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ORIGINAL ARTICLE

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Diagnosis of acute rubella infection during pregnancy

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OBJECTIVE(S) : To study prevalence and method of diagnosis of acute rubella infection during early pregnancy.

METHOD(S) : Clinical signs and symptoms of acute rubella infection were looked for in 100 pregnant women booked before 12 weeks of gestation. Serial rubella specific IgG and IgM serologic testing was done in these 100 women before 12 weeks of pregnancy, after 3 weeks, and again at 18-20 weeks of gestation. Ultrasound was done at 12-14 weeks and at 18-20 weeks of gestation for detecting malformations.

RESULTS : No woman had clinical signs and symptoms of rubella infection. One woman was IgM positive at 9 weeks of pregnancy; 79 were IgG +ve but IgM -ve initially and also on repeat sampling after 3 weeks; while 20 women were nonimmune (IgG and IgM negative) in the first trimester, after 3 weeks, and again at 18-20 weeks.

CONCLUSION(S) : Acute rubella infection was diagnosed by serial serologic screening in 1% women in early pregnancy.

Key words : rubella, pregnancy

Introduction

Rubella virus is one of the most teratogenic agents known. If primary rubella infection occurs during pregnancy, the virus may cross the placenta and induce fetal infection, depending upon the gestational period [1]. The classic triad of defects associated with congenitally acquired rubella consists of cataracts, heart defects, and sensorineural deafness, but many other anomalies have also been described [2]. The pathological potential of intrauterine rubella, the congenital rubella syndrome (CRS) has greatly expanded [3]. Cases of CRS are still being reported in India, as in most other countries, despite the availability of rubella vaccine since 1969 [3,4].

Women at high risk for contracting rubella in pregnancy are those who are nonimmune to rubella and are exposed to the infection. More than half of the women infected with rubella do not show the classical signs and symptoms of fever and 3 day rash. Hence, serologic tests are used to diagnose acute infection in the pregnant woman. In general, IgM production is the acute reaction, followed by IgG in 1-3 weeks. Diagnosis of acute maternal infection is made by seroconversion (IgG -ve mother becoming IgG +ve), a four fold increase in IgG serial titer over 2-3 weeks, or the demonstration of pathogen specific IgM [5,6].

In India, a woman's serologic status is rarely known before pregnancy and there are no studies on serial screening for diagnosis and prevalence of acute rubella infection during pregnancy. This study was, therefore, planned to diagnose acute rubella infection during pregnancy, clinically and by serial immunological testing.

Methods

This cohort study was carried out from July 2001 to December 2002. One hundred consecutive pregnant women attending the antenatal clinic in the first trimester of pregnancy were included in the study. Women with documented previous rubella infection, birth of a CRS baby, recent rubella vaccination, and those more than 12 weeks pregnant were excluded. The following protocol for diagnosis of acute rubella infection by serology was carried out :

1. At < 12 weeks gestation, positive rubella specific IgG and IgM.

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2. If IgM negative and IgG positive, repeat IgG levels after 3 weeks for evidence of significant (3-4 times) rise in titres, signifying acute infection.
3. At 18-20 weeks, repeat estimation of IgG and IgM levels in seronegative women for evidence of seroconversion.

Clinically fever, rash, and any other signs and symptoms of acute rubella infection were looked for and IgG and IgM levels determined for confirmation.

Estimation of all IgG and IgM levels were by standard sandwich ELISA and μ capture ELISA respectively at the Institutional Referral Laboratory only [7,8].

Routine antenatal care was provided, with a detailed ultrasound scan performed at 12-14 weeks and 18-20 weeks for structural malformations.

Results

Clinical Features : No woman had any clinical evidence of rubella, fever or rash, in the first half of pregnancy.

Serology

Before 12 weeks – one woman was IgM +ve (acute infection) at 9 weeks (Group 1), 79 women were IgG +ve and IgM -ve (Group 2), and 20 women were with IgG and IgM negative (Group 3).

After 3 weeks, repeat serology showed that none of the 79 women who were +ve for IgG in Group 2 showed any rise in IgG titres and none of the 20 women who were IgG and IgM negative in Group 3 showed seroconversion.

At 18-20 weeks IgG and IgM levels were still negative in the 20 seronegative women of Group 3.

Thus acute infection was documented in only one out of the 100 pregnant women. She opted for medical termination of pregnancy.

None of the remaining 99 women had evidence of CRS in her baby at birth.

Discussion

Though rubella is mainly a disease of childhood (3-10 years), over 70% cases occur in people more than 15 years of age and in the reproductive age [7]. The disease is world wide in distribution and tends to occur in epidemics in non-immunized populations every 4-9 years in a seasonal pattern during late winter and spring. The virus was isolated in 1962, and the attenuated vaccine was developed in 1967 which became commercially available since 1969 [3,5].

The nonimmune pregnant woman can get infected directly by droplets from the nose and throat on contact with a clinical or more often a subclinical case of rubella. There could be a history of contact with a child/adult having fever and rash. The incubation period is 14-18 days, but may be as long as 21 days. Infectivity probably ranges from a week before symptoms to about a week after the rash appears, and it is maximum when the rash is erupting [1,3]. The vaccine virus is not communicable.

In a typical clinical case of acute rubella infection there are :

a) Prodromal symptoms of coryza, sore throat and low-grade fever, which herald the onset of viremia.
b) Postauricular and posterior cervical lymphadenopathy may appear even 7 days before the rash and remain for 10-14 days after the rash.
c) Minute, disecrete, macular facial rash may appear within 24 hours of the onset of prodromal symptoms. Rash may spread to the trunk and extremities and dispappear within 3 days, as compared to the longer lasting measles rash.
d) Rarely, complications such as arthralgia, encephalitis and thrombocytopenic purpura can occur [1,9].

Differential diagnosis include parvovirus B-19, enterovirus, measles and some arbovirus infections.

The clinical diagnosis of acute rubella infection in pregnancy is extremely difficult. The rash is not very specific nor particularly apparent, and most infectious cases are subclinical [8]. Therefore, demonstration of seroconversion and presence of high IgM titres is the primary mode of diagnosis of acute rubella in pregnancy. If a woman has been exposed to or is in contact with a case of rubella or if infection is suspected because of rash or fever, serology – especially with paired acute and convalescent samples – can diagnose acute infection if there is seoconversion [1,7,8,10]. Viral isolation from the throat or blood is confirmatory [7].

The very widely used serologic test is the hemagglutination inhibition (HAI) test developed in 1966. Two blood samples – first within 5 days of exposure or onset of illness and the second 2 weeks later – should be examined. A four fold rise of HAI Ab in this paired sera or presence of IgM in a single serum sample is diagnostic of recent, acute rubella infection. More sensitive serologic tests are the ELISA test and the radio-immuno assay [8,10.11].

Women who are immune to rubella after natural infection or

vaccination demonstrate lifelong IgG antibodies. Presence of natural immunity (IgG +ve) is a parameter of protection from infection during pregnancy, the same as offered by vaccination. Hence, prepregnancy screening of all women and demonstration of high immunity places a woman at relatively no risk of rubella infection during pregnancy.

If primary rubella infection occurs during pregnancy, the rubella virus will cross the placenta, and induce fetal infection depending upon the time of gestation. Infection occurring in the first 12 weeks of pregnancy causes congenital rubella infection in 90%, with almost a 100% risk of congenital defects. From 13 to 17 weeks the risk of infection is about 60%, and risk of defects about 50%. From 18 to 24 weeks the risk of infection is about 25%, with hardly any risk of congenital defects [1,6,10].

Hence, it is very important that if rubella screening is done at all, testing should be done serially as in our study protocol, starting in the early first trimester. A baseline prepregnancy screen is most useful for the immunological status which also enables prescription of vaccination 1-3 months before planning a pregnancy in seronegative women [3,5]. Many cases are referred to us with rubella IgG positive report and request for prenatal diagnosis or even termination of pregnancy. Most often than not the serology is done late in pregnancy with either IgG or IgM values only, at a laboratory where serum samples are not stored for repeat testing of paired samples. In such a scenario, it is most often impossible to diagnose or time the infection to the exact/approximate period of gestation. This causes great anxiety to the couple and also to the referring obstetrician and to the referral fetal medicine center specialist. Thus, knowledge of the pathogenesis of the infection and interpretation and correct timing of testing in relation to period of gestation is vital for diagnosis of rubella in pregnancy [12]. At present, in India, data is scant and not uniform [7,13] and ideally screening protocols should not be done outside research trials to study the magnitude of the problem and their cost effectiveness. Attention may be focused by specific laboratory tests on the high risk group of women, those with clinical signs and symptoms of suspected rubella infection, and complications in pregnancy. Universal serial screening in pregnancy for seroconversion is expensive and therefore not a cost effective venture. Pre-pregnancy universal vaccination is more practical in developing countries like India [14,15].

Conclusion

The incidence of acute infection in nonepidemic situations is relatively low, as demonstrated in this pilot study, and is diagnosed mainly by serology. This is the first research study on diagnosis of acute rubella infection during the vulnerable weeks of pregnancy, clinically and by serial immunological serologic testing in India.

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