

Different modes of delivery and hormonal stress response

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ABSTRACT

Objectives: The aim of the study was to determine how the type of delivery affects the stress response cycle and the level of cortisol, progesterone and corticoliberin.

Material and methods: The study was conducted among 26 pregnant women admitted to the Gynecology and Obstetrics Ward due to an approaching delivery date or the onset of labor. The participants were aged between 20 and 41 years, with a mean age of approximately 30 years. After delivery, blood was drawn in parallel from the maternal antecubital vein, the umbilical cord vein and the umbilical cord artery. The levels of stress hormones were assessed by ELISA. The results were subjected to statistical analyses, and correlation coefficients were calculated for individual variable pairs. The analysis also examined the participation of pregnant woman in antenatal education.

Results: A high correlation was observed between cortisol and progesterone levels in venous and arterial cord blood and physiological delivery. The mean cortisol level was 247.37 ng/mL in venous cord blood and 233.59 ng/mL in arterial blood and the respective mean progesterone levels were 331.81 ng/mL and 342.36 ng/mL. The highest cortisol concentration was determined in the primiparas umbilical cord blood (236.182 ng/mL in the vein, 230.541 ng/mL in the artery). Correlation between cortisol level in venous and arterial cord blood and prenatal education was also noted (venous cord blood: $r = -0.5477$; $F = 10.2833$; $p = 0.0038$; cord arterial blood: $r = -0,4436$; $F = 5.8789$; $p = 0.0232$).

Conclusions: The results obtained emphasize the importance of the hypothalamic-pituitary-adrenal (HPA) axis as one of the potential mechanisms actively involved in childbirth. The determined levels of cortisol and progesterone in the maternal and umbilical cord blood varied significantly depending on the type of delivery, with higher concentrations being observed in the case of natural delivery. In addition, the highest levels of cortisol were determined in primiparas; however, lowered umbilical cord blood cortisol levels were observed in pregnant women who had participated in antenatal education, regardless of the number of deliveries.

Key words: physiological delivery; cesarean section; stress hormones; cortisol; progesterone; corticoliberin

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INTRODUCTION

Stress is now an integral part of human life. During pregnancy, both the mother and the developing fetus are exposed to various environmental stimuli. A number of stress-related hormonal reactions occur during labor, and these affect the presence of stress markers in the maternal and fetal blood. Perinatal care has improved significantly in developed countries over the past 100 years, but psychological support is probably the most neglected aspect of obstetric medicine, despite being acknowledged as key for the well-being of the pregnant woman and her future child [1, 2].

Stress is defined as a state of disharmony present in the body or as a state of destabilization of homeostasis [3]. An important role in stressful situations is played by the hypothalamic-pituitary system, which includes corticoliberin (CRH), vasopressin (AVP), glucocorticosteroids and catecholamines (adrenaline, noradrenaline). Stressful situations are also associated with an increase in the secretion of cortisol, prolactin and proopiomelanocortin metabolites, which include adrenocorticotrophic hormone (ACTH) and beta-endorphin (BE). Exposure to stress in the early prenatal period or exposure to stress during childbirth may affect the individual stages of neonatal development [4].

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During pregnancy, the CRH produced by the placenta increases gradually in the maternal and fetal circulation, mainly during the third trimester and during labor, reaching maximum values of 1000–10000 pg/mL. This causes an increase in cortisol concentration, which inhibits hypothalamic CRH secretion [3, 4].

During pregnancy, the amount of progesterone produced by the secretory tissue increases with the growth of the placenta. However, the correlation between placental weight and maternal progesterone concentration is negligible, indicating that other important factors regulate its synthesis. The mechanism involved in the spontaneous onset of labor in women remains indefinite, but it is thought that high levels of progesterone are necessary for active labor [3].

Objectives

The aim of this study was to assess the effect of the type of delivery on the concentration of cortisol, progesterone and corticotropin present in maternal and umbilical cord blood serum. Other perinatal factors, such as antenatal education, were also included in the analysis. The obtained results were compared with available medical literature.

MATERIAL AND METHODS

Study group

The study was conducted among 26 pregnant women from the Obstetrics and Perinatology Clinic, Department of Obstetrics and Perinatology, Medical University of Lodz, and the Gynecology and Obstetrics Ward, Maria Skłodowska-Curie Memorial Provincial Specialist Hospital in Zgierz. Pregnant women were admitted to the ward in response to an approaching delivery date or the onset of labor. The participants were aged between 20 and 41 years old, with an mean age of about 30 years. Of the 26 participants, 13 cesarean sections and 13 physiological deliveries were performed during the period April 15, 2019 to May 15, 2019. All pregnancies were single ones and delivery took place between 34 and 40 weeks of gestation (mean value about 37 weeks). In addition, 21 pregnant women received anesthesia, and 18 underwent antenatal education.

Pregnancy was accompanied by a number of conditions. Among the study group, hypothyroidism was experienced by two participants, hypertension by two, and gestational diabetes by two. In addition, individual patients suffered from systemic lupus erythematosus, endometriosis, bronchial asthma and multiple sclerosis.

Blood samples were obtained in parallel from both mother and fetus. Briefly, 5–8 mL of blood was collected from the maternal antecubital vein and 5–8 mL from the venous and arterial cord blood. The samples were then centrifuged at 4000 rpm for 10 minutes. The obtained serum

was frozen and sent in dry ice to the Department of Biopharmacy, Faculty of Pharmacy, Medical University of Lodz, Poland. Samples were stored at -70°C until analysis. The study was conducted with the consent of the Bioethical Committee of the Medical University of Lodz — resolution No. RNN/43/19/KE of March 12, 2019.

Assay

The levels of cortisol, progesterone and corticotropin in the maternal blood serum and umbilical cord blood serum were determined by ELISA, based on a competitive test. The following kits were used: CORTISOL ELISA DiaMetra, PROGESTERONE ELISA DiaMetra, ELISA For Corticotropin Releasing Hormone (CRH) Cloud-Clone Corp.

Statistical methods

The results were subjected to statistical analysis using STATISTICA 13.1 software. The arithmetic mean and standard deviation were calculated, the minimum and maximum values and the median were determined. The obtained results were analyzed. Correlation coefficients were determined at the significance level $p < 0.05$.

RESULTS

The mean postnatal condition of the newborn assessed on the Apgar scale was 9.4. In the group of pregnant women for whom pregnancy was completed by physiological delivery (mean age 31.5 years). The mean advancement of pregnancy in which the delivery took place was 37.7 weeks. In the study group, 53.85% underwent antenatal education. The mean body weight of the newborn was 3068 g, with five male and eight female newborns. The mean postnatal condition of the newborn was 9.4, assessed on the Apgar scale.

Among the group who underwent caesarean section (mean age 30.2 years) and 84.62% participated in antenatal education. The mean stage of gestation at delivery was 37.9 weeks. There were five male newborns delivered in the study group, and eight females. The mean newborn body weight was 3120 g. The mean postnatal state of the newborn expressed was 9.5 on the Apgar scale. The characteristics of the participants are presented in Table 1.

Higher cortisol levels were observed in the umbilical cord blood of the women who underwent natural labor (Fig. 1): 247.3734 ng/mL for venous cord blood and 233.5890 ng/mL for arterial blood. The minimum and maximum values were 133.2070 ng/mL and 404.7190 ng/mL in venous cord blood, and 90.7540 ng/mL and 370.7240 ng/mL in arterial cord blood. The median value was 245.6940 ng/mL in venous cord blood and 238.9290 ng/mL in the arterial blood; the standard deviations were 79.0383 ng/mL in venous cord blood and 79.0020 ng/mL in arterial blood.

Table 1. Characteristics of pregnant women		
Mother/fetus details	Physiological delivery (n = 13)	Delivery by caesarean section (n = 13)
Mother's age	31.5 ± 5.77	30.2 ± 4.93
Week of pregnancy	37.7 ± 1.93	37.9 ± 1.72
Antenatal education [%]	53.85	84.62
Birth weight [g]	3068 ± 493	3120 ± 543
Newborn gender (male/female)	5/8	5/8
Apgar score	9.4 ± 1.04	9.5 ± 0.88

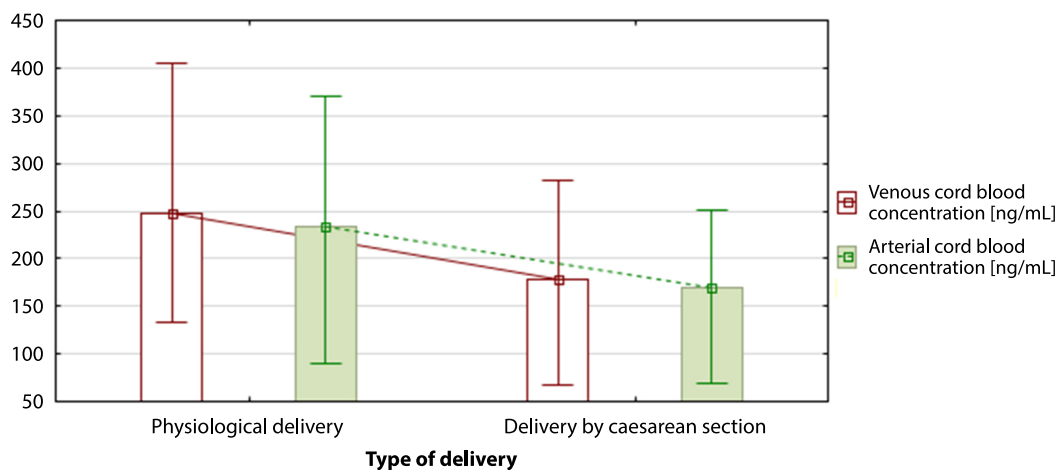


Figure 1. The mean cortisol concentration in umbilical vessels according to the type of delivery

In the case of natural labor, higher levels of progesterone were observed in umbilical cord blood (Fig. 2), with progesterone concentrations of 331.8078 ng/mL in venous cord blood and 342.3588 ng/mL in arterial blood. The minimum and maximum values were 275.1470 ng/mL and 389.6970 ng/mL in venous umbilical cord blood, and 312.8570 ng/mL and 383.3860 ng/mL in arterial blood. The median values were 328.8580 ng/mL in venous cord blood and 335.2240 ng/mL in arterial blood; the standard deviations were 28.25252 ng/mL in venous cord blood and 22.3280 ng/mL in arterial blood.

The CRH concentrations in maternal blood and in venous and arterial cord blood did not significantly correlate with the type of delivery: maternal blood ($r = 0.2090$; $F = 1.0966$; $p = 0.3054$), venous cord blood ($r = 0.3687$; $F = 3.776$; $p = 0.0638$), arterial cord blood ($r = 0.0466$; $F = 0.0523$; $p = 0.8211$) (Fig. 3.)

The highest cortisol concentration was determined in the primiparas umbilical cord blood (236.182 ng/mL in the vein, 230.541 ng/mL in the artery) (Fig. 4).

Participation in antenatal education women significantly correlated with the cortisol concentrations of both venous and arterial cord blood during delivery: venous cord blood

($r = -0.5477$; $F = 10.2833$; $p = 0.0038$), arterial cord blood ($r = -0.4436$; $F = 5.8789$; $p = 0.0232$) (Fig. 5.).

DISCUSSION

Literature data concerning cortisol show clearly that its concentration is closely related to the method of termination of pregnancy. A study conducted in 1976 showed that vaginal delivery increases cortisol levels as opposed to caesarean section. Farquharson et al. [3] showed an increase in cortisol concentration in children born by sudden caesarean section compared to planned surgery or vaginal delivery. A significant correlation was observed between umbilical cord cortisol concentration and the type of delivery (Fig. 1). Cortisol concentration also correlated with the number of deliveries, with a significantly higher level observed in the first child than in the following ones (Fig. 4). The mechanism of this difference is not fully understood, however, these results are consistent with earlier studies on the cortisol concentration in primiparas and multiparas [3]. A correlation was also observed between umbilical cord blood cortisol concentration and the antenatal education of pregnant women (Fig. 5). Lower venous and arterial cord blood cortisol concentrations were observed in pregnant

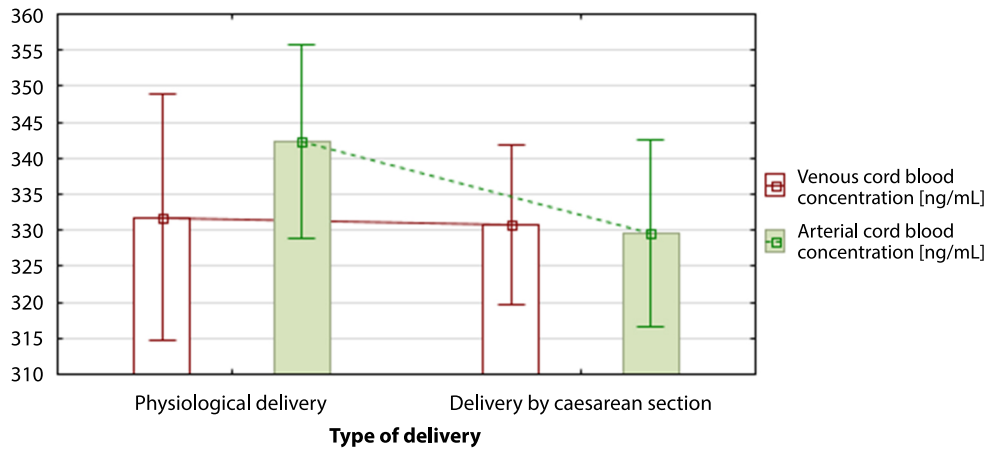


Figure 2. The mean progesterone concentration in umbilical cord blood according to the type of delivery

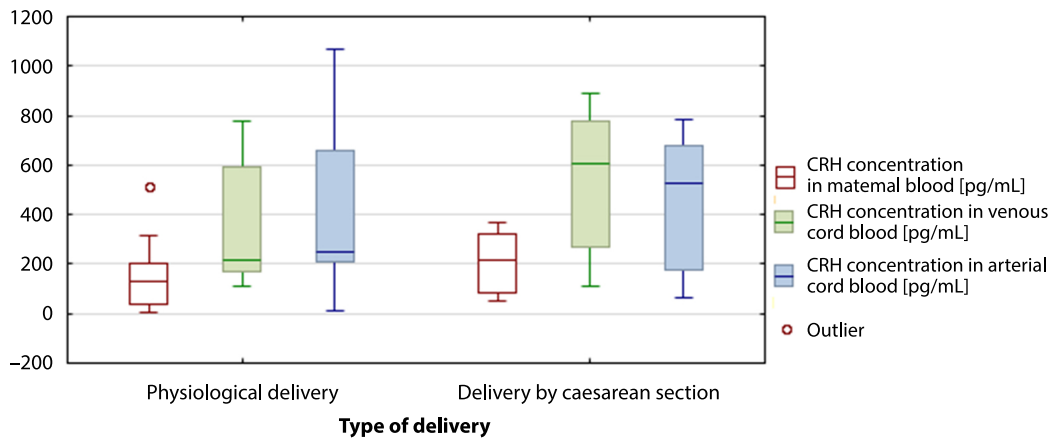


Figure 3. Corticosteroid concentration in maternal blood, as well as in venous and arterial cord blood according to the type of delivery; CRH — corticosteroid

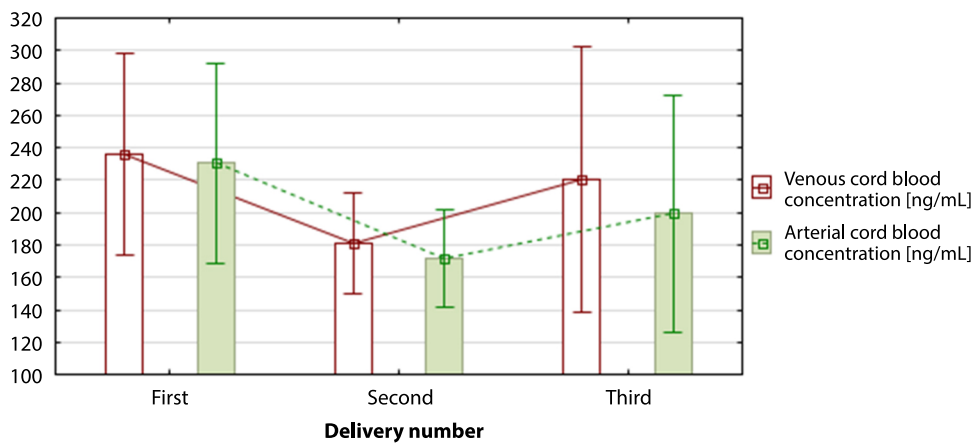


Figure 4. The mean umbilical cord blood cortisol concentration according to the order of delivery

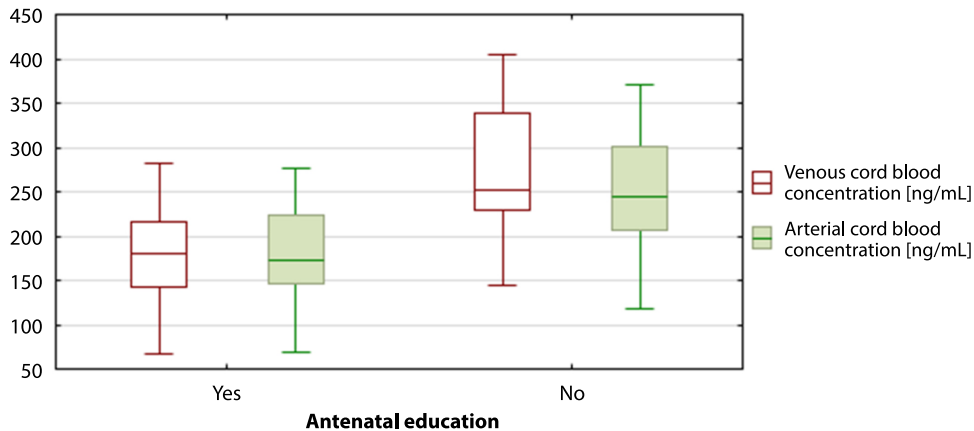


Figure 5. Correlation between cortisol concentration in venous and arterial cord blood and participation in antenatal education

women who participated in antenatal education compared to those who did not.

Data on the role of progesterone as a stress biomarker during termination of pregnancy are disputable. Löfgren et al. [3] report significantly higher serum concentrations of progesterone in mother and child as a result of natural delivery than during planned caesarean section. Aisien et al. [4] also found elevated progesterone levels in the blood of a fetus exposed to stress during delivery. This may be one way to protect the fetus against stress factors and the consequence of hypoxia. The results of this study show that higher levels of progesterone in umbilical cord blood were determined in the group of pregnant women giving birth naturally than in the case of caesarean section.

Our findings regarding the relationship between corticotropin concentration and the method of completion of pregnancy are not in line with those of previous studies. Earlier studies have reported the presence of higher levels of CRH, a similar hormone to cortisol, in blood following vaginal delivery [3]. The CRH neuropeptide is released from hippocampal neurons using environmental signals, including stress. During pregnancy, it is produced by the placenta, which also stimulates the release of cytokines. Consequently, it is difficult to distinguish the source of CRH production during labor.

Births, both natural one and those occurring as a result of caesarean section, took place around the 37th of pregnancy. No significant correlation was observed between the increase in individual hormones and the week of completion of pregnancy.

CONCLUSIONS

The obtained results emphasize the importance of the hypothalamic–pituitary–adrenal axis (HPA) as one of the potential mechanisms actively participating in labor.

The concentration of cortisol and progesterone in the blood of mother and fetus correlates with the type of delivery. Physiological delivery increases the release of most of the tested hormones, in contrast to the caesarean section. In addition, participation in antenatal education reduces the cortisol level in umbilical cord blood.

The first delivery is associated with greater stress and higher cortisol level compared to subsequent deliveries.

The age of the pregnant woman does not affect the concentration of stress hormones during childbirth.

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Conflict of interest

None.

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