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Complete Blood Count Indices in Pregnancies With Isolated Intrauterine Growth Restriction

İzole İntrauterin Gelişme Kısıtlılığı Olan Gebeliklerde Tam Kan Sayım Parametreleri

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ABSTRACT

Aim: Our aim was to compare the complete blood count indices in intrauterine growth restriction (IUGR) with healthy pregnant controls and to investigate whether any hematological changes have predictive value for the prediction of adverse pregnancy outcomes in IUGR.

Material and Methods: Mean platelet volume (MPV), platelet distribution width (PDW), plateletcrit (PCT), platelet large cell ratio (P-LCR) and red cell distribution width (RDW) levels of 35 pregnant women with isolated IUGR and 105 healthy pregnant women were retrospectively evaluated.

Results: Women with IUGR had significantly higher MPV (mean 11.21 ± 0.99 vs. 9.99 ± 0.84; P<0.001), PDW (mean 14 ± 2.51 vs. 28.22 ± 6.99; P<0.001) and P-LCR (median 31.5 U/L vs. 44.7 U/L; P<0.001) values, when compared with controls. Statistically significant negative correlations were found between RDW and gestational age at birth (r:-0.39, p:0.02) and also between PCT and 1-min APGAR scores (r:-0.34, p:0.04).

Conclusion: Cheap and easily measurable complete blood count indices including MPV, PCT, PDW, P-LCR and RDW levels may be valuable markers of IUGR.

Key Words: Intrauterine growth restriction, complete blood count indices

ÖZET

Amaç: Çalışmamızda intrauterin gelişme kısıtlılığı (İUGK) olan gebelikler ile sağlıklı gebelikler arasında tam kan sayım parametrelerini karşılaştırılması ve İUGK varlığında hematolojik değişikliklerin istenmeyen gebelik sonuçları üzerinde belirleyici değerinin olup olmadığını araştırılması hedeflenmiştir.

Gereç ve Yöntemler: İUGK ile komplike 35 gebenin ve 105 sağlıklı kontrolün ortalama platelet hacmi (OPH), platelet dağılım genişliği (PDG), plateletcrit (PCT), platelet büyük hücre oranı (P-BHO) ve kırmızı hücre dağılım genişliği (KDG) retrospektif olarak değerlendirilmiştir.

Bulgular: IUGK olan gebelerde kontrol grubuna göre, OPH (ortalama 11.21 ± 0.99 vs. 9.99 ± 0.84; p<0.001), PDG (ortalama 14 ± 2.51 vs. 28.22 ± 6.99; p<0.001) ve P-BHO (median 31.5 U/L vs. 44.7 U/L; p<0.001) istatistiksel olarak anlamlı düzeyde yüksekti. Ayrıca KDG ve doğumda gestasyonel hafta arasında (r:-0.39, p=0.02) ve PCT ve 1. dakika APGAR skorları arasında (r:-0.34, p=0.04) istatistiksel olarak anlamlı negatif korelasyon bulunmuştur.

Sonuç: Ölçümü kolay ve ucuz olan OPH, PCT, PDG, P-BHO ve KDG gibi tam kan parametreleri İUGK'da faydalı belirteçler olabilir.

Anahtar Kelimeler: İntrauterin gelişme kısıtlılığı, tam kan sayım parametreleri

Introduction

Intrauterine growth restriction (IUGR) is one of the most common problems in obstetrics complicating approximately 7-15% of all pregnancies and defined as a fetus with an estimated weight of < 10th percentile for gestational age (1). The underlying mechanism varies due to the maternal, fetal and placental etiologies but finally all share the common end-point namely insufficient uteroplacental and fetal perfusion. IUGR is also reported to be one of three clinical conditions that constitute ischemic placental disease and the others are preeclampsia and placental abruption (2). The pathophysiological mechanism leading to these complications have been suggested to be uteroplacental ischemia and placental insufficiency beginning at the very early stages of gestation during implantation (3). On the way resulting with ischemia, pathologies like thrombosis, coagulation defects, inflammation and infection seem to play important roles (4).

Complete blood count (CBC) indices such as plateletcrit (PCT), red cell distribution width (RDW) and mean platelet volume (MPV) have been already studied in various diseases other than those seen in pregnancy and reported to be associated with inflammatory, ischemic and thrombotic states such as myocardial infarction and stroke (5-8). Moreover, it has been already proved that MPV values indicate the higher platelet consumption and activity that

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may lead to hypercoagulability, microcirculatory disturbances and vascular reactivity in placental bed leading to fetal complications and altered Doppler velocimetry profiles in IUGR and preeclampsia (9-10). Besides higher RDW levels were reported to be associated with preeclampsia which is the one of the defined ischemic placental diseases (11).

In the current study we aimed to compare the complete blood count indices in IUGR with age-matched healthy pregnant controls and to investigate whether any hematological changes have predictive value for the prediction of adverse pregnancy outcomes in IUGR.

Material and Methods

This retrospective study was carried out in Zekai Tahir Burak Women's Health Education and Research Hospital. We reviewed the data of 35 pregnant women with isolated IUGR between January and June 2014. IUGR was defined as a fetus with an estimated weight of < 10th percentile for gestational age according to the biometric measurements on ultrasonography and as a birth weight of the neonate < 10th percentile of the standard growth curve. Another 105 age- and BMI-matched healthy pregnant women without any maternal and/or fetal complications were recruited as control group.

Patients were excluded if any of the following disorders were present: multiple pregnancies, the presence of any fetal congenital anomalies, placental anomalies and any maternal diseases resulting in the impairment of the fetal growth restriction such as diabetes mellitus, preeclampsia and others.

Clinical information including age and body mass index were collected. Hematologic data of the patients, obtained in the third trimester of pregnancy, were achieved from their medical records. The data regarding platelet count, mean platelet volume (MPV), platelet distribution width (PDW), plateletcrit (PCT), platelet large cell ratio (P-LCR) and red cell distribution width (RDW) were evaluated. CBC parameters were measured by automated blood counter within two hours of blood sampling using a Beckman-Coulter Gen-S system device. Pregnancy and neonatal outcomes were collected from medical records. The pregnancy outcomes studied in our study were; gestational age at delivery, birth weight, 1- and 5-minute Apgar scores and neonatal intensive care unit (NICU) admission.

The study was approved by the local ethic committee of Zekai Tahir Burak Women's Health Education and Research Hospital.

BM SPSS Statistics for Windows, Version 18.0 (Armonk, NY: IBM Corp.) was used for statistical analysis. Continuous variables were tested for normality by the Kolmogorov–Smirnov test. Normally distributed data are presented as mean ± standard deviations. Categorical comparisons were performed using the Chi-Square Test. For data not normally distributed, median with data range (minimum to maximum) were used. We used the independent samples t-test and Mann-Whitney U test for parametric and nonparametric groups respectively. For the correlation of normally distributed data a Pearson correlation coefficient was used and for data not normally distributed, correlation was performed using spearman's rho test.

Results

A total of a hundred and thirty nine participants (35 IUGR patients and 104 age-matched healthy pregnant controls) were enrolled in the study. The baseline anthropometric characteristics, CBC parameters and the birth weight, APGAR scores and neonatal unit admission of the neonates of IUGR patients and controls are given on Table 1. There were no statistically significant differences among age, BMI, white blood cell (WBC) counts, platelet counts, PCT and RDW values between groups.

Women with IUGR had significantly higher MPV (mean 11.21 ± 0.99 vs. 9.99 ± 0.84; P<0.001), PDW (mean 14 ± 2.51vs. 28.22 ± 6.99; P<0.001) and P-LCR (median 31.5 U/L vs. 44.7 U/L; P<0.001) values, when compared with controls.

The mean birth weight of the neonates were 2215 ± 337.6 gr and 3279 ± 517.9 gr, in IUGR and control groups, respectively (P<0.001). The NICU admission rate was 31.4% in IUGR group and no need for NICU admission was existed in the control group (P<0.001). There were statistically significant differences among 1- and 5-minute APGAR scores of the neonates, with lower values in IUGR group when compared with the control group (P<0.001) (Table-1).

Table 1. Baseline demographic, obstetric characteristics and laboratory values in patients with IUGR and the control group

	IUGR (n:35)	Control (n:104)	*P**
Age	26.6 ± 4.32	27.82 ± 3.91	0.09
BMI	27.28 ± 5.31	27.79 ± 5.48	0.7
Gravida	2 (1-6)	3(1-8)	**<0.001**
Parity	0(0-2)	1(0-5)	**<0.001**
Gestational age at birth	38 (32-40)	39 (35-42)	**<0.001**
C/S rate (%)	%71.4 (n:25)	%48.1 (n:50)	**0.017**
Birth weight (gr)	2215 ± 337.6	3279 ± 517.9	**<0.001**
Apgar-1 min	7 (5-7)	7	**<0.001**
Apgar-5 min	9 (7-9)	9	**<0.001**
NICU admission (%)	%31.4 (n:11)	-	**<0.001**
Platelet count ($\times 10^3/\mu L$)	232.142 ± 54.511	234.596 ± 72.576	0.83
MPV (fl)	11.21 ± 0.99	9.99 ± 0.84	**<0.001**
PCT (%)	0.24 (0.13-1.21)	0.24 (0.09 -0.49)	0.5
PDW (ratio)	14 ± 2.51	28.22 ± 6.99	**<0.001**
PLCR	31.5 (14.3 -51.2)	44.7 (37.4-70.4)	**<0.001**
RDW (%)	13.9 (12.4-18.7)	14.3 (11.7-26.3)	0.06

**;P< 0.05 is statistically significant, BMI: body mass index, C/S; cesarean section, NICU; neonatal intensive care unit, WBC; White Blood Cells count, NLR; neutrophil to lymphocyte ratio, MPV; mean platelete volume, PCT; plateletcrit, PDW; platelet distribution width, PLCR; platelet large cell ratio, RDW; red cell distribution width.*

Further analysis was performed based on the laboratory values and pregnancy outcomes of IUGR group. Gestational age at birth, birth weight, 1- and 5-minute Apgar scores and NICU admission were again evaluated in order to determine if any correlations with CBC parameters are present or not. No statistically significant correlations between pregnancy outcomes and MPV, PDW and P-LCR values were found (Table-2). Statistically significant positive correlation was present between platelet count and 1-min APGAR scores (r:0.37, p:0.03). Also statistically significant negative correlations were found between RDW and gestational age at birth (r:-0.39, p:0.02) and also between PCT and 1-min APGAR scores (r:-0.34, p:0.04) (Table-2).

Table-2 Association of laboratory parameters with adverse pregnancy outcomes

	Apgar-1	Apgar-5	NICU	Birth weight	Gestational age at birth
Platelet	**r:0.37 p*:0.03**	r:0.31 p:0.06	r:0.077 p:0.65	r:0.1 p:0.54	r:0.087 p:0.62
MPV	r:-0.29 p:0.086	r:-0.27 p:0.1	r:0.28 p:0.09	r:-0.24 p:0.14	r:-0.22 p:0.19
RDW	r:0.26 p:0.12	r:0.22 p:0.18	r:-0.29 p:0.82	r:0.26 p:0.13	**r:-0.39 p*:0.02**
PCT	**r:-0.34 p*:0.04**	r:0.16 p:0.36	r:-0.74 p:0.67	r:0.19 p:0.25	r:0.16 p:0.33
PDW	r:-0.16 p:0.33	r:-0.18 p:0.28	r:0.25 p:0.13	r:-0.15 p:0.36	r:-0.24 p:0.16
PLCR	r:-0.21 p:0.22	r:-0.25 p:0.13	r:-0.03 p:0.98	r:-0.19 p:0.26	r:-0.26 p:0.12

**;P< 0.05 is statistically significant, BMI: body mass index, C/S; cesarean section, NICU; neonatal intensive care unit, WBC; White Blood Cells account, NLR; neutrophil to lymphocyte ratio, MPV; mean platelete volume, PCT; plateletcrit, PDW; platelet distribution width, PLCR; platelet large cell ratio, RDW; red cell distribution width.*

Conclusion

In the present retrospective study of CBC indices among IUGR patients, statistically significant higher levels of MPV, PDW and P-LCR were found when compared with the control group. Besides, RDW and PCT levels showed statistically significant negative correlation with gestational age at birth and 1-min Apgar scores, respectively.

Platelet indices such as MPV, PDW, PCT and P-LCR measured by simple complete blood count are suggested to be determinant for platelet function and are of great interest as surrogate markers of platelet activation (12,13). As larger platelets contain more prothrombotic materials including thromboxane A2 abd B2, they are more aggregable and more reactive than the smaller ones (14,15). Considering the fact that the possible mechanism leading to IUGR is placental ischemia, we hypothesized whether increased platelet activation is the underlying factor or not. Higher levels of MPV, PDW and P-LCR are found in IUGR group in the present study. Our results are in consistence with Wasiluk et al. suggesting increased levels of MPV, PDW, PCT and large platelet count are characteristic in small for gestational age newborns (16). Marumoto et al also reported increased levels of MPV in maternal serum of the women delivering IUGR babies, suggestive of the presence of the high platelet consumption (17). Besides, MPV values were previously found to be associated with unimpaired Doppler velocimetry profiles in both umbilical and uterine arteries (9). Again it has been already proved that MPV values indicate the higher platelet consumption and activity that may lead to hypercoagulability, microcirculatory disturbances and vascular reactivity in placental bed leading to fetal complications and altered Doppler velocimetry profiles in IUGR patients (9,10). All these reports are consistent with the present study, since we found negative correlation between PCT levels and 1-min Apgar scores.

RDW, another parameter easily detectible in simple CBC, have been already proposed to be reflective of systemic inflammation (18), Correlations between RDW and other inflammatory markers such as C-reactive protein (CRP), erythrocyte sedimentation rate, interleukin-6 (IL-6) and tumor necrosis factor have been reported (19,20). As inflammation is proposed to be another underlying factor in IUGR and previously reported to be associated with increased levels of CRP and IL-6, we evaluated RDW levels in IUGR pregnancies and found a negative correlation with gestational age at birth in the present study (21,22). Similarly, a recent study by Garofoli et al., evaluating RDW levels in IUGR full-term infants, suggested that RDW and gestational age at birth were negatively correlated and high RDW levels were predictive for the determination of critical newborns (23).

In conclusion, cheap and easily measurable CBC indices including MPV, PCT, PDW, P-LCR and RDW levels may be valuable markers of IUGR. Further prospective studies are needed to evaluate the association of these indices with IUGR and the relation of them with adverse pregnancy outcomes as well

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