Placental Transfer of Respiratory Syncytial Virus-Specific IgG in Iranian Mothers

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ABSTRACT

Background: Respiratory Syncytical virus infection is the most common cause of bronchiolitis and viral pneumonia in infancy. **Objective:** To investigate the placental transfer of RSV-specific IgG in Iranian mothers. **Methods:** The antibodies were measured in sera of 146 mother/newborn pairs using a commercially available indirect Enzyme Linked Immunosorbent Assay (ELISA). The studied subjects were among healthy pregnant women who attended to the Zeinabieh Hospital of Shiraz University of Medical Sciences in a one year period. **Results:** A highly significant correlation was observed between RSV-specific IgG in newborns and mothers ($r = 0.88$). However, mean RSV-specific IgG antibodies in neonates was significantly higher than that of their mothers ($P = 0.019$). In addition, the mean cord/maternal ratio of RSV-specific IgG was detected to be 1.27 ± 0.60. Maternal blood group, age, parity, previous abortions and neonatal gestational age had no correlation with placental transfer of RSV-specific IgG antibodies. **Conclusion:** Our finding demonstrates that placental transfer of RSV-specific IgG antibodies is an active process and the main factor that influences this transfer is maternal concentration of these immunoglobulins.

Key words: IgG, Iranian, Placental Transfer, RSV

INTRODUCTION

Respiratory Syncytial Virus (RSV) is a member of Pneumovirus genus of Pnemovirinae sufamily (1). The virus is the most common cause of viral lower respiratory tract infection in infants and young children. Infected children suffer from bronchiolitis and viral pneumonia with a peak at age 2-6 months (1). Infection among infants is sometimes very severe and results in hospitalization of children

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(2), which is suggested to be associated with birth weight, maturity, immune function, socioeconomic class and gender of infants (3,4,5,6,7,8). Among infants, age below 3 months is considered a main factor for severity of the disease (2,9,10,11).

Epidemiological studies have shown that most adults have antibodies against RSV virus, however, the level of these antibodies differ among individuals (1). Most of children become infected before 2 years of age; however, the symptomatic disease appears only in a fraction of infected children (12,13). The annual rate of RSV-related mortality among children below 5 years of age is estimated to be 600000 to 1000000 deaths (14,15). In addition, there is a correlation between RSV bronchiolitis in childhood and developing respiratory diseases in the adulthood (16).

An intact and competent immune system can resolve the infection and produces partial resistance to further infections (15,17,18,19). Both humoral and cellular immune responses are essential in the immunity to the virus (18,19). The most important role of RSV-specific antibodies is decreasing the severity of infection and rate of hospitalization of infants (12,18). Maternal antibodies which can pass placenta during gestation decrease the risk of infection and severe disease among infants especially in high risk populations (20). In this regard, RSVIG and RSV-IVIG can decrease the rate of hospitalization and duration of hospitalization by 55% (7,19). Recently, it has been shown that a humanized IgG monoclonal antibody (Palivizumab) can decrease the rate of hospitalization of high risk children (14,15,21).

Since the highest rate of RSV-related infection and disease occurs in 2-7 month-old infants, vaccination against this virus has not been a successful attempt (19). Immaturity of immune system in infancy and preventive role of maternally transferred antibodies are among the major barriers for vaccination of infants (19).

In this study the level of maternal and neonatal RSV-specific IgG immunoglobulins was investigated in a group of low-socioeconomic mothers in Shiraz, Iran.

SUBJECTS AND METHODS

Study population. In total, 146 pregnant women who attended to the Zeinabieh hospital of Shiraz University of Medical Sciences in 1999 were included in this study. After informed consent, 5 ml blood was collected from mothers by venipuncture and 5 ml umbilical cord blood was collected for each infant at the time of delivery. Sera were separated from blood samples on the same day of sampling, were aliquoted in 0.5 ml volumes and stored at –20°C until used. Demographical and clinical data including gestational age, previous abortions, parity, mothers' blood group and newborns weights were recorded from patients' files.

RSV-specific IgG detection. A commercially available indirect Enzyme Linked Immunosorbent Assay (ELISA) (IBL, Germany) was used for measuring RSV-specific IgG in cord and maternal sera according to the manufacturer's instructions. An antibody level of >10 IU/ml was considered as positive.

Statistical analyses. Student's *t*-test for paired samples was used to compare the mean concentration of maternal and neonatal RSV-specific IgG. Spearman's test was

used for testing correlation of maternal and neonatal RSV-specific IgG. χ^2 test was used to evaluate the effect of different factors on seropositivity rate. ANOVA and Mann-Whitney tests were used to compare mean maternal and neonatal RSV-specific IgG and cord/maternal ratios between different blood groups. Statistical analyses were performed using SPSS for Windows software version 10.0 and Microsoft Excel version 97.

RESULTS

Mean maternal age was 23.72 ± 5.80 years and median age of mothers was 23 years. The mean ± S.D. weights of newborns was 3234 ± 431 g. Table 1 summarizes the main characteristics of the studied cases.

Table 1. Characteristics of patients

	No. of cases
Gestational age	
⩾37 weeks	**125**
<37 weeks	**13**
Unknown*	**8**
Abortion	
No abortion	**121**
One abortion	**17**
Two abortions	**3**
Three abortions	**1**
Unknown	**4**
Delivery	
Normal vaginal	**132**
Cesarean section	**11**
Unknown	**3**
Blood group	
A+	**40**
B+	**32**
AB+	**10**
O+	**46**
A-	**4**
B-	**4**
AB-	**1**
O-	**4**
Unknown	**5**
Parity	
≤3	**111**
>3	**28**
Unknown	**7**
Total	**146**

*Data were not available.

The mean ± S.D. of RSV-specific IgG in neonatal and maternal sera were 32.03 ± 33.73 IU/ml and 28.90 ± 33.78 IU/ml, respectively, which indicates a significant higher level of RSV-specific IgG in newborns (P = 0.019). There was also a

Table 2. Mean RSV-specific IgG level in mothers and neonates according to type of delivery.

Type of Delivery	Number	Maternal IgG(IU/ml)	Neonatal IgG(IU/ml)	C/M ratio
NVD*	132	26.05 ± 31.21	28.11 ± 29.37	1.27 ± 0.61
Cesarean Section	11	58.96 ± 37.90	69.85 ± 42.98	1.34 ± 0.46
Unknown**	3			
Total	146			

* NVD = Normal Vaginal Delivery
** Data were not available.

significant correlation between maternal and neonatal RSV-specific antibodies (r = 0.88).

Of 146 studied mother/newborn pairs, 56(38.36%) had cord/maternal ratios less than 1, 1(0.69%) had cord/maternal ratio equal to 1 and 89(60.95%) had cord/maternal ratios greater than 1. The mean cord/maternal ratio of RSV-specific IgG antibodies was found to be 1.27 ± 0.60.

In total, 60.27% of mothers and 64.38% of neonates had a level of RSV-specific IgG antibodies in their sera. Comparison of the rate of seropositivity in mothers with different blood groups indicated no significant difference. A significant difference in the mean RSV-specific IgG level was observed between mothers and newborns according to the type of delivery (P = 0.002 and P = 0.001, respectively). RSV-specific IgG concentration was higher in newborns and mothers who had Cesarean section compared to those who had normal vaginal delivery (table 2). However, no difference was observed in the cord/maternal ratio of the two groups (P = 0.58).

No correlation was observed between level of placentally transferred RSV-specific IgG antibodies and maternal age, parity, neonates' weight, maternal previous abortions and neonatal gestational age.

DISCUSSION

In previous investigations the protective role of RSV-specific antibodies has been suggested (22,23,24). In addition, a higher level of RSV-specific IgG antibodies has been detected in non-infected infants compared to infected infants in an African population (20). In the present study a relatively high percentage of mothers (40%) did not have RSV-specific antibodies in their sera. Since our studied population was selected from a low-socioeconomic group of mothers in Shiraz, it is logical to assume that the rate of seronegativity among mothers in other areas be higher. Therefore, a high percentage of infants are fully susceptible to RSV infection at birth.

A cord/maternal ratio of RSV-specific IgG antibodies greater than 1 was observed in this study which is indicative of active placental transfer of these antibodies in southern Iranian mothers. This finding is in accordance with a previous study which reported cord/maternal ratios equal to 1.02 for RSV A-specific and 1.03 for RSV B-specific antibodies (25). In this study no correlation was observed between placental transfer of RSV-specific IgG antibodies and maternal ABO blood groups. In

previous studies on the placental transfer of rubella-specific, tetanus-specific and Helicobacter-specific IgG antibodies on the same population, we observed a different pattern of specific IgG transfer in B+ mothers compared to the A+ and O+ mothers (26,27,28). The lack of association between maternal blood group and placental transfer of RSV-specific IgG antibodies implies that the observed correlation is microorganism-specific.

A highly significant difference was observed between mean RSV-specific IgG antibodies in mothers and neonates according to the type of delivery. However, there was no difference in the cord/maternal ratios of RSV-specific IgG antibodies of mothers with normal delivery compared to those with Cesarean section. Therefore, it is logical to assume that the observed difference has been simply due to the different concentrations of RSV-specific IgG in mothers.

Lack of correlation of maternal and neonatal RSV-specific IgG with maternal age is in accordance with previous studies in African and American populations (25,29).

It has been shown that the mean level of RSV-specific IgG in premature infants (<37 weeks) is less than that of mature infants (≥37 weeks). This effect has been suggested to be related to the malarial and HIV infection of African mothers resulting in low-birth-weight of the infants as there has been no difference in the level of maternally transferred antibodies in premature and mature infants with normal birth weight (29,30). Previous studies have also suggested that the level of RSV-specific IgG antibodies in low-birth-weight infants is less than those with normal birth weight (29,30). However, in our study no difference was observed between these groups as the mean birth weight of all infants was considerably high. Accordingly, the mean birth weight of premature infants in our study was 2669.39 ± 997.80 g which is much higher than the birth weight of premature infants in African populations.

In conclusion, our data suggest that placental transfer of RSV-specific IgG is an active process and the concentration of these antibodies in neonates strongly correlates with maternal antibodies.

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