

Placental transfer of tetanus-specific immunoglobulin G in Iranian mothers

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Objectives: To investigate placental transfer of anti-tetanus immunoglobulin (Ig)G antibodies in Iranian mothers.

Methods: Sera collected from 209 pregnant women and their paired infants were evaluated for tetanus-specific antibodies by a commercial enzyme-linked immunosorbent assay.

Results: In total, 15 (7.2%) out of 209 mothers and 12 (5.7%) out of 209 newborns were negative for anti-tetanus IgG. A highly significant correlation was observed between maternal and fetal anti-tetanus IgG ($r = 0.80$). The mean cord/maternal blood ratio of anti-tetanus IgG was 1.22 ± 0.97 . The mean cord/maternal blood ratio of anti-tetanus IgG in mothers with blood groups B+ and AB+ was lower than in mothers with other blood groups ($p = 0.027$). In addition, among mothers who had more than 0.5 IU/ml anti-tetanus IgG, a higher percentage of cases with cord/maternal blood ratio of < 1 was observed in carriers of blood groups B+ and AB+ compared to those with other blood groups (45.2% vs. 41.8%). Parity of more than 4 had a significant negative effect on both frequency of high positive sera and the mean of anti-tetanus IgG level in maternal and neonatal sera.

Conclusions: A relatively high percentage of pregnant women were not immune against tetanus. It was also found that the main factors that affect infants' tetanus-specific IgG are maternal concentration of this immunoglobulin, parity and maternal blood group.

Key words: IRAN; PLACENTAL TRANSFER; TETANUS; NEONATE

INTRODUCTION

Tetanus, caused by *Clostridium tetani*, is an acute disease which may affect neonates at the time of delivery or in perinatal life. It is estimated that neonatal tetanus results in 400 000 deaths annually¹. In addition to neonates, maternal death due to postpartum tetanus infection may occur². Neutralizing antibodies against tetanus toxoid are protective and it is well established that a serum antibody level of ≥ 0.01 IU/ml can be life saving³.

Based on the World Health Organization records, Iran is among the countries that have eliminated neonatal tetanus with only 21 cases reported in 1997^{4,5}. However, since the causative bacterium of the disease is ubiquitous and cannot be eradicated from the environment, the immunity status of newborns is important in disease prevention. The existence of anti-tetanus antibodies is especially important for neonates born to mothers in unsanitary conditions, where the placentally transferred antibodies are the only route of protection of newborns against neonatal tetanus.

To assess the degree of anti-tetanus immunity among Iranian mothers and transfer of this immunity to their newborns, anti-tetanus immunoglobulin (Ig)G titer was determined in 209 mothers and their newborns.

SUBJECTS AND METHODS

Study population

In total, 209 pregnant women who attended the hospitals of Shiraz University of Medical Sciences in 1999 were included in this study. After informed consent was obtained, 5 ml blood was collected from mothers by venipuncture and 5 ml umbilical cord blood was collected from each infant at the time of delivery. Sera were separated from blood samples on the day of sampling, were aliquoted in 0.5-ml volumes and stored at -20°C until used. For 155 women, demographic and clinical data were available. These data, including gestational age,

previous abortions, parity, mothers' blood group and newborns' weights were recorded from the patients' files.

Anti-tetanus IgG detection

A commercially available indirect enzyme-linked immunosorbent assay (ELISA) (IBL, Germany) was used for measuring anti-tetanus IgG in cord and maternal sera according to the manufacturer's instructions. An antibody level of ≥ 0.01 IU/ml was considered positive.

Statistical analysis

Student's *t* test for paired and unpaired samples was used to compare the mean concentration of anti-tetanus IgG between study groups. Spearman's test was used for testing the correlation of maternal and neonatal anti-tetanus IgG. The F test for equality of variance was used to compare the variance of the groups. The χ^2 test was used to evaluate the effect of different factors on seropositivity rate. The Mann-Whitney test was used to compare mean maternal and neonatal tetanus-specific IgG according to parity. Statistical analyses were performed using SPSS for Windows software version 6.0 and Microsoft Excel version 97.

RESULTS

The mean maternal age, among 155 mothers with known histories, was 23.89 ± 5.73 years; the median age of mothers was 23 years. The mean $\pm$ SD of newborns' weights was 3171 ± 414 g. Table 1 summarizes the main characteristics of 155 of 209 studied cases.

In total, 15 (7.2%) out of 209 mothers and 12 (5.7%) out of 209 newborns were negative for anti-tetanus IgG. The mean $\pm$ SD of anti-tetanus IgG in maternal and newborn sera was 2.12 ± 1.45 IU/ml and 2.32 ± 1.51 IU/ml, respectively, which indicates a significantly higher level of anti-tetanus IgG in newborns ($p = 0.003$). There was also a good correlation between maternal and fetal anti-tetanus IgG ($r = 0.80$). The mean cord/ maternal blood ratio of anti-tetanus IgG was 1.22 ± 0.97 (range 0.06–3.96). The mean maternal IgG in cases with cord/maternal blood ratio greater than 1 was 2.08 ± 1.32 IU/ml, while this value in mothers with cord/maternal blood ratio less than 1 and equal to 1 was 2.18 ± 1.61 and 3.33 ± 1.42 IU/ml, respectively.

In Table 2, the mean maternal and neonatal anti-tetanus IgG according to the parity of the mothers is shown. As is indicated, there was a trend towards a decrease in both maternal and neonatal IgG with parity of > 4 . The mean anti-tetanus IgG in mothers with parity of ≤ 4 was 2.25 IU/ml compared to 0.94 IU/ml in mothers with parity of > 4 ($p = 0.008$). There was also a significant difference

Table 1 Characteristics of patients

	Number of cases
<i>Gestational age</i>	
≥ 37 weeks	133
< 37 weeks	19
Data not available	57
<i>Abortion</i>	
No abortion	134
One abortion	17
Two abortions	3
Three abortions	1
Data not available	54
<i>Delivery</i>	
Normal vaginal	132
Cesarean section	23
Data not available	54
<i>Blood group</i>	
A+	49
B+	29
AB+	8
O+	55
A–	4
B–	6
AB–	1
O–	1
Data not available	56
<i>Parity</i>	
0	72
1	40
2	18
3	8
4	7
5	4
6	3
7	2
8	1
Data not available	54
Total	209

between mean anti-tetanus IgG in neonates of these mothers (2.34 vs. 0.95 IU/ml; $p = 0.004$). In addition, a significant difference between frequency of high positive sera (anti-tetanus IgG > 0.5 IU/ml) and frequency of low positive sera (anti-tetanus IgG < 0.5 IU/ml) was observed in cases with parity of < 4 compared to cases with parity of > 4 ($p = 0.0009$). Therefore, parity of > 4 had a significant negative effect on both frequency of high positive sera and the mean of anti-tetanus IgG level in maternal and neonatal sera. Although only four women with parity of > 4 were aged less than 30 years, there was no difference

Table 2 Mean maternal and neonatal anti-tetanus IgG according to parity

Parity	Mean maternal IgG (IU/ml)	Mean neonatal IgG (IU/ml)
0	2.18	2.27
1	2.18	2.33
2	2.23	2.45
3	2.91	2.56
4	2.73	2.64
5	1.14	1.08
6	1.4	1.38
7	0.18	0.35
8	0.26	0.36

Table 3 The cord/maternal blood ratio of anti-tetanus IgG according to maternal blood group

Maternal blood group	Cord/maternal blood ratio
A+	1.08
B+	0.97
AB+	0.78
O+	1.18
A-	1.00
B-	1.37

Two cases with blood groups AB- and O- were negative for anti-tetanus IgG

between mean maternal and neonatal IgG in women younger than 30 (2.17 and 2.25 IU/ml) and older than 30 (2.15 and 2.24 IU/ml) ($p = 0.47$ and 0.49 , respectively).

When results were categorized according to the maternal blood group, it was noted that the mean cord/maternal blood ratio of anti-tetanus IgG in mothers with blood groups B+ and AB+ was lower than in mothers with other blood groups (Table 3). F test for equality of variance revealed a significant difference of variance between these groups ($p = 0.008$) and the t test for two samples with unequal variance revealed a significant difference between cord/maternal blood ratio in these groups ($p = 0.027$). Considering those mothers who had more than 0.5 IU/ml anti-tetanus IgG in their sera, a higher percentage of cases with cord/maternal blood ratio of < 1 was observed in carriers of blood groups B+ and AB+ compared to carriers of other blood groups (45.2% vs. 41.8%).

No correlation was observed between anti-tetanus IgG in neonates and type of delivery, neonates' weight, previous abortions and neonatal gestational age.

DISCUSSION

Fetal and neonatal lives depend on maternal health and immunity. One of the main routes of protection of neonates is the presence and transfer of maternal antibodies. Vaccination of mothers before and during pregnancy has been a successful way of eliciting protective levels of maternal antibodies. However, in many cases, the immunization success rate is not 100%. In addition, there are reports concerning lack of antibody transfer from mother to fetus⁶. Even an immune mother may not maintain a protective level of antibodies for her infant. The immunization coverage rate of tetanus for women of reproductive age in Iran was 82% in 1995⁷. In the present study we detected anti-tetanus IgG seropositivity rates of 92.8% and 94% among Iranian mothers and their newborns. The 15 (7.2%) seronegative mothers were aged between 14 and 35 years. These mothers and their newborns are fully susceptible to maternal and neonatal tetanus and should be regarded as a population at risk. More attention to this pool of susceptibility and more adherence to the immunization programs is needed. In addition, awareness in the general population, especially high-school-age girls and young mothers, could be effective.

We observed a significant positive correlation between maternal and neonatal anti-tetanus IgG. Moreover, neonatal tetanus levels were significantly higher than those of their mothers, with a cord/maternal blood ratio greater than 1. This finding is in agreement with previous reports and indicates an active process of anti-tetanus IgG transfer from mother to fetus⁸. There was no difference between mean anti-tetanus IgG in cases with cord/maternal blood ratio greater than, equal to or less than 1. Therefore, maternal anti-tetanus IgG level had no effect on cord/maternal blood ratio of this antibody.

High parity (i.e. parity more than 4) had a significant negative effect on both frequency of high positive sera and the mean anti-tetanus IgG level in mothers and newborns. The same effect has been reported for total serum IgG and measles-specific IgG by Goncalves and co-workers⁹. The effect was independent of maternal age and might be related to the chronic pregnancy-induced immunosuppression in these high-parity mothers.

We observed a slightly lower level of antibody transfer from mothers with blood groups B+ and AB+ compared to mothers with other blood groups. This was in accordance with our results from a previous study, in which we observed a significant difference between mean anti-rubella IgG in newborns born to mothers with blood group B+ in comparison to newborns born to mothers with blood groups A+ and O+¹⁰. Although the correlation of ABO blood group antigens with many different bacterial, fungal, viral or parasitic diseases has been reported extensively, the nature of this association has not been clear in many

cases^{11–16}. The present data need to be confirmed in other studies and the mechanisms involved need to be elucidated.

In this study we investigated the placental transfer of tetanus-specific antibodies in Iranian mothers and newborns. A relatively high percentage of pregnant women were not immune against tetanus. It was also found that the main factors that affect infants' tetanus-specific IgG are maternal concentration of this immunoglobulin, parity and maternal blood group.

ACKNOWLEDGEMENT

This work was financially supported in part by Shiraz Institute for Cancer Research, Shiraz, Iran.

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