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ORIGINAL ARTICLE

Routine Screening for Rubella and CMV Antibodies During Pregnancy: Is it Justifiable?

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Abstract
Background Rubella and cytomegalovirus (CMV) screening during pregnancy is routinely carried out in India. However, its value has been questioned due to the absence of clearly effective intervention.
Objectives This retrospective study evaluates the usefulness of rubella and CMV antibody screening during pregnancy.
Materials and Methods Serum samples received from pregnant women and children were tested for rubella- and CMV-specific IgM antibodies by capture ELISA. The data were analyzed to determine the incidence of rubella and CMV infection during pregnancy and in congenital infections.
Results In asymptomatic pregnant females ($n = 505$), rubella positivity was 3.16 % and in women with bad obstetric history (BOH) ($n = 220$), it was 7.72 %, while CMV positivity was 5.9 % in both asymptomatic pregnant women and in women with BOH. In children ($n = 200$), the overall positivity for rubella- and CMV-specific IgM antibodies was 15 and 25 %, respectively. A declining trend was observed in the incidence of both rubella and CMV infections in pregnant women and in women with BOH. In children, the incidence of congenital rubella syndrome has declined, but the incidence of CMV infection has remained almost the same in 5 years.
Conclusion The incidence of rubella has reduced over the past 5 years and can further be prevented by providing direct protection to women and school girls with rubella vaccines. Primary CMV infection in pregnancy is the main problem, and due to the unavailability of efficient and safe treatment, routine antenatal screening for rubella and CMV should be reserved for women with obstetric complications only.

Keywords Rubella and CMV antibodies · Routine screening · Pregnant women

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Introduction

Infections acquired in utero or during the birth process are a significant cause of fetal and neonatal morbidity and important contributors to early and later childhood morbidity [1]. Human CMV and rubella virus are increasingly being recognized as important causes of congenital infection. The endemicity of the rubella virus has already been established in India [2]. Even without a global recommendation, some countries have added the rubella vaccine to their national immunization programs, reflecting the high coverage levels (>80 %). Childhood vaccines in these countries [3], intrauterine transmission of CMV to the baby can occur irrespective of prior maternal exposure [2].

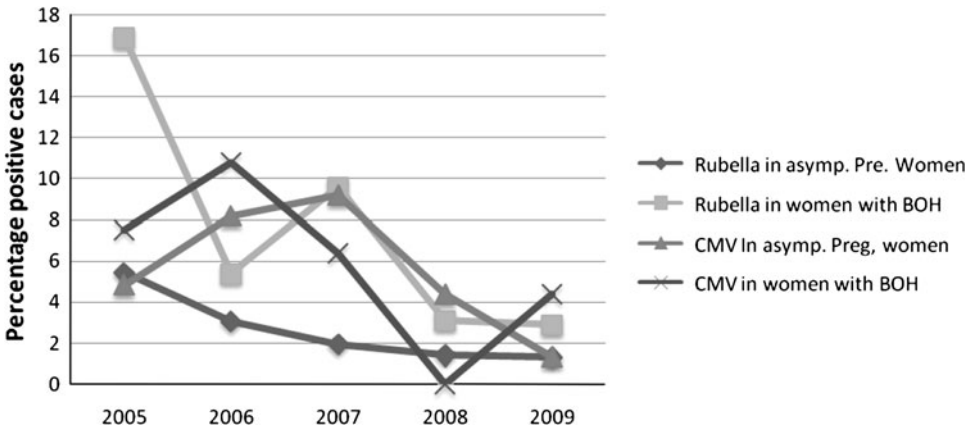

Fig. 1 Annually reported cases of rubella and CMV in pregnant women

Routine screening of pregnant women at the first prenatal visit for rubella and CMV antibodies is common in many parts of the world. However, the value of this testing has been questioned [4–6]. The utility of rubella and CMV titers as an effective tool is doubtful because of overuse and consistent lack of interpretability and reliability [7]. Moreover, for CMV, there is an absence of clearly effective intervention [8, 9]. In our hospital, we routinely screen pregnant women for rubella and CMV IgM antibodies in order to determine the maternal antibody status. This retrospective study was carried out to assess the usefulness of routine screening for rubella and CMV antibodies during pregnancy.

Materials and Methods

Study Population

Nine hundred and twenty-five cases were screened for CMV and rubella antibodies from Jan 2005 to Dec 2009 in the virology laboratory of Maulana Azad Medical College. The samples belonged to following three groups:

1. Children suspected of suffering from intrauterine infection ($n = 200$), referred by the pediatrics department of Lok Nayak Hospital.

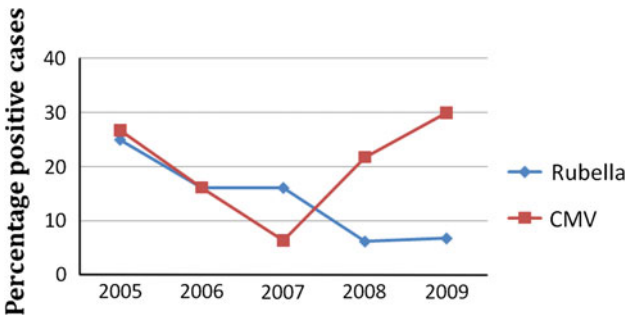

Fig. 2 Annually reported cases of rubella and CMV in children

2. Pregnant women with BOH ($n = 220$)(BOH > 2 consecutive abortions, still births or intrauterine growth retardation, and/or history of congenital fetal malformation) attending the antenatal clinic at Lok Nayak Hospital.
3. Asymptomatic pregnant women ($n = 505$) attending the antenatal clinic at Lok Nayak Hospital.

Antibody Detection

Venous blood was collected from all the patients; serum was separated and stored at −20 °C until further processing. Serum samples were tested for the presence of CMV IgM and rubella IgM antibodies by M capture enzyme immunoassay (Adaltis, Italy). IgG avidity assay (Euroimmune AG kit) was used in combination with IgM Elisa for monitoring pregnant women with primary CMV and rubella infection. The tests were performed and interpreted as per the manufacturer's instructions.

Data Analyses

Data were analyzed to determine the incidence of rubella and CMV infection in pregnancy and congenital infections. Statistical analysis was done using Chi square test and student's t test. Statistical significance was assigned to a p value <0.05. Odds ratio and risk ratio were calculated for rubella and CMV infections in asymptomatic women and women with BOH.

Results

Out of 925 cases, 505 were asymptomatic pregnant women, 220 were pregnant women with BOH, and 200 were children with suspected intrauterine infection. On analyzing the year-wise data (Figs. 1, 2), a declining trend was observed in prevalence of rubella and CMV infections

(5.4 and 4.8 %, respectively, in 2005 and 1.3 % for both in 2009) in asymptomatic pregnant women and in women with BOH (16.9 and 7.54 %, respectively, in the year 2005 to 7.72 and 5.9 % in the year 2009). Similarly, in children, the incidence of congenital rubella syndrome has declined from 25 % in 2005 to 11 % in 2009. However, the incidence of CMV infection has remained almost same during the five years (26 % in 2005 and 30 % in 2009).

Among the asymptomatic pregnant women who were screened, rubella and CMV positivity was observed in 3.16 % (30/505) and 5.9 % (30/505), respectively. However, in pregnant women with BOH, IgM antibodies against rubella and CMV were observed in 7.72 % (17/220) and 5.9 % (13/220) cases, respectively. Among the asymptomatic rubella- and CMV-positive pregnant women, primary infections (IgG avidity index less than 40) were not seen in any of them, while the pregnant women with BOH showed primary rubella (IgG avidity index < 40) infections in 29.4 %(5/17) cases and primary CMV (IgG avidity index < 40) infections in 46.1 % (6/13) cases. There was a significant difference in prevalence of rubella in asymptomatic pregnant women and in women with BOH (p Value < 0.05). However, there was no significant difference in prevalence of CMV in asymptomatic pregnant women and in women with BOH (p value > 0.05). The odds ratio was 2.6 and risk ratio was 2.7 for rubella infection in the two groups, implying that the risk of rubella infection is 2.7 times more in women with BOH than in pregnant women. On the other hand, the odds ratio was 0.96 and risk ratio was 1.1 for CMV infection in the two groups, implying that the risk of CMV infection is the same in pregnant women and in women with BOH. Age-wise distribution of the cases shows that the positivity of rubella and CMV was the highest in the age group of 20–24 years among the pregnant women of both the groups. The prevalence of rubella and CMV in different age groups did not show a significant difference (Table 1).

Out of the 200 children suspected of having congenital infections, rubella- and CMV-specific antibodies were observed in 15 % (30/200) and 25 % (50/200), respectively. On analyzing the age-specific prevalence, rubella positivity was high in the 0–29-day-old children and in children >1 year, and CMV positivity was high in children of the age group 1 month–1 year. The prevalence of rubella and CMV in different age groups did not show a significant difference (p value = >0.05) (Table 2). The common symptoms observed in these children were cardiac defects, congenital cataract, hepatomegaly with jaundice, and microcephaly (Table 3). Children suspected of having CMV infection were referred to the pediatric OPD where they were treated with ganciclovir, while those with rubella were placed on conservative management.

Discussion

Over the past 5 years (2005–2009), we received 925 cases in our virology laboratory to screen for rubella and CMV antibodies. The data were analyzed in three clinically distinct groups. Rubella positivity was 15 % in children with suspected congenital infection, with a declining trend in the incidence from 25 % in the year 2005 to 11 % in the year 2009. However, the incidence of congenital rubella syndrome was seen only in 2.8 % of children by Singh et.al. [2], but the declining incidence of congenital rubella syndrome in our study was similar to other studies [2, 9]. Rubella IgM positivity in asymptomatic pregnant women was 3.16 %. This observation was similar to studies by other investigators [10–12], wherein IgM positivity for rubella was 3–9 %. Rubella positivity in women with BOH was 7.72 %. Similar observations were obtained in other studies [11–14] where 10–28 % of women with BOH were positive for rubella antibodies. This may be due to the fact that a majority of the women in the Indian population are immune to rubella as proven by studies conducted by Yadav et al. and Gupta et al. [15, 16]. Therefore, the authors believe that routine screening for rubella should be reserved for women with BOH only. In addition to these findings, we observed that the prevalence of primary rubella infection was less in asymptomatic women as compared to the women with BOH (0 % in asymptomatic women and 29.3 % in women with BOH). It may be suggested that it is the low rubella immunity status that makes

Table 1 Age-specific prevalence of rubella and CMV IgM antibodies in pregnant women

Age group	Women with BOH			Asymptomatic pregnant women		
	Total cases	Rubella-positive	CMV-positive	Total cases	Rubella-positive	CMV-positive
15–19	2	0 (0 %)	0 (0 %)	12	0	0 (0 %)
20–24	29	4 (13.1)	3 (10.3 %)	265	8	21 (7.9 %)
25–29	165	12 (7.2 %)	8 (4.8 %)	161	3	6
30–34	20	1 (5 %)	2 (10 %)	55	2	3 (5.4 %)
>35	4	0 (0 %)	0 (0 %)	12	0	0 (0 %)
Total	220	17 (7.7 %)	13 (5.9 %)	505	13 (3.16 %)	30 (5.9 %)

Table 2 Specifics of rubella IgM in age prevalence and CMV antibodies in Children

Age group	Total cases	Rubella-positive cases	CMV-positive cases
0–29 day	34	6 (3 %)	5 (2.5 %)
1 month–1 Year	138	19 (9.5 %)	43 (21.5 %)
>1 Year	28	5 (2.5 %)	2 (1 %)
Total	200	30 (15 %)	50 (25 %)

Table 3 Clinical features attributable to congenital rubella and CMV infections

Features	Rubella-positive	CMV-positive	Total cases
Cardiac malformation/PDA	8	1	9
Cataract	11	12	23
Hepatomegaly and jaundice	6	17	23
Encephalitis	1	2	3

an individual susceptible to rubella infections. Hence, immunization of females against rubella, before contemporary pregnancy, will prevent repeated abortions and the birth of infants with congenital rubella syndrome. It is important that countries like India which include the rubella vaccine in their national immunization program should insure that their strategies should include women in childbearing age.

In our study, CMV positivity in asymptomatic pregnant women and in women with BOH was almost similar (5.9 %). The risk of CMV infection was also the same (odds ratio = 0.96 and relative risk = 1.1) in pregnant women and in women with BOH. Singh et al. [2] also had similar observations in the study, with no difference in IgM positivity among asymptomatic pregnant women and those with obstetric complications. CMV positivity of 8–27 % in women with BOH has been reported by other studies [14, 17]. We have observed higher CMV positivity (25 %) in children suspected of congenital infections. Studies conducted by Broor et al. and Ganghoke et al. [18, 19] have also reported high CMV positivity of 20 and 18.7 %, respectively, in children with congenital infections. However, the incidence of CMV infection has almost remained the same in the last 5 years among children, but a declining trend has been observed in pregnant women (4.8 % in 2005 to 1.3 % in 2009). Similar to rubella infections, the prevalence of primary CMV infections was also found to be less in asymptomatic women as compared to pregnant women with BOH (0 %). Considering the observations in our study, it is felt that there is no need for routine screening of pregnant women for CMV because efficient and safe treatment for CMV infection is still not available. Only women with obstetric complications should undergo testing for CMV antibodies, and recent primary infection should be proved which is really the problem during pregnancy Moreover, females who were diagnosed with rubella or CMV infection in the first trimester were advised to terminate their pregnancy and those who came in the later trimesters were counseled for the consequences by the treating obstetrician. So, even if the rubella and CMV status is known, no specific standard treatment guidelines for managing such cases are available in India and obstetricians just end up counseling and reassuring the patients.

To conclude, CMV infection is more common than rubella in India. The incidence of rubella has decreased over the past 5 years and can further be prevented by providing direct protection to adolescent girls and women of the reproductive age group with rubella vaccine in addition to childhood immunization. Routine screening of rubella should be reserved for women with BOH only. Primary CMV infection is the main problem during pregnancy, and therefore routine screening for CMV infection can be justified only when reliable tests are used for diagnosis like detection of CMV-specific IgM antibody complemented with IgG avidity which will prove or disprove primary infection.

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