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**ORIGINAL ARTICLE**

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# Seroprevalance of rubella in BOH cases - A 5 year study.

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**OBJECTIVE(S) :** To study the rubella seroprevalance rates in children, in newborns with congenital anomalies, and in women with bad obstetric history.

**METHOD(S) :** A total of 489 blood samples were collected by veinous puncture from both women, and children attending out patient departments of pediatrics, and obstetrics and gynecology. Samples were tested for the presence of rubella specific IgM antibody by ELISA.

**RESULTS :** Fifteen out of 334 women (4.49%) and 11 out of 155 children (7.9%) were positive for rubella specific IgM antibodies.

**CONCLUSION(S) :** The prevalence of rubella specific IgM antibodies in women with affected children and newborns (7.09%) with congenital anomalies was higher than that in women with bad obstetric history (4.9%). There is a need to screen all the women attending antenatal clinic for the presence of rubella specific IgM antibodies which indicates recent infection with rubella virus. This would prevent pregnancy wastage and congenital anomalies in the newborns.

**Key words :** rubella virus, IgM antibodies, congenital rubella syndrome, bad obstetric history.

## Introduction

Rubella is a mild exanthematous disease of world wide distribution. Rubella virus accounts for majority of intrauterine infections; however there is a risk of infection to the fetus and subsequent congenital defects when it infects susceptible pregnant women [1]. Maternal infection with rubella virus plays a critical role in pregnancy wastage and its occurrence in patients with bad obstetric history (BOH) has significant consequences. Risk of rubella defects is high in infants whose mothers are infected by rubella virus in the first 16 weeks of pregnancy. WHO estimates that world wide more than 100,000 children are born with congenital rubella syndrome (CRS) each year, most of them in developing countries [2,3]. A study in Southern India during 1993-94 found that CRS was the cause of 26% of cases of children born with congenital anomalies. WHO recommended that case definition for probable rubella is a patient with fever, maculopapular rash, cervical, suboccipital or postauricular lymphadenopathy and arthralgia/arthritis. Because of the difficulty of clinical diagnosis of rubella, laboratory confirmation is required. This involves specific IgM test on a serum specimen obtained within 28 days after the onset of rash. WHO recommended that case definition for clinically confirmed CRS is an infant with two of the complications described in (a) or with one of those in (a) and one in (b) below [4,5] –

(a) cataract, congenital glaucoma, congenital heart disease, loss of hearing, pigmentation, retinopathy.

(b) purpura, splenomegaly, microcephaly, mental retardation, meningo-encephalitis, onset of jaundice within 24 hours of birth, radioluscent bone disease.

Laboratory confirmation of CRS involves a rubella specific IgM test on a blood specimen obtained within the first year of life, preferably within first 6 months. Nearly 50% of rubella infections are subclinical and an infected health care worker may therefore unknowingly transmit the virus to a patient or

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to other staff. This poses a risk of CRS if a woman becomes infected with rubella in the early months of pregnancy [6]. This paper reports the results of a 5 year (January 2000 - December 2005) serological study of rubella specific IgM antibodies among newborns, children with congenital anomalies, and women with BOH attending out patient departments of Pediatrics, and of Obstetrics and Gynecology.

## Methods

The study group comprised of newborns and children suspected of CRS attending the out patient department of Pediatrics and women with BOH attending the out patient department of Obstetrics and Gynecology from January 2000 to December 2005. A detailed history with special reference to past rubella virus like infection, immunization against rubella, and adverse pregnancy outcomes if any was recorded.

A total of 155 children upto 5 years of age and 334 women with BOH between 26 and 45 years of age were studied. Blood samples were collected by veinous puncture under strict aseptic conditions. Sera were separated and stored at $4^0$C until tested for IgM antibodies. The serum samples were examined by microcapture ELISA. The sera were tested for the presence of rubella specific IgM antibodies. Sera yielding corrected absorbance values of more than 70% of that obtained with the positive control serum were considered positive. The test was performed and interpreted as per the manufacturers instructions (EQUIPAR). The optical density was measured at 450 nm using ELISA reader. The absorbance values of the standard controls provided in the kit and of the test sera were plotted on a graph. The results were interpreted as positive, negative and equivocal as per the manufacturer's guidelines.

## Results

Out of 489 cases screened for rubella infection 26 (5.4%) were diagnosed as having acute rubella infection. Clinical conditions of the patients positive for rubella IgM antibodies are given in Table 1 and 2.

We found a higher percentage (33.33%, 5/15) of prevalence of IgM antibodies in mothers with history of still birth/ abortions. Similarly higher percentage of rubella specific IgM antibodies was detected in children with bilateral congenital cataract (27.27%, 3/11) and also in cases of hepatosplenomegaly (27.27%,3/11). Our study also showed a higher prevalence of IgM antibodies in children (7.09%) than that in women with bad obstetric history (4.49%).

**Table 1. Women with bad obstetric history and their relative seropositivity.**

| Clinical diagnosis | Number (Percent) | Seropositivity of rubella IgM antibodies by ELISA Number (Percent) |
|---|---|---|
| Mothers with history of still birth/abortions | 136 (40.7) | 5 (3.6) |
| Mothers with previous congenitally malformed babies | 43 (12.8) | 3 (6.97) |
| Mothers with history of intrauterine deaths | 58 (17.3) | 4 (6.89) |
| Mothers with previous intrauterine growth retarded babies | 21 (6.2) | 2 (9.52) |
| Mothers with no significant past clinical history | 76 (22.7) | 1 (1.31) |
| Total | 334 | 15 (4.49%) |

**Table 2. Clinical presentation of children with congenital rubella syndrome and their relative seropositivity (n=155).**

| Clinical presentation | Number | Seropositivity of rubella IgM antibodies by ELISA Number (Percent) |
|---|---|---|
| Bilateral congenital cataract | 50 | 3 (6) |
| Neonatal jaundice | 10 | 1 (10) |
| Intrauterine growth retardation | 20 | 2 (10) |
| Hepatosplenomegaly | 50 | 3 (6) |
| Developmental delay with or without microcephaly | 10 | 1 (10) |
| Miscellaneous group (seizures, pneumonia, cerebral palsy, etc.) | 15 | 1 (6.6) |
| Total | 155 | 11 (7.09) |

## Discussion

Rubella is a mild viral illness in children which can occasionally infect adults. Rubella infection has been incriminated as one of the causes of BOH and seroconversion of pregnant women has been considered as one of the reasons for medical termination of pregnancy[7]. The diagnosis of rubella is very often missed as the infection is mild and the rash and lymphadenopathies are transient. Infection from rubella virus is particularly serious if contracted during the first 3 months of pregnancy [8]. Primary virus infection during pregnancy may lead to teratogenic effects on the fetus. It is highest in cases of infection during first 3 months of pregnancy (40-60%) and progressively decreases during the fourth and fifth months (10-20%). Women of child bearing age may also be infected as a result of occupational exposure [9]. Episodes of increased incidence of rubella are reported to occur every 3-4 years. Since 10-30% of women in child bearing age are susceptible to rubella infection, increased incidence of rubella will lead to increased reporting of pregnant women with rubella infection. Serodiagnosis is the most useful and reliable method to detect the infection[10,11]. In general, following primary infection IgM antibodies can usually be detected within 4 days of onset of rash, but the duration of response is variable. IgM antibodies persist for 6-12 weeks although some patients may exhibit a more prolonged response which may extend for as long as a year. In the present study rubella infection was diagnosed in 15 out of 334 pregnant women (4.9%) by detecting virus specific IgM antibodies using Elisa. This shows the importance of diagnosing rubella in pregnant women from a single serum specimen. ELISA tests are not only sensitive but also do not need serum pretreatment and can be adapted to detect specific IgM antibodies. Detection of IgM antibodies is evidence of immunity as there is only one serotype of rubella virus. To accurately confirm a recent rubella infection, which is critically important in a pregnant woman, either a rise in antibody titer must be demonstrated between two serum samples taken at least 10 days apart or rubella specific IgM antibodies must be detected in a single specimen using ELISA [12-14]. Intrauterine infection with rubella is associated with chronic persistence of the virus in the new born. Viral excretion may last for 12-18 months after birth but the level of shedding gradually decreases with age. Rubella infection if acquired early in pregnancy may result in spontaneous abortion or congenital anomalies in the infant. Fetal abnormalities may be heaptosplenomegaly, psychomotor retardation, bone alterations, cardiopathies, and neuropathies. Congenital rubella infection usually causes permanent developmental defects resulting in cataract, sensory and neural deafness, cardiac defects, and bony lesions [9].

Demonstration of virus specific IgM antibodies in infancy is considered a definitive evidence of intrauterine infection. Hence the higher incidence of seropositivity observed in women presenting with adverse pregnancy outcomes suggests that rubella could be a cause of repeated pregnancy wastage in these women. It is evident from the present study that rubella virus infection is prevalent among newborns and children and also women with BOH.

## Conclusion

There is a need to screen all pregnant women, for presence of rubella specific IgM antibodies to prevent pregnancy wastage and congenital anomalies.

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