Original Article

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Comparison of Interleukin-6 (IL-6) Serum Levels in Neonates Born via Vaginal Delivery and Caesarean Section

I. Mohammadzadeh (MD)[1], Z. Akbarianrad (MD)[1], D. Dehbandi (MD)[2], H. Hosseinnia (BSc)[3], M. Haghshenas Mojaveri (MD)*[1]

1.Non-Communicable Pediatric Diseases Research Center, Health Research Institute, Babol University of Medical Sciences, Babol, I.R.Iran
2.Babol University of Medical Sciences, Babol, I.R.Iran
3.Department of Clinical Research Development, Rouhani Hospital, Babol University of Medical Sciences, Babol, I.R.Iran

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ABSTRACT

BACKGROUND AND OBJECTIVE: Interleukin-6 (IL-6) plays a pivotal role in hematopoiesis, immune system and acute phase response. This cytokine is found in umbilical cord blood and is a protective marker for neonatal stress and infection. This study aimed to compare serum levels of IL-6 in neonates born via vaginal delivery and caesarean section.

METHODS: This cross-sectional study was conducted on 35 neonates born via cesarean section and 46 neonates born via term vaginal delivery at Ayatollah Rohani Hospital of Babol, Iran in 2012. Neonates had appropriate weight for gestational age, one-minute and five-minute Apgar scores of ≥8 and no clinical and laboratory evidence of neonatal infection. To determine IL-6 serum levels, 5 ml of blood was obtained from the umbilical cord of each neonate, and blood samples were analyzed using enzyme-immunoassays methods. Moreover, data such as maternal age, infant age and sex, number of pregnancies and parity were recorded and compared.

FINDINGS: In this study, mean age of mothers with vaginal and caesarean delivery was 28.6±4.8 and 25.5±5.7 years, respectively (p=0.011). In total, 20(43.5%) and 16(45.7%) neonates in vaginal and cesarean delivery groups were male, respectively. Mean of IL-6 serum concentration in neonates born via vaginal delivery (10.9±3.11) was higher compared to cesarean group (6.6±3.15); however, this difference was not statistically significant.

CONCLUSION: According to the results of this study, neonates born via vaginal delivery and cesarean section had no significant difference in terms of IL-6 serum levels.

KEY WORDS: Natural delivery, Caesarean Section, Infant, Umbilical cord, Interleukin-6.

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***Corresponding Author: M. Haghshenas Mojaveri (MD)**
Address: Neonatal Intensive Care Unit, Ayatollah Rohani Hospital, Babol University of Medical Sciences, Babol, I.R.Iran
Tel: +98 11 32238384
E-mail: matia.mojaveri@yahoo.com

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Introduction

Neonates are susceptible to infections due to dysfunctional defense mechanisms. Creation and maintenance of adaptive immune response are regulated through interactions between intracellular glycoproteins and phospholipids, also known as cytokines. Production of proinflammatory cytokines by mother and infant protects the neonate against infections after birth. Lack of these cytokines could lead to disease and mortality, increased risk of early neonatal infection, necrotizing enterocolitis, bronchopulmonary dysplasia and hypoxic-ischemic brain injury (1).

Cytokines such as interleukin 1-β, interleukin-6 (IL-6) and tumor necrosis factor α are directly involved in term and preterm deliveries. Biosynthesis triggers prostaglandins, which stimulate contractions in the myometrium and open up the cervix. During the transition period, fetus is transferred from sterile intrauterine environment to an ectopic environment and has contact with several antigenic stimulants. Evidently, the immune system of infant has a key role during the transition period. By regulating biological functions, cytokines alter the immune status of fetus; such examples are phagocytosis and emergence of binding molecules on the surface of other cells (2).

Stimulation of monocytes in blood flow results in the production of IL-6 (3). After lipopolysaccharide stimulation, monocytes obtained from the neonate could produce sufficient amounts of IL-6 (4). These findings could justify higher IL-6 serum levels associated with vaginal delivery since this mode of childbirth involves more intense physical exertion of the mother compared to cesarean section. On the other hand, some other studies have reported no significant correlation between IL-6 serum levels in the umbilical cord and mode of delivery (5). Few international studies have evaluated the production of proinflammatory cytokines, such as IL-6, in mother and neonate to prevent neonatal infections. Since no research has been performed in this regard in Iran, this study aimed to investigate changes in serum concentration of IL-6 in neonates born via vaginal delivery and cesarean section..

Methods

This cross-sectional study was conducted on neonates born via vaginal delivery and cesarean section in 2012 at Ayatollah Rohani Hospital of Babol, Iran. Study protocol was approved by the Ethics Committee of Babol University of Medical Sciences. Considering At alpha: 0.05 and Beta: 0.8, a sample size of 40 cases per group was calculated and our sample size was calculated at 80 neonates (40 in each group).

However, due to restrictive inclusion and exclusion criteria, we only evaluated 35 neonates born via cesarean section and 46 neonates born via vaginal delivery.Neonates were selected via simple random sampling. Inclusion criteria of the study were appropriate weight for gestational age, one-minute and five-minute Apgar scores of ≥8 and no clinical and laboratory evidence of neonatal infection. Exclusion criteria of the study were as follows: 1) maternal corticosteroid use; 2) maternal diseases; 3) use of medications that affect immune system; 4) use of antibiotics within two weeks before delivery and 5) preterm labor.

Arteriovenous blood samples were obtained from umbilical cord of neonates at the time of delivery. After adding anticoagulant, blood samples were preserved at temperature of 4-8°C at the labor room of hospital. Samples were transferred to the laboratory of hospital daily for centrifuge and separation of serum, and afterwards, they were maintained at temperature of -20°C.

Analysis of blood samples was performed using enzyme immunoassays methods at Cellular and Molecular Biology Research Center of Babol University of Medical Sciences, Iran. Other data including maternal age, infant gender, term or preterm labor, number of pregnancies and parity were recorded as well.

Data distribution was determined using Kolmogorov-Smirnov test, and data were compared using Fisher's exact test. In addition, mean age of study samples was calculated using T-test, and for inter-group comparison of data on IL-6 concentration (without normal distribution), Mann-Whitney test was used. In this study, P value of less than 0.05 was considered significant

Results

In total, 46 neonates were evaluated in vaginal delivery group, and 35 neonates were evaluated in elective cesarean group. Mean of maternal age in vaginal delivery and elective cesarean groups was 28.6±4.8 and 25.5±5.7 years, respectively (vaginal

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delivery group: gravida 2, para 1). In the study population, 20 (43.5%) and 16 (45.7%) neonates in vaginal delivery and cesarean groups were male, respectively (p=0.841).

Mean of IL-6 concentration in neonates born via vaginal delivery and cesarean section was estimated at 3.11 and 3.15, respectively. According to our findings, concentration of IL-6 was higher in female neonates born via vaginal delivery compared to elective cesarean group. Moreover, IL-6 serum levels were higher in both male and female neonates born via natural vaginal delivery; however, this difference was not statistically significant.

It is notable that this difference was quite close to the significance level determined for this study. In terms of gender, concentration of IL-6 was significantly higher in male neonates compared to female neonates in vaginal delivery group (p=0.036). However, no significant difference was observed between female neonates in cesarean group in this regard (table 1).

Since data were not normally distributed in this study, parametric tests could not be performed. As such, mean of IL-6 concentration in vaginal delivery group (10.9) was higher than the cesarean group (6.6).

Table 1. Mean and Median of IL-6 Serum Levels in Neonates Born via Vaginal Delivery and Caesarean Section Based on Gender

Gender	Group	Mean±SD	Median	P-value
Male	Natural Vaginal Delivery	17.1±3.16	5.2	0.054
	Caesarean Section	10.9±2.18	3.7	
Female	Natural Vaginal Delivery	6.3±0.7	4.1	0.091
	Caesarean Section	3.3±0.2	3.1	

Discussion

According to the results of this study, serum levels of IL-6 were higher in neonates born via vaginal delivery compared to cesarean section; however, this difference was not statistically significant. In one study, De Jongh et al. reported no significant association between IL-6 concentration and mode of delivery (3). Similarly, results obtained by Fukdah et al. were indicative of no significant difference in serum levels of IL-6 in neonates born via vaginal delivery and cesarean section (7).

In another study, Takahashi et al. also observed that IL-6 serum concentration was similar in infants born via natural vaginal delivery and caesarean section (8). Correspondent to the aforementioned studies, findings of Sarandakou denoted no correlation between serum levels of IL-6 and mode of delivery (9), which is in line with the results of the present study.On the other hand, some studies have reported different results suggesting a significant correlation between serum concentration of IL-6 and mode of delivery.

For instance, Zanardo et al. claimed that serum concentration of IL-6 in the umbilical cord of infants born via cesarean section was significantly lower compared to neonates born via natural vaginal delivery (5). In another study by Malamiri-Puchner et al., it was reported that serum levels of IL-6 were significantly higher in infants born via vaginal delivery compared to cesarean section (10).

On the same note, results obtained by Berner et al. indicated that plasma levels of IL-6 were higher in infants born via vaginal delivery compared to caesarean section (11).In one of their studies, Haghshenas et al. stated that serum concentration of IL-6 was significantly higher in women who have vaginal delivery compared to those with elective cesarean section (12). Conflicting results presented in our research and previous studies emphasize the need for further investigation of this subject.

It is possible that physical stress imposed during vaginal delivery activates certain physiological functions in mother's body, which lead to increased secretion of inflammatory cytokines. These cytokines cross through the placenta and reach the fetus to protect the neonate against infections after birth. In cesarean section, prior to the activation of related physiological functions, labor is terminated through surgical intervention.

According to our findings, serum levels of IL-6 were higher in infants born via natural vaginal delivery compared to cesarean section group in both male and female neonates. One of the limitations of the current study was the relatively small sample size, which resulted in no statistically significant difference between study groups in terms of IL-6 serum concentration.

Nevertheless, in male neonates, this difference was close to the determined significance level of the study.

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According to our observations, serum concentration of IL-6 was significantly higher in male infants born via natural vaginal delivery compared to female infants. However, no significant difference was observed between neonates born via cesarean section in this regard. In the literature, there is limited data on the correlation between serum levels of IL-6 and gender of infants. For instance, findings of Poggi et al. revealed that concentrations of IL-6 and interleukin-10 in the amniotic fluid of male and female neonates had no significant difference (1).

In conclusion, results of the present study indicated that serum concentration of IL-6 was not significantly different between neonates born via natural vaginal delivery and cesarean section.

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