide more than 100,000 children are born with CRS each year. Most of these children are born in developing countries. Several guidelines suggest routine rubella serology testing in women trying for pregnancy. Objectives: This study was conducted to assess immunity (seroprevalence) to rubella among Indian women of childbearing age attending subfertility clinic and to observe the trend over the years.

**Material and methods:** Women attending subfertility clinic had serum sample tested to determine the seropositivity as part of subfertility work up. Rubella seropositivity was determined by estimating IgG antibodies to rubella virus using CLIA method.

**Results:** The study period was from January 2011 to December 2018. Three hundred and seventy seven women were tested for estimation of Rubella IgG. Overall seronegativity was 29.4%. Interestingly this seronegativity rate was very similar over the study period, demonstrating overall nearly one-third of the subfertile women were susceptible to rubella.

**Conclusion:** These observations indicate high rubella susceptibility among women in the childbearing age group trying for pregnancy. There is a need for detection of seroprevalence in subfertile population in Eastern India; so that appropriate vaccination can prevent this preventable tragedy of perinatal / neonatal morbidity. Further study is needed to determine the magnitude of problem in other settings (Government hospital, rural population, low socioeconomic status).

**Keywords:** Rubella Infection, Congenital Rubella Syndrome, Subfertility, Seronegativity

In case of early pregnancy infection, there is 90% chance of passage of virus to the embryo. Hearing loss, eye problem (congenital cataract), cardiac problem are three main disabilities in children. They may also suffer from diabetes mellitus and thyroid dysfunction. These problems may require costly therapy, surgeries and other expensive care. The link between maternal rubella infection and congenital rubella syndrome was first suggested by the Australian ophthalmologist Norman Gregg. Gregg noticed a substantial increase in the number of congenital cataract cases seen in his practice during 1941, and was able to link a history of maternal German measles in 78 of these cases.<sup>3</sup>

Rubella vaccination or previous rubella infection gives immunity to this disease. Upto 4 babies in every 1000 live births were born with CRS before the worldwide introduction of vaccine. In the surveillance sites during 2016-18, 21.2% were laboratory confirmed CRS and 1.2% were congenital rubella infection. Structural heart defects, cataract or glaucoma, and deafness were the main clinical features. Significance of rubella infection as a persistent

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health problem was indicated in this data.<sup>4</sup>

A single dose of rubella vaccine (live attenuated strain) gives more than 95% long lasting immunity. Available vaccines are either monovalent or in combinations with other vaccines. Measles and rubella vaccine (MR); mumps, measles and rubella (MMR); mumps, measles, rubella, varicella (MMRV) are available in Indian market. Safety and efficiency studies of MMR/MMRV shows favourable results.<sup>5</sup>

A global Measles and rubella initiative covers the period from 2012 – 2020.<sup>2</sup>

Highest incidence of CRS has been noted in countries where rubella vaccination was adapted slowly as national programme. In 2010, an estimated 40000 cases of CRS was detected in India, which a significant burden in the society. At that time, RCV was only available in private-sector health facilities in India. Measles – Rubella campaign is introduced by Government of India from February 2017. The target children group is from 9 months to below 15 years. This huge programme is targeting nearly 41 crore children over a period of two to three years. This programme aims to reduce measles mortality and reduce CRS related disabilities.<sup>6</sup>

Additional studies will be needed to determine the cost effectiveness strategies in low income countries.<sup>4</sup>

Muliyil DE et al<sup>7</sup> conducted a sero-survey among pregnant women attending antenatal clinics of six hospitals in India which also function as sentinel sites for CRS surveillance, to estimate the prevalence of IgG antibodies against rubella. Among 1800 tested sample 83.4% were sero positive and 1.3% were indeterminate and 15.2% were seronegative. High seropositivity in absence of routine childhood immunization

indicates continued transmission of rubella virus. We don't have similar kind of data from women of childbearing age attending subfertility clinic of Eastern India.

The main aim of this study was to access the seropositivity to rubella among Indian women of childbearing group attending subfertility clinic and to observe the trend over the years.

## MATERIAL AND METHODS

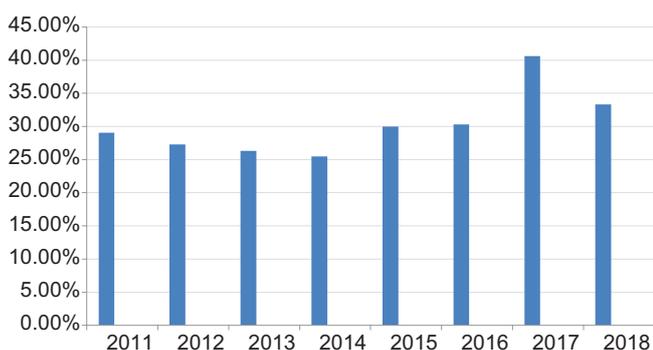
This was a cross sectional study of prospectively collected data from January 2011 to December 2018 of women attending subfertility clinic in a semi urban tertiary care private hospital of eastern India. Ethics committee approval was waived and verbal consent was taken. All women had undergone estimation of rubella – specific IgG as a part of routine infertility work up. The serum sample had undergone measurement of rubella-specific IgG chemiluminescence assay method (CLIA). This method combines the highly-sensitive chemiluminescence assay with highly-specific immune response and affinity of antibodies. Values less than 10 IU/ml was considered negative and equal to or more than 10 IU/ml was considered positive. Women with seronegative report were advised to have rubella vaccine within first few days of her next period and advised against conception for one month. Captured data were analyzed by Microsoft Office Excel 2007.

## RESULTS

A total of 377 cases were analyzed. 111 women had negative report indicating lack of immunity to rubella. This translates to overall 29.4% of the studied population lacked immunity to rubella and therefore needed vaccination. Table 1 illustrates the year wise distribution of patients and their

Year	Number of patients	Number of nonimmune patients	Percentage of nonimmune patients	Number of immune patients	Percentage of immune patients
2011	62	18	29.03%	44	70.9%
2012	66	18	27.27%	48	72.72%
2013	57	15	26.31%	42	73.68%
2014	51	13	25.49%	38	74.50%
2015	40	12	30.0%	28	70.0%
2016	33	10	30.30%	23	69.69%
2017	32	13	40.62%	19	59.37%
2018	36	12	33.33%	24	66.66%
Total	377	111	29.44%	266	70.55%

**Table-1:** Rubella seroprevalence by years (2011 – 2018)



**Table-2:** Trends of seronegativity over the years (2011-2018)

immune status. Table 2 demonstrates the year wise trend of Seronegativity.

## DISCUSSION

Based on data from sentinel surveillance (2016-18), a study of epidemiology of Congenital Rubella Syndrome (CRS) in India, Murhekar M et al<sup>4</sup> has indicated the need for continued surveillance of rubella control programme.

A retrospective survey between January 2005 and December 2015 analyzed medical records of children discharged with a diagnosis of congenital rubella syndrome (CRS) from a tertiary care hospital from North India. This study

highlighted the urgent need for effective CRS surveillance. They also suggested initiating preventive measures including appropriate vaccination against rubella.<sup>8</sup>

Susceptibility to rubella infection of adolescent girls, women of non pregnant reproductive age group, women with fertility problem and in pregnant women has been published in several studies. These studies are not only in different population group but also in different settings.

In a study of one hundred and forty healthy girls, aged 9-12 years (the mean age of the girls was 10.7 years), attending pediatric out-patient department from Delhi, 10 per cent were found to be seronegative prior to immunization.<sup>9</sup> In a community based rubella serosurvey in five blocks of Tamil Nadu, 13.5 per cent in 10-16 year age group population were found to be susceptible to rubella infection.<sup>10</sup>

Sero-surveillance to assess immunity to rubella was conducted in Jammu, India, in two public schools. Among these school children, aged 11-18 years 32.7% were found to be seronegative.<sup>11</sup> In a large study conducted on 1,329 female adolescents in 12 districts of Maharashtra, India, to assess their serological status of rubella exposure, Sharma HJ et al<sup>12</sup> found 23.6% girls are nonimmune to rubella.

A community-based observational study was conducted at a randomly selected rural area of Kozhikode District, Kerala, among adolescent girls. Among 250 girls, 32% was found to susceptible to rubella infection.<sup>13</sup>

In 580 women including 80 women of medical community of district Amritsar seroprevalence of Rubella was determined, by ELISA test. The overall rubella IgG seropositivity was 68.8%. Seropositivity in women of medical community was 80%. Significantly higher rates were observed in women of urban areas and those belonging to lower socioeconomic class.<sup>14</sup> Susceptibility to rubella were assessed in a study of 770 women of childbearing age attending the Obstetrics and Gynecology department and Reproductive Medicine Unit of Christian Medical College, Vellore. The level of susceptibility to rubella was 12.5%.<sup>15</sup>

Data of all women who attended a private assisted reproduction center at Kerala, India for evaluation of infertility or for pre-pregnancy counseling between January 2012 and October 2017 was collected retrospectively. A total of 1671 cases were analyzed. 418 cases found to have insufficient immunity and therefore needed vaccination. This study concluded that one in four women was at risk of developing rubella during pregnancy.<sup>16</sup> A study from Bijapur, India evaluated the seroprevalence of anti-rubella virus in both pregnant and non-pregnant women. This study included 240 female subjects. The age range was 16-45 years. Among the 115 non-pregnant women tested, 20.86% were positive for rubella IgG antibodies. This shows a 79.14% woman to be susceptible to rubella. This is one of studies which reported the highest susceptible group of women.<sup>17</sup>

The prevalence of rubella immunity was investigated in a cross sectional study of 485 pregnant women in their first trimester. The women were attending the antenatal clinics of three government maternity hospitals in the city of Thiruvananthapuram, Kerala, during 2003–06. 65.7%

were IgG-positive and thus had immunity against rubella.<sup>18</sup> Another study from Lucknow, India, pregnant women attending antenatal clinics was investigated to determine the rubella seropositivity. They found 11.8% of women were sero negative. No relationship was observed between parity and seronegativity.<sup>19</sup>

Our results show that nearly one in three women of childbearing age needs vaccination at this time to prevent CRS. This high percentage of susceptible women in Eastern India is a matter of concern. The newly introduced MR vaccine (GOI) targets a younger age group and not adults. This programme will not be effective to prevent CRS in the near future. Until then, we need to actively screen women planning pregnancies and vaccinate the susceptible women. This process need to be continued till we reach a stage of disease elimination.

At present the best ways to screen the women is in premarital clinic, prepregnancy clinic, subfertility clinic and also in the antenatal clinic. Unfortunately this screening is not widely practiced in this part of India. Increased screening advice for the eligible women will be a significant move to prevent this preventable tragedy.

## CONCLUSION

Rubella infection and congenital rubella syndrome can be prevented by rubella vaccination. Our observations indicate high rubella susceptibility among women in the childbearing age group trying for pregnancy. The current vaccination programme by Government of India which is initiated in 2017 will not cover these women as they are not the targeted vaccination group. There is a need for determination of serological status among the women in the reproductive group especially in premarital clinic, subfertility clinic, prepregnancy clinic, and also in the antenatal clinic, so that appropriate vaccination can be offered. Further study is needed to determine the magnitude of problem in other settings (Government hospital, rural population, low socioeconomic status).

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