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## **Peripheral, Placental and Cord Cytokines Profile in Spontaneous Labor and Elective Caesarean Section**

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## SHORT PAPER

# Peripheral, Placental and Cord Cytokines Profile in Spontaneous Labor and Elective Caesarean Section

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### ABSTRACT

**Background:** Cesarean section delivery can lead to much maternal morbidity. Different cytokines have been reported to be influenced by the mode of delivery. **Objective:** To investigate the influence of mode of delivery on maternal, placental and cord sera of interferon gamma (IFN- $\gamma$ ), interleukin-4 (IL-4) and interleukin-10 (IL-10) levels. **Methods:** These three cytokines were measured using ELISA in peripheral, placental and cord sera of two groups of women (38 in each group), either delivering vaginally or by elective cesarean section. **Results:** Concentrations of IFN- $\gamma$ , IL-4 and IL-10 in the peripheral and placental sera were higher in vaginal delivery, while cord cytokines were not significantly different in the two groups. Cord sera contained significantly less concentrations of these cytokines than the peripheral and placental sera. **Conclusion:** It appears that the levels of IFN- $\gamma$ , IL-4 and IL-10 are influenced by the mode of delivery.

**Keywords:** Cytokines, Cesarean, Labor, Vaginal

### INTRODUCTION

The rate of cesarean section is rising worldwide and Sudan is not an exception (1, 2). Cesarean section delivery can lead to higher maternal morbidity and is associated with increased risks of asthma and atopy in the delivered children (3, 4).

Cytokines play an important role during labor and they influence immunity of the fetus and neonate. The mode of delivery might influence the establishment of the infant's microflora (1). Thus, during the transitional period from the normally sterile intrauterine environment to the extrauterine one- which is characterized by exposure to multiple antigenic stimuli- neonatal defense is going to be built accordingly (2). Recently, production of different cyto-

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kines and their balance have been reported to be influenced by the mode of delivery (7-9). Further understanding of the relationship between mode of delivery and immune system of the newborn is needed. The current study was conducted to investigate the influence of mode of delivery on maternal, placental and cord sera IFN- $\gamma$ , IL-4 and IL-10 levels.

## MATERIALS AND METHODS

The study was conducted at the labor ward of New Halfa hospital, eastern Sudan in the period of October 2006 through March 2007 to investigate whether maternal, placental and cord cytokine profiles depend on mode of delivery.

Healthy women -vaginal or elective cesarean delivery- and their singleton neonate were approached to participate in the study. A structured questionnaire was administered to gather socio-demographic characteristics.

The study received ethical clearance from the Research Board at the Faculty of Medicine, University of Khartoum.

Immediately after delivery, 5 mL of maternal, placental and cord blood were collected, using the biopsy-pool method for placental blood. The samples were centrifuged and the sera were kept at -20 until processed for cytokines in the laboratory.

Sera were analyzed by ELISA for IFN- $\gamma$ , IL-4 and IL-10 levels according to the manufacturer's instructions (eBioscience, Inc. 6042 Cornerstone Court West San Diego, CA 92121, USA).

**Statistical Analysis.** Data were analyzed using SPSS for Windows. The socio-demographic characteristics were compared using Student's t-test. Cytokines data, which were not normally distributed, were compared by Mann-Whitney U and Kruskal-Wallis tests. Correlations between continuous variables were assessed by the Spearman rank test. P-values less than 0.05 were regarded as significant.

## RESULTS AND DISCUSSION

Seventy six (38 in each group) women and their neonates were enrolled. The two groups were well matched in the basic data; age, parity, gestational age, haemoglobin and birth weight (Table 1).

**Table 1. The mean (SD) of the demographic characteristics of the two groups of women, delivering either vaginally or by elective cesarean section**

Variable	Vaginal delivery	Cesarean section
Age, years	25.7(7.3)	26.3(6.1)
Parity	3.1(2.5)	2.4(2.1)
Weight, Kg	51.1(13.1)	59.9(12.5)
Birth weight,g	2932.0(585.4)	2922.2(502.9)

Concentrations of IFN- $\gamma$ , IL-4 and IL-10 in the peripheral and placental sera were higher in vaginal delivery, while the levels of these cytokines were not significantly different in the cord sera. Significantly less concentration of these cytokines were noted in cord sera than in the peripheral and placental ones (Table 2).

**Table 2. The median (interquartile range) of cytokine levels in vaginal and cesarean section delivery**

Cytokines, pg/ml	Maternal	Placental	Umbilical	Pv
IFN- $\gamma$				
vaginal	352.8(169.6-732.2)	289.8(181.0- 559.0)	123.8(77.9-238.3)	S
cesarean section	215.4(169.6-307.0)	244.0(186.8-344.3)	83.7(40.7- 166.3)	S
Pv	S	S	NS	
IL-4				
vaginal	28.3(17.6-65.6)	30.3(17.3-60.9)	5.0(1.0-13.0)	S
cesarean section	23.6(18.3-31.0)	24.3 (18.0-31.6)	7.6 (1.0-16.0)	S
Pv	S	S	NS	
IL-10				
vaginal	168.3 (94.0-387.1)	180(103.7-277.7)	51.0 (31.5-90.1)	S
cesarean section	105.7(82.3-156.6)	109.7(85.2-217.1)	70.6 (33.4-106.7)	S
Pv	S	S	NS	

\*N = not, S = significant

Strong positive correlations were observed between each cytokine in peripheral and placental sera: IFN- $\gamma$  ( $r = 0.89$ ,  $p < 0.05$ ); IL-4 ( $r = 0.82$ ,  $p < 0.05$ ); and IL-10 ( $r = 0.15$ ,  $p < 0.05$ ). There was no correlation between peripheral and cord ( $r = 0.2$ ,  $p = 0.06$ ), or placental and cord sera concentrations ( $r = 0.12$ ,  $p = 0.2$ ) of IL-4. Similarly a lack of correlation between peripheral and cord sera IL-10, ( $r = 0.13$ ,  $p = 0.2$ ), or between placental and cord sera concentrations of this cytokine ( $r = 0.1$ ,  $p = 0.3$ ) was observed.

The current study was conducted to investigate the influence of the mode of delivery on cytokine levels. The peripheral and placental levels of IFN- $\gamma$ , IL-4 and IL-10 were significantly higher in women who delivered vaginally, with strong positive correlations between peripheral and placental levels. The cord levels of these cytokines were not significantly different between the two groups, but cord levels were lower than the peripheral and placental levels. These results are in agreement with previous reports demonstrating that peripheral and placental and not the umbilical cord cytokine productions depend on the mode of delivery (7, 8). Cytokines play an important role in the defense against infections and the regulation of the immune response; therefore, their increase during labor is implicated in the protection of the mother and the neonate against perinatal infections.

In a previous report, no association was reported between cesarean section and the neonatal levels of IL-10 (9), a cytokine with inhibitory effects on the secretion of Th1 and Th2 cytokines (10). Yet an elevated level of IFN- $\gamma$  at birth was found to associate with asthma and atopy in childhood (11).

Our study did not show any difference in the cord sera concentrations of these cytokines. Ly et al., reported that the cytokine levels were significantly higher in cesarean delivery (9). Interestingly, in the current study, there were positive correlations between the peripheral and placental cytokines. This indicates the interactions between the two sources of these cytokines mainly the maternal and the placental ones. In summary, it seems that levels of IFN- $\gamma$ , IL-4 and IL-10 are influenced by mode of delivery.

## REFERENCES

- 1 Hamilton BE, Martin JA, Ventura SJ, Sutton PD, Menacker F. Births: preliminary data for 2004. Natl Vital Stat Rep. 2005; 54:1-17.
- 2 Ahmed ES, Mirghani OA, Gerais A, Adam I. Ceftriaxone versus ampicillin/cloxacillin as antibiotic prophylaxis in elective caesarean section. East Mediterr Health J. 2004 ;10:277-88
- 3 Kero J, Gissler M, Gronlund MM, Kero P, Koskinen P, Hemminki E et al. Mode of delivery and asthma -- is there a connection? Pediatr Res. 2002;52:6-11
- 4 Bager P, Melbye M, Rostgaard K, Benn CS, Westergaard T. Mode of delivery and risk of allergic rhinitis and asthma. J All

Levels of IFN- $\gamma$ , IL-4 and IL-10 are influenced by mode of delivery

- ergy Clin Immunol. 2003; 11:51-6.
- 5 Groñlund MM, Lehtonen OP, Eerola E, Kero P. Fecal microflora in healthy infants born by different methods of delivery: permanent changes in intestinal flora after cesarean delivery. *J Pediatr Gastroenterol Nutr.* 1999; 28: 19-25.
  - 6 Romero R, Gomez R, Yoon BH, Mazou M, Edwin SS, Berry SM. A fetal systemic inflammatory response is followed by the spontaneous onset of preterm partuition. *Am J Obstet Gynecol.* 1998; 179:186-93.
  - 7 Malamitsi-Puchner A, Protonotariou E, Boutsikou T, Makrakis E, Sarandakou A, Creatsas G. The influence of the mode of delivery on circulating cytokine concentrations in the perinatal period. *Early Hum Dev.* 2005; 81:387-92.
  - 8 Cindrova-Davies T, Yung HW, Johns J, Spasic-Boskovic O, Korolchuk S, Jauniaux E et al. Oxidative stress, gene expression, and protein changes induced in the human placenta during labor. *Am J Pathol.* 2007; 171:1168-79.
  - 9 Ly NP, Ruiz-Pérez B, Onderdonk AB, Tzianabos AO, Litonjua AA, Liang C et al. Mode of delivery and cord blood cytokines: a birth cohort study. *Clin Mol Allergy.* 2006; 4:13.
  - 10 Akdis M, Verhagen J, Taylor A, Karamloo F, Karagiannidis C, Cramer R et al. Immune responses in healthy and allergic individuals are characterized by a fine balance between allergen-specific T regulatory 1 and T helper 2 cells. *J Exp Med.* 2004, 199:1567-75.
  - 11 Rowe J, Heaton T, Kusel M, Suriyaarachchi D, Serralha M, Holt BJ et al. High IFN-gamma production by CD8+ T cells and early sensitization among infants at high risk of atopy. *J Allergy Clin Immunol.* 2004; 113:710-6.