Brief Reports

Influence of Gestational Age on Cord Blood Immunoglobulin and Complement Levels

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The immaturity of immune defenses in the neonate, particularly in the preterm infant, is the main reason for increased susceptibility to infection in this age group. Assessment of the immunological status of neonates provides insight into the specific deficiencies of the immune system which, in turn, may have therapeutic implications. Therefore, the present study was undertaken to determine the influence of gestational age on the levels of immunoglobulins and complements in cord blood.

Material and Methods

The sample consisted of 51 neonates, of whom 15 were preterm and 36 term infants. The gestational age of all infants was determined by using maternal menstrual dates and Dubowitz Scoring System. Only healthy appropriate for gestational age infants were studied. Neonates were categorized as appropriate for gestational age (birth weight between 10th and 90th centile for gestation) according to previously published data (l). Newborns with Apgar scores of $\leq$6 at 1 and 5 minutes, fetal distress, infection, respiratory distress, hemolytic disease of the newborn and congenital malformations was excluded from the study. Maternal infection, prolonged rupture of membranes (>24 hours), meconium stained liquor and anemia (<10g/dl) precluded entry into the study.

Five ml of cord blood was collected in plain vials by venipuncture from the placental vessels immediately after the delivery of the placenta. Serum was maintained after separation at -20° c until analysis. IgG, IgM, IgA, C_3 and C_4 were determined in cord sera using single radial immunodiffusion method (2). Statistical analysis was done by the Student's 't' test.

Results

Cord blood samples tested were all from healthy appropriate for gestational age infants. The material was divided into five groups according to weeks of gestation *(Table I).* IgA was not detected in any of the cord blood specimens. As calculated by the Student's 't' test, cord blood IgG levels during week 41 were significantly higher than during weeks $\leq$34 and 37 to 38 ($p<0.05$). IgG levels during weeks 39 to 40 were statistically elevated as compared with those during weeks $\leq$34, 35 to 36 and 37 to 38 ($p<0.05$). In contrast to IgG, IgM levels showed no significant change in relation to gestational age. C_3 concentrations were significantly higher during weeks 39 to 40 than during weeks 35 to 36 ($p<0.05$). C_4 levels showed no significant change with increase in gestational age.

Discussion

The present study demonstrated that IgG levels in cord blood were influenced by gestational age. IgG concentrations were significantly elevated in term infants than in preterm infants. IgG levels in cord blood are determined by the length of gestation (3-5). Although IgG synthesis in human fetus begins at 12 weeks of gestation (6),

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TABLE-I Cord Blood Immunoglobulin and Complement Levels (Mean + SD) in Relation to Gestational Age

Gestation (weeks)	IgG (mg/dl)	IgM (mg/dl)	C_3 (mg/dl)	C_4 (mg/dl)
< 34 (n=7)	738.3 ± 109.6 [a,b]	9.2 ± 3.2	41.2 ± 27.3	12.7 ± 3.4
35-36 (n=8)	803.3 ± 161.2 [c]	9.0 ± 2.0	43.4±21.1 [f]	15.6±9.6
37-38 (n= 21)	832.4 ± 150.4 [d,e]	10.4±3.0	64.9±41.6	16.4±7.7
39-40 (n= 10)	966.4 ± 176.8 [a,c,d]	10.7 ± 3.0	72.0±34.5 [f]	13.8±7.1
41 (n=5)	1037.5 ± 286.9 [b,e]	12.5 ± 4.4	75.7±50.0	15.2±6.8

Level of significance of differences between mean values are indicated with the following letters: a,b,c,d,e,f ($p< 0.05$). For example, the letter 'a' shows comparison of IgG levels at gestational ages ≤34 weeks vs 39-40 weeks, the letter 'b' compares IgG levels at gestational ages ≤ 34 weeks vs 41 weeks and so on. Similarly, the letter 'f' compares C_3 levels at gestational ages 35-36 weeks vs 39-40 weeks. Only significant differences ($p< 0.05$) between mean values have been mentioned.

nearly all the cord IgG is maternal in origin because fetus synthesizes very little IgG due to lack of exposure to antigenic stimuli. Placental transfer of IgG is both a passive and an active process which takes place mainly in the third trimester (7). Therefore, infants born prematurely tend to have lower IgG levels compared with those born at term.

The mean cord blood IgG levels in the present study were lower as compared with other studies (5,8-10). However, the neonates studied by these workers had elevated levels of IgM and IgA in their cord blood, in addition to high IgG concentrations. It appears that these neonates had sub clinical infection which led to the production of abnormal levels of immunoglobulins in response to exposure to antigenic stimuli *in utero.* This may explain the discrepancy in IgG levels between this study and previous studies. Other factors which may influence the IgG levels in cord blood are genetic background, socioeconomic status, and method of detection.

Elevated IgM levels in cord blood serve as an important marker for intrauterine infection. The values above 20 mg/dl are considered significant (6). IgM does not cross the placenta and cord blood levels reflect fetal synthesis which commences at 11 weeks of intrauterine life (6). All the neonates in the present study had IgM levels of less than 17 mg/dl in their cord blood There are conflicting reports in literature regarding the effect of gestational age on cord blood IgM levels. IgM levels in cord blood may or may not be influenced by gestational age (4,ll-13). In this series, gestational age did not appear to influence the cord IgM levels.

IgA could not be detected in any of the cord blood specimens. This is in accord with previous studies (13-15). The lower limit of detection for IgA in this study was 5 mg/dl. Using better method, Cederqvist *et al(4)* could detect low levels of IgA in almost all samples of cord blood. So the inability to detect IgA in cord blood reflects the methodologic problem rather than its true absence. Like IgM, IgA does not cross the placenta and is of importance for diagnosis of intrauterine infection. The upper limit of normal IgA levels in cord blood is considered to be 5 mg/dl (16).

At term, complement components C_3 and C_4 are 50% to 65% of the corresponding levels in normal adult serum or paired maternal serum (6). Low birth weight infants have much lower levels of C_3 and C_4, and these are reduced in proportion to the degree of prematurity (6,17,18). In this study, C_3 levels were influenced by gestational age, while C_4 levels remained unaffected. Reduced complement activity in neonates may contribute to opsonic defects and predispose them to infection.

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