

Fetal risk associated with rubella mass vaccination

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Introduction

In previous reports to CDC, approximately 2% of infants born to susceptible vaccinee had serologic evidence of subclinical infection, regardless of rubella vaccine strain.^[1]

In response to the above concern, a descriptive study was designed to find clinical congenital Rubella syndrome (CRS) and congenital rubella infection (CRI) in newborns of inadvertently vaccinated pregnant women after a mass campaign with Measles RA27/3 rubella vaccine in Yazd, Iran, during 2004.

Materials and Methods

A descriptive cross-sectional study was carried out in Yazd, Iran, from 8th July 2004 to 29th December 2004. We found 442 parturient women ≤ 26 years old who had been inadvertently vaccinated against measles and rubella (MR) while pregnant or who became pregnant within 3 months after vaccination, and they were enrolled in a study for determination of CRS and CRI.

Before carrying out the study, midwifery staff of hospitals was given training on various aspects of the study. A questionnaire containing parturient women's age; dates of last menstrual period, delivery and vaccination; newborns' weight, height and head circumference, whether born alive or dead was provided. All newborns were examined by pediatrician for signs of CRS. Plasma samples from cord blood stored at -80°C were examined for rubella-specific IgM and IgG by ELISA method.

Information was collected for 437 neonates and their mothers. One hundred ninety-seven fetal cord blood samples were examined for both rubella-specific IgM and IgG, 179 samples were examined only for IgG due to laboratory error, 5 intrauterine fetal death products could not provide any blood and 61 neonates were examined by pediatrician but their blood samples were either lost or discarded because of inadequate storage.

Study subjects were finally classified in one of the four following categories:

1. Confirmed cases of CRS, a newborn that has both congenital anomalies compatible with rubella and serologic evidence of rubella infection at birth
2. Clinical congenital rubella syndrome, a newborn that has only congenital anomalies compatible with rubella without serologic confirmation at birth
3. Confirmed case of CRI without CRS, a newborn without any congenital anomaly compatible with rubella but with serologic evidence of rubella infection at birth (i.e., positive specific IgM in fetal cord blood)
4. Healthy newborn, with neither congenital anomalies nor serologic evidence of rubella infection ^[2]

Ethical clearance was obtained from ethical board of the funding university. Analysis was done after determining the frequencies and coding the information.

Results

We gathered information about 437 neonates, including 5 twins, to find the frequency of CRS or confirmed congenital rubella infection. Seven deaths (including 2 stillborns) within 3 hours of birth were registered. All of the remaining 430 neonates were free of defects compatible with CRS. Other congenital abnormalities are presented in [Table - 1].

In 197 serum samples examined for both rubella-specific IgM and IgG, 2 (1.01%) reacted positive for IgM (ISR >1.1) and negative for IgG (<6.5 IU/ml); both were free of defects compatible with CRS and so were labeled as confirmed congenital Rubella infection. First had normal weight; her mother had been vaccinated while 3 weeks pregnant. The second neonate weighed 2,400 gm; her mother became pregnant 1 month after vaccination.

One serum sample reacted negative for both IgM (ISR <0.9) and IgG, and the remaining 194 serum samples reacted negative for IgM and positive (>8.2 IU/ml) for

IgG (12.7-195.5 IU/ml). Three deaths (out of 7) occurred in this group; one was low birth weight associated with hypoplasia of lungs, hepatomegaly and oligohydramnios; and one was premature.

All of 179 newborns whose serum samples were examined only for IgG at birth reacted positive (8.6-84.7 IU/ml); none had defects compatible with CRS. Two deaths (out of 7) occurred in this group (weighed 2,100 gm and 2,700 gm).

In 61 neonates whose blood samples were lost or discarded no congenital anomaly compatible with CRS was observed; two deaths occurred among them (weighed 1,100 gm and 1,400 gm).

In follow-up of 2 CRI cases, one at 28 months and the other at 30 months of age, no abnormality was observed in development, vision and hearing.

Discussion

No clinical CRS was observed in 430 alive neonates examined in this study. A prospective study in 94 women exposed to rubella vaccine 3 months pre- or post-conception revealed the same result.^[3] In another study, 119 women susceptible to rubella received RA 27/3 vaccine; none of them gave birth to a living infant with abnormality compatible with CRS.^[4] In a report to CDC, none of the 505 newborns whose mothers had been vaccinated with RA 27/3 had defects compatible with CRS.^[1]

Confirmed CRI was seen in 2 (1.01%) of the 197 neonates in the present study. Although pre-vaccination immunity status of our study subjects was individually unknown, yet in a study performed to evaluate the immune status against rubella before and after the mass campaign vaccination in the same country, 92.2% of subjects had anti-rubella antibody using HI test.^[5] So 2 confirmed cases of CRI in neonates of about actually 15 to 16 susceptible women (out of 197) were observed (approximately 13%).

The rate in the present study is higher than that reported (0.8%) by another study which was carried out in women susceptible to rubella before vaccination with RA 27/3 vaccine.^[4] It was lower than that (1.44%) reported to CDC.^[1] They cannot be compared with our rate because they obtained those rates in women susceptible to rubella before vaccination. If we take the susceptible section of our study population into consideration, the corrected rate will become higher than the rate reported in both studies. This may be due to more potent virus in vaccine used in campaign.

Only moderate and severe cases of CRS are typically recognized at birth. In mild forms of the disease, however, the anomalies may not be obvious at birth but become apparent within the first year of life. Often such cases are diagnosed long after birth as clinical manifestations become gradually apparent. So we examined two CRI cases, but we did not find any abnormality in them at 28 and 30 months of age and CRS was ruled out.

Regarding anomalies, polydactyly, folded ear lobes and bilateral clubfoot observed in this study were not mentioned in CDC report. ^[1]

Conclusion

No doubt pregnancy remains a contraindication to rubella vaccine because of the theoretical risk of CRS, and reasonable precautions should be taken to preclude vaccination of pregnant women; yet if vaccination does occur within 3 months before or after conception, the risk of CRS is so small as to be negligible.

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