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Mean Platelet Volume (MPV) and Neonatal Outcomes Of Infants Born To Mothers With Preeclampsia

Preeklamptik Anne Bebeklerinde Ortalama Platelet Hacmi (MPV) ve Neonatal Sonuçlar

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ÖZ

Amaç: Preeklampsi hem maternal hem de neonatal komplikasyonlara yol açabilen bir hastalıktır. Hastalığın fetal ve neonatal komplikasyonlarına uteroplasental yetersizliğin yol açtığı düşünülmektedir. Güncel bilgiler doğrultusunda hastalığın etyolojisi ve patogenezinde inflamasyonun da maternal bulgulardan sorumlu olduğu görülmüş ve neonatal bulguların da inflamasyonla ilişkili olabileceği düşünülmüştür. Bu amaçla, preeklampsi olan gebelerde yüksek olduğu görülen MPV'nin (mean platelet volume) preeklamptik anne bebeklerinde de değerlendirilmesi planlanmıştır.

Gereç ve yöntemler: Bu çalışma, Hacettepe Üniversitesi Ihsan Doğramacı Çocuk Hastanesi Yenidoğan Yoğunbakım Ünitesi'ne yatışı yapılmış olan 148 preeklamptik anne bebeği ve kontrol grubu için tabakalı örnekleme sistemi ile seçilmiş 147 bebeğin değerlendirmeleri ile yapılmıştır. Gruplar arasında hematolojik parametreler (MPV, hemoglobin değerleri, beyaz küre trombosit sayısı) ve sık görülen neonatal morbiditeler (SGA (gebelik haftasına göre düşük ağırlık), respiratuar distres sendromu, nekrotizan enterokolit, intraventriküler kanama, PDA (patent ductus arteriosus)) karşılaştırılmıştır.

Bulgular: Preeklamptik annelerin bebeklerinde MPV ve hemoglobin değerleri anlamlı olarak (p<0.0001, p:0.032) yüksek, beyaz küre ve trombosit sayıları anlamlı olarak düşük (p:0.002, p:0.011) bulunmuştur. Preeklamptik anne bebeklerinde SGA oranı anlamlı olarak (p<0.0001) yüksek bulunmuş olup diğer morbiditeler açısından belirgin fark bulunmamıştır. Hematolojik parametler incelenirken MPV ve trombosit sayısının ters orantılı olduğu, SGA bebeklerde MPV yüksek olduğu ve PDA olan bebeklerde MPV düşük olduğu görülmüştür.

Sonuç: Preeklampsi olan gebelerde olduğu gibi inflamasyonla seyreden birçok hastalıkta MPV yüksekliği dikkat çekmektedir. Preeklamptik anne bebeklerinde MPV artışı bulgularımıza dayanarak, preeklampsinin neonatal komplikasyonlarının da inflamatuar bir süreçle ilişkili olabileceği düşünülmüştür.

Anahtar kelimeler: preeklampsi, inflamasyon, sFLT-1, sVEGFR-1, soluble endoglin

ABSTRACT

Aim: Preeclampsia may cause both maternal and neonatal complications. Uteroplacental dysfunction is one of the reasons of fetal and neonatal complications in preeclampsia. Recent findings about the etiology and pathogenesis of the disease shows that inflammation is one of the factors responsible for maternal complications, thus neonatal complications should be associated with the same inflammatory process. We considered evaluating mean platelet volume (MPV) of infants born to mothers with preeclampsia, based on the findings of elevated MPV values in pregnant women with preeclampsia.

Materials and methods: This study was carried out at the Neonatal Intensive Care Unit of Hacettepe University Ihsan Dogramacı Children's Hospital and consisted of 148 infants born to mothers with preeclampsia and 147 infants as a control group which were selected by stratified sampling system. Hematological parameters (mean platelet volume, hemoglobin values, white blood cell and platelet counts) and common neonatal morbidities (small for gestational age, respiratory distress syndrome, necrotizing enterocolitis, intraventricular hemorrhage and patent ductus arteriosus) were evaluated between groups.

Results: The infants of mothers with preeclampsia had significantly elevated MPV and hemoglobin values (p<0.0001, p:0.032) and significantly lower platelet and white blood cell counts than the control group (p:0.002, p:0.011). Small for gestational age (SGA) ratio was higher in infants of preeclamptic mothers (p<0.0001) and there was no difference between groups for other morbidities. When examining the hematological parameters, MPV and platelet counts were inversely proportional. MPV was higher in SGA infants and lower in infants with patent ductus arteriosus.

Conclusion: Elevated MPV values are noticed in various diseased associated with inflammation like preeclampsia. Interpreting our findings of elevated MPV values of infants born to mothers with preeclampsia, neonatal complications of preeclampsia should be related with an inflammatory process.

Keywords: preeclampsia, inflammation, sFLT-1, sVEGFR-1, soluble endoglin

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INTRODUCTION

Preeclampsia is a pregnancy complication that can lead to both maternal and neonatal outcomes. The etiology of preeclampsia has not yet been fully resolved, but abnormal placentation, which is also influenced by genetic and immunological factors, is the most agreed mechanism. Due to the impaired placental structure, it is thought that some clinical findings have emerged due to the effect of some cytokines passed through the maternal circulation.(1)

The main complication of preeclampsia, affecting the fetus and therefore the newborn, is uteroplacental ischemia. Occurrence of ischemia and infarct areas in the placenta may even cause ablatio placenta and fetal death. Intrauterine growth restriction (IUGR), fetal distress and hematological problems are more common in infants of mothers with preeclampsia due to the insufficiency of placental flow in addition to the increased risk of premature birth. In recent years, it has been shown that not only uteroplacental insufficiency but also cytokines causing preeclampsia may be responsible for neonatal complications.(1)

The increase in mean platelet volume (MPV) values in many diseases with endothelial damage and inflammation attracts researchers attention in recent years. MPV values in preeclamptic pregnancies were investigated and found to be higher than those in non-preeclamptic pregnancies, since preeclampsia is a disease associated with both increased thrombotic activity and inflammation with endovascular impairment.(2) Similar effects may be seen in infants when it is taken into account that cytokines are effective in the mechanism of preeclampsia that affect the fetus; however there are not enough studies to study MPV values in infants of preeclamptic mothers. In this study, MPV, other hematologic parameters and common neonatal morbidities were examined in the infants born to preeclamptic pregnancies, which were compared with non-preeclamptic pregnancies.

MATERIAL AND METHODS

This study was carried out with a retrospective evaluation babies whose mother had preeclampsia, eclampsia or hemolysis, elevated liver enzymes and low platelets (HELLP) syndrome during the pregnancy and whose complete blood counts were studied at the 6th hour of their life were taken into the study group. Since hematologic problems are common in infants born to preeclamptic pregnancies, complete blood counts were evaluated in every infant admitted to our unit. For this reason, almost all of the infants who were admitted as infants born to preeclamptic pregnancies constitute the study group. A control group was selected among infants whose mothers had no preeclampsia, eclampsia or HELLP syndrome, and who had complete blood counts at the 6th hour of life.

The study and control groups were divided into three groups according to gestational age as 29, 30-33 and 34-36 weeks. Since there were only seven patients in the study group for 37 and above weeks, babies 37 and above weeks were not included in the study group. Considering the possibility of prematurity and complications related to prematurity affecting the MPV values, a stratified sampling system was used while the control group was being formed, and therefore the infants in the same weeks with the study group were selected. The complete blood count obtained in the first 6 hours of infants was evaluated in both groups to rule out the effects of the supportive care after birth, medications used for treatment and the diseases came along.

The patients in the study group who had expiratory grunting, tachypnea, intercostal or subcostal retractions and cyanosis, those whose arterial oxygen pressure (PaO2) in the room air is less than 50 mmHg or those who require oxygen support to keep PaO2 above 50 mmHg and have diffuse reticulonodular ground glass appearance with air bronchograms on the anterior-posterior chest X-ray were accepted as respiratory distress syndrome (RDS). Patients diagnosed with pneumatosis intestinalis, portal vascular gas or pneumoperitoneum in direct abdominal x-rays, with abdominal distension or bloody stool finding, were accepted as necrotizing enterocolitis (NEC). Patients detected blood in the germinal matrix, ventricles or cerebral parancyme by routine transfontanel ultrasonography scan were diagnosed intraventricular hemorrage (IVH). Patients with persisting murmur and nonhealing respiratory problems were evaluated by pediatric cardiologist and patent ductus arteriosus (PDA) was diagnosed by anatomically imaging by echocardiography. Those whose birth weight was less than 10 percentile by gestational week were accepted as small for gestational age (SGA).

Patients with major congenital malformation, intrauterine infection, metabolic disease, immune or nonimmune hydrops fetalis findings, chromosomal abnormality or genetic disease, early-onset neonatal sepsis and neonatal thrombocytopenia (other than preeclampsia) were excluded. However, atrial septal defect (ASD) and ventricular septal defect (VSD) which did not lead to hemodynamic instability were not included among the exclusion criteria from the study groups.

Gestational weeks at birth, birth weight, weigth for gestational

age, gender; hemoglobin, white blood cell (WBC) count, platelet count and MPV values; whether they were diagnosed with RDS, NEC, IVC or PDA in follow-up were recorded by examining epicrisis and complete blood count reports from the hospital system, belonging to the infants in both groups.

Hemoglobin values, white blood cell counts, platelet counts and MPV values from complete blood count results that were obtained in Hacettepe University Hospital Clinical Pathology and Microbiology Laboratories by using Beckman Coulter LH780 Analyzer (22 parameters) device.

Statistical Review

SPSS Statistics 21.0 program was used to evaluate the data. The statistical study was done together with Hacettepe University Faculty of Medicine Biostatistics Department. Whether the continuous variables fit the normal distribution was determined by the Shapiro-Wilk test. When descriptive statistics were made, mean and standard deviation values were used for continuous variables that fit normal distribution, and median and interquartile range was used for those that do not fit the normal distribution. The p value <0.05 was regarded as statistically significant. When the study and control groups were compared in terms of discontinuous variables, the chi-square test was used and when they were compared in terms of continuous. variables, the Mann-Whitney U test was used.

Spearman's correlation test was used when the relationship between continuous variables was investigated. When the correlation coefficient (r) was less than 0.4 it was evaluated as weak relationship, between 0.4-0.6 as moderate relationship, between 0.6-0.8 as strong relationship and when it was bigger than 0.8 as very strong relationship.

RESULTS

In this study, a total of 295 patients were studied, 148 were in the study group and 147 in the control group. Because stratified sampling system was used when the patients were selected in the control group, the number of patients in study and control groups were very close to each other when they were evaluated by gestational weeks. There were no differences between the groups in terms of gender.

When the groups were compared in terms of the neonatal morbidities, the SGA ratios in the study group were statistically significantly higher. Therefore there was no difference in the incidence of RDS, NEC, IVH and PDA (Table 1).

Table 1: Neonatal morbidities between groups

Morbidity	Study group	Control group	p
SGA	53 (%67)	26 (%33)	**<0.0001**
RDS	52 (%49.5)	53 (%50.5)	0.869
NEC	14 (%70)	6 (%30)	0.108
IVH	6 (%37.5)	10 (%62.5)	0.297
PDA	43 (%54.5)	36 (%45.5)	0.376

When examined separately according to the gestational weeks, it was seen that the SGA and PDA ratios were statistically significantly higher in the study group between 30-33 gestational weeks than the control group. Other morbidities were not different when examined by gestational weeks.

Hemoglobin and MPV values were found to be statistically significantly higher in study group, WBC and platelet counts were statistically significantly lower (Table 2).

Table 2: Hematological parameters between groups

	Study group	Control group	p
Hemoglobin (gr/dL)	17.5 (±2.5)	16.9 (±2.6)	**0.032**
WBC(/µL)	10500 (3000-48000)	11900 (2300-99300)	**0.011**
Platelets (/µL)	190 000 (±82 000)	219 000 (±73 000)	**0.002**
MPV (fL)	7.8 (4.6-10.3)	7.5 (5.5-10.2)	**<0.0001**

Platelet counts were lower in study group in all gestational weeks in addition to MPV values were high, but statistically significant differences were found in babies of 30-33 and 34-36 gestational weeks (Table 3 and table 4).

Table 3: Platelet counts between groups

Platelets	Study group /µL (SD)	Control group /µL (SD)	p
29 week	193 000 (±113 000)	212 000 (±65 000)	0.417
30-33 weeks	196 000 (±71 000)	229 000 (±73 000)	**0.013**
34-36 weeks	180 000 (±70 000)	212 000 (±79 000)	**0.045**
Total	190 000 (±82 000)	219 000 (±73 000)	**0.002**

Table 4: MPV levels between groups

MPV	Study Group fL (min-max)	Control Group fL (min-max)	p
29 week	7.7 (6.7-10.3)	7.8 (5.5-10.0)	0.664
30-33 weeks	7.7 (6.1-10.2)	7.5 (6.2-10.2)	**0.012**
34-36 weeks	7.9 (4.6-9.5)	7.4 (6.3-10.2)	**0.005**
Total	7.8 (4.6-10.3)	7.5 (5.5-10.2)	**<0.0001**

MPV values were found to be higher in SGA infants. However, MPV values were found to be lower in infants with PDA. When the study and control groups were examined, the difference in the control group was not statistically significant, but it was significant in the study group. There was no significant difference

in MPV values in morbidities such as RDS, NEC and IVH (Table 5).

Table 5: MPV values by the neonatal morbidities

		Study group (fL)	Control group (fL)	Total (fL)
SGA		7.9 (4.6-10.3)	7.7 (6.4-10.0)	7.8 (4.6-10.3)
No SGA		7.7 (6.4-10.2)	7.5 (5.5-10.2)	7.6 (5.5-10.2)
	p	0.199	0.138	**0.013**
RDS		7.7 (6.4-10.3)	7.7 (6.1-10.2)	7.7 (6.1-10.3)
No RDS		7.9 (4.6-10.2)	7.4 (5.5-10.2)	7.6 (4.6-10.2)
	p	0.109	0.448	0.597
NEC		7.8 (6.5-8.9)	7.5 (5.5-9.6)	7.8 (5.5-9.6)
No NEC		7.8 (4.6-10.3)	7.5 (6.1-10.2)	7.7 (4.6-10.3)
	p	0.364	0.902	0.846
IVH		7.8 (6.9-9.6)	7.5 (6.5-10.0)	7.7 (6.5-10.0)
No IVH		7.8 (4.6-10.3)	7.5 (5.5-10.2)	7.7 (4.6-10.3)
	p	0.676	0.978	0.995
PDA		7.5 (6.4-10.3)	7.5 (6.1-10.0)	7.5 (6.1-10.3)
No PDA		7.9 (4.6-10.2)	7.5 (5.5-10.2)	7.7 (4.6-10.2)
	p	**0.002**	0.631	**0.021**

DISCUSSION

In this study, hematological parameters such as MPV and hemoglobin values were high in preeclamptic mothers, while platelet and WBC values were low. When we examined common morbidities, we found that SGA ratio was higher in infants of preeclamptic mothers and there was no significant difference in terms of other morbidities. When MPV values were analyzed in relation to hematological parameters, MPV and platelet counts were inversely proportional. The relationship between morbidities and MPV was found out that MPV was higher in SGA infants and lower in infants with PDA.

Thrombocytopenia is also one of the most common hematologic complications in infants born to mothers with preeclampsia and the platelet counts in the study group were significantly lower than the case group (p: 0.002) according to the results of our study. Negative correlation (p <0.0001) was also observed when the relationship between MPV values and platelet counts were examined. The pathophysiology of thrombocytopenia, a very common complication in preeclamptic pregnancies, is not fully elucidated, but the fact that both the mother and the infant spontaneously recover within 7-10 days, suggests that the factors causing preeclampsia are effective on thrombocytopenia. The most common mechanism is reduced platelet production. (3) Thrombocytopenic infants from pregnancies with placental insufficiency have been shown to have decrease in megakaryocyte counts, and to return normal in parallel with increased platelet counts after birth.(4) It is known that VEGF and PlGF mediators are also effective in the maturation of medulloblastocytes and platelet production. Increased sFLT-1 in preeclampsia is believed to bind to these mediators, leading to a reduction in their concentrations in blood, thus leading to prevent megakaryocyte maturation and end up with thrombocytopenia.(5,6)

While there are many studies examining MPV values in pregnancies with preeclampsia, very few studies have examined the MPV values in infants born to mothers with preeclampsia. Our study was one of a large number of cases with a total of 295 patients with 148 cases and 147 control groups.

MPV is known to be elevated in thrombopoietic disorders or in conditions of elevated thrombotic activity but has also been shown to increase in inflammatory diseases and diseases causing inflammation indirectly such as endothelial damage in recent years.(7) Preeclampsia has both increased thrombotic activity and increased inflammatory response with endothelial damage, which accounts for the increase in MPV values.(8)

There are very few studies on the MPV values of infants born to preeclamptic mothers. In a study by Akcan et al.(9) MPV values in 63 infants were analysed and the infants born to mothers with preeclampsia were recorded higher MPV values than those in control group. Also MPV values were higher in thrombocytopenic patients when only infants born to mothers with preeclampsia were examined, but the differences were not statistically significant. Similarly, in our study, MPV values in infants born to mothers with preeclampsia were found to be statistically significantly (p <0.0001) higher. The higher number of patients in our study was considered to have statistically more powerful results.

MPV values were studied by Çekmez et al.(10) in very preterm infants for neonatal morbidities and found that high MPV values are related with NEC, bronchopulmonary dysplasia (BPD) and IVH but not related with sepsis or ROP. Another study about MPV was by Canpolat et al.(11) presents the results of MPV values are higher in RDS. In our study, there was no relationship between MPV values and RDS, NEC and IVH but lower MPV values were found in PDA.

CONCLUSION

MPV values in infants to preeclamptic mothers were significantly higher than infants to non-preeclamptic mothers. Low platelet counts are thought to be related to MPV elevation. Hemoglobin values were found to be high in the infants to preeclamptic mothers while white blood cell values were found low. SGA ratios were also found high in infants to preeclamptic mothers. These findings may be attributed to placental insufficiency due to preeclampsia, but may be associated with cytokines such as sFLT-1 and sEng involved in the preeclampsia mechanism. It is concluded that studies investigating the relationship between these cytokines and neonatal morbidities are needed.

Author contribution

SNS: Data collection, writing

MY: Design, critical review

SY: Critical review

Statistical analysis: Hacettepe University, Department of Bioistatistics

Conflict of interest

The authors have no conflicts of interest to declare.

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