Study of Incidence of Congenital Rubella and cytomegalovirus infections in Children’s, Attending in Tertiary care Hospital at New Delhi

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Abstract
Objective: The present study was undertaken to determine the role of Rubella and cytomegalovirus (CMV) infections of children and pregnant woman.

Materials and Methods: A total of 232 children were screened for suspected Rubella infection and 276 children were screened for CMV infection. A total of 34 asymptomatic pregnant women were screened for CMV and 112 Asymptomatic Pregnant women for Rubella infection. Pregnant woman with obstetric complications were screened for CMV (n=66) and Rubella (n=282). Blood samples from pregnant woman (Asymptomatic and also woman with obstetric problems) and children (suspected of intrauterine infections) were collected and send to laboratories for tests. The samples were tested for Rubella and CMV specific IgM antibodies by CMIA methods.

Results: In children, overall positivity for Rubella and CMV specific IgM antibodies was 3.44% and 12.67% respectively. In asymptomatic Pregnant females Rubella positivity was 0.89%, while with obstetric complication it was 4.96%. IgM antibody positivity in cases of CMV was 8.82% in asymptomatic pregnant woman and 7.57% in woman with obstetric complications.

Conclusion: The study indicated that infection with CMV is more common than the rubella virus. The incidence of rubella infections were decreases in the past few years. Hence, screening for rubella infection may be reserved for women with obstetric complications only. The routine screening for CMV among all antenatal cases is a debatable issue.

Keywords: Cytomegalovirus, congenital infection, IgM antibodies, rubella.

Introduction
Human cytomegalovirus (CMV) and rubella virus are increasingly being recognized as important causes of congenital infection. Intrauterine transmission of CMV to the baby can occur irrespective of prior maternal exposure; whereas, in rubella, a previous exposure actually prevents the virus from crossing the placenta by generating protective antibodies. The incidence of congenital CMV from 0.5-3.0% in all live births. CMV is also linked to late abortions and still births. A rubella virus infection has also been increases in India. If contracted during the first trimester of pregnancy, it can infect the foetus leading to congenital rubella syndrome. Congenital CMV infection usually presents as hepatosplenomegaly.
with or without jaundice, low birth weight, chorioretinitis, or anemia. On the other hand, congenital rubella syndrome usually manifests in the form of developmental defects like cataract, hearing, or cardiac defects. Following the rubella vaccination practices, the incidence of rubella has been reduced drastically but the World Health Organization (WHO) still estimates over 100,000 children worldwide are born with congenital rubella syndrome and more so in developing countries. This study was carried out to assess the prevalence of CMV and rubella viral infections in children with suspected congenital infection and pregnant females by detection of virus specific IgM antibodies.

**Materials and Methods**

The present study was conducted in the Department of Paediatrics, P.G.I.M.E.R. & R.M.L Hospital New Delhi with the help of Department of obstetrics and Gynaecology, during the period of January 2012 to December 2013. The samples belonged to patients from the following clinical groups:

1. Children suspected of suffering from intrauterine infections these children presented with one or more of the following clinical manifestations – fever, pneumonia, jaundice, encephalitis, cardiac anomalies, hearing defects, nephrotic syndrome, growth retardation, or ascites. A total of 232 children were screened for suspected rubella infection and 276 children were screened for CMV infection.

2. Pregnant women, These samples belonged to the following groups:
   a. Asymptomatic pregnant women in the age group of 21-36 years who were screened for CMV (n = 34) and rubella (n = 112) as part of a routine antenatal check-up.
   b. Pregnant women with obstetric complications like bad obstetric history (BOH> 2 consecutive abortions or still births) or intrauterine growth retardation (IUGR) and/or congenital foetal malformations (CFM) detected antenatally by ultrasonogram who were screened for CMV (n = 66) or rubella (n = 282) depending on clinical suspicion.

Venous blood samples were collected from all the patients, serum was separated and stored at – 20°C until tested. The samples were tested for CMV and rubella-specific IgM antibodies by CMIA methods (Abbott diagnostics). The manufacturer's instructions were strictly adhered to in the performance and interpretation of the tests.

**Result**

Of the children with suspected congenital infection, rubella and CMV specific IgM antibodies were detected in 3.44% (8/232) and 12.67% (35/276), respectively. These children were divided into 3 age groups: 0-29 days, 1 month-1 year and > 1 year. The rubella and CMV seropositivity in these groups is shown in Table 1. Dysmorphism was the common clinical presentation in rubella IgM positive cases whereas sepsis, pneumonia and neonatal jaundice were the presenting feature in CMV positive cases.

Among the asymptomatic pregnant females screened, IgM antibodies to rubella and CMV could be detected in 0.89% (1/112) and 8.82% (3/34) of the females.

| Table – 1 Age-specific prevalence of rubella-and cytomegalovirus-specific IgM antibodies in children |
|--------------------------------------------------------|
| Age group | Serology performed | No. tested | IgM positive | Percent positivity |
|-----------|--------------------|------------|--------------|--------------------|
| 0-29 days | Rubella            | 69         | 3            | 1.29               |
|           | CMV                | 94         | 5            | 1.81               |
| 1 month-1 year | Rubella       | 112         | 3            | 1.29               |
|           | CMV                | 135        | 25           | 9.05               |
| > 1 year  | Rubella            | 51         | 2            | 0.86               |
|           | CMV                | 47         | 5            | 1.81               |
| Total     | Rubella            | 232        | 8            | 3.44               |
|           | CMV                | 276        | 35           | 12.67              |
Table-2 Rubella and Cytomegalovirus positivity in pregnant females

| Patient group                                      | Viral serology | No. tested | No. of positive cases | Percent positivity |
|---------------------------------------------------|----------------|------------|-----------------------|--------------------|
| Asymptomatic Pregnant females                      | Rubella        | 112        | 1                     | 0.89               |
|                                                   | CMV            | 34         | 3                     | 8.82               |
| Pregnant women with obstetric problems            | Rubella        | 282        | 14                    | 4.96               |
| a) Bad obstetric history                          | CMV            | 66         | 5                     | 7.57               |
| b) Intrauterine growth retardation                | Rubella        | 201        | 9                     | 4.47               |
| c) Congenital foetal malformation                 | CMV            | 40         | 5                     | 12.5               |
|                                                   | Rubella        | 51         | 3                     | 5.8                |
|                                                   | CMV            | 23         | 0                     | 0                  |
|                                                   | Rubella        | 30         | 2                     | 6.6                |
|                                                   | CMV            | 3          | 0                     | 0                  |

Discussion
In present study, we have analysed for rubella and CMV infection in a tertiary care hospital of New Delhi. The study was carried out in three clinically distinct groups. The evidence of congenital rubella was seen in 3.44% of children with suspected congenital infection, which is at par with the declining trend in the incidence of congenital rubella syndrome from 34.5% in 1988 to 0% in 2002 as observed by Gandhoke, et al. and is much less than the earlier reports of 10-20%. Out of 112 asymptomatic pregnant females screened for rubella in the present study, 1 (0.89%) were found to be positive. The observation was similar in recent studies where in IgM positivity was observed only in 1% of pregnant women. However, 3-9% rubella IgM positivity has been shown in asymptomatic pregnant women by other investigators. Recent studies have shown that the majority of pregnant women in the Indian population are immune to rubella, thereby leaving only a few susceptible to contract acute rubella infection. In this study, the overall IgM positivity in women with obstetric complications was 4.96%. Singla, ET al. has reported higher positivity (10.4%) in women with adverse pregnancy outcomes as compared with those with normal obstetric performance (3.6%). The positivity in BOH cases in this study was 4.47%, which is much less than earlier studies that have observed a positivity of 10-28%. In our study, the rubella virus could be attributed in 5.8% of IUGR cases and 6.6% of congenital foetal malformation cases. Rubella virus is known for its teratogenicity and can also cause intrauterine growth retardation. If primary rubella infection occurs during the first trimester of pregnancy, the incidence of congenital rubella is 90% and the risk decreases to 25% during the third trimester. In India, the serological status of most women is not known before pregnancy. A baseline pre-pregnancy screening of rubella is necessary because a demonstration of high immunity puts women at relatively no risk of infection during pregnancy. Also, it will enable prescription of vaccination 1 to 3 months before conception in seronegative women thereby further reducing the incidence of congenital rubella syndrome.

In this study, laboratory evidence of CMV infection in the form of IgM antibodies were found in 12.67% of suspected infants with congenital infection. Broor, et al. and Ganghoke, et al. have reported IgM positivity of 20% and 18.75% in infants and children, respectively with congenital infection. Presently, the overall incidence of CMV in women of child bearing age was 8.82%. Only minimal difference was observed in IgM positivity among asymptomatic pregnant women and those with obstetric complications. Considering the fact that transmission to foetus occurs in about 40% of the cases with primary infection and results in the delivery of about 10-15% symptomatic and 85-90% asymptomatic congenitally-infected newborns, so need for routine screening for CMV in all antenatal cases. The 8.82% IgM positivity in asymptomatic pregnant women seen in our study is similar to earlier Delhi-based studies. However,
some studies from India have observed a higher positivity of 13-20% in asymptomatic pregnant women. This study shows a seropositivity of 7.57% in women with obstetric problems. A positivity of 8-27% in women with BOH and other obstetric problems has been reported previously.

In present study, we observed significantly higher CMV positivity in infants presenting with hepatosplenomegaly with or without jaundice, sepsis, or pneumonia, whereas significantly higher rubella positivity was seen in infants presenting with dysmorphism. No significant difference was noted in the relative prevalence of CMV and rubella infection in infants presenting with other clinical manifestations. Thus, the findings of the present study are in agreement with earlier observation.

**Conclusion**

As of now, there is no strict treatment regimen for patients infected with rubella and CMV in India. However, limited clinical trials have shown an improvement in hearing loss in children infected with CMV following Ganciclovir treatment. Since it is well known that all children infected with these viruses may not develop clinical manifestations of the disease during the first year of life.

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