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Significance of the platelet distribution width as a severity marker for the development of preeclampsia

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ABSTRACT

Objective: To evaluate the platelet distribution width (PDW) and other platelet indices as potential severity markers of preeclampsia (PE).
Study design: A total of 935 pregnant women who had received continuous prenatal care and had undergone delivery were included. The participants were classified into 3 groups: healthy pregnant women ($n = 816$), pregnant women with mild PE ($n = 59$), and pregnant women with severe PE ($n = 60$). Blood samples were collected during antenatal care or at the time of admission, and the platelet indices were compared among the three groups.
Results: Among the three groups, the platelet count and plateletcrit decreased as the disease progressed. The mean platelet volume and the PDW, however, increased as the disease progressed. When compared to the levels of other platelet indices, the PDW showed significant elevation in the severe PE group. In the mild and severe PE groups, the PDW was statistically correlated with the mean arterial pressure (MAP) ($r = 0.231$, $p < 0.05$), whereas other platelet indices were not. In the receiver operating characteristics curve analysis, the area under the curve of the PDW to predict severe PE was 0.74.
Conclusions: Among platelet indices, the PDW is significantly higher in women with severe PE than in women with mild PE, and is positively correlated with the MAP. Therefore, the PDW can serve as a candidate marker for predicting the severity of PE.

1. Introduction

Preeclampsia (PE) is a major cause of maternal and fetal morbidity and mortality in pregnancy [1]. PE is a multi-organ disease with an unknown etiology, and many studies have investigated this condition. A decreased platelet count is observed during the progression of PE, and is considered a marker of the severity of PE. Although PE is defined by hypertension and proteinuria, transition of the coagulation function between platelet and endothelial vascular cells is believed to play an important role in the pathogenesis of PE [2].

PE involves a multi-organ system, and it is therefore difficult to identify severity markers of PE. Severe PE is diagnosed by the presence of one or more of the following symptoms in a pregnant woman on bed rest: a systolic blood pressure of ≥160 mmHg or a diastolic blood pressure of ≥110 mmHg obtained on two occasions after a difference of 6 h or more; proteinuria with the excretion of ≥5 g of protein in a 24-h urine specimen or ≥3+ protein obtained in two random samples of urine collected after four hours or more; oliguria with the excretion of <500 mL of urine in 24 h; pulmonary edema or cyanosis; impairment of liver function; visual or cerebral disturbances; pain in the epigastric area or right upper quadrant; decreased platelet count; and intrauterine growth restriction.

Among these clinical signs and symptoms, decreased platelet count is an important character and is associated with hemolysis, elevated liver enzyme levels, and low platelet counts (HELLP), a syndrome where there is an increased risk of adverse maternal and fetal outcomes [3,4]. A low platelet count is supposed to be a characteristic of worsening PE. When pregnant women with PE have a normal platelet count, platelet-related parameters are not seriously analyzed until it significantly changes. However, although the etiology of PE is unknown, several studies have

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demonstrated that uncontrolled platelet activation and aggregation are expected in thrombocytopenic PE and even in non-thrombocytopenic PE [5,6].

Platelet indices calculated from the platelet count include the mean platelet volume (MPV), plateletcrit (PCT), and platelet distribution width (PDW). Platelet indices are potentially useful markers for thromboembolic disease, and MPV and PDW in particular represent platelet activation [7]. The PDW is calculated by measuring the width of the size distribution curve (in femtoliters (fL)) at the 20% level when the peak distribution curve is taken as 80% or 100% [8]. It represents the heterogeneity in platelet morphology and is clinically related to platelet activation [7]. Large platelets are usually more reactive than smaller ones due to the increased number and size of the pseudopodia [9]. This possibly causes an increase in the PDW value. Many studies have evaluated the platelet indices and have reported that the MPV increases during pregnancy, and is higher in women with PE. The MPV may therefore be a valuable tool for evaluating the severity of PE [10,6,11–13]. Also, in some studies, it has been suggested that the PDW instead of MPV can be a practical tool to evaluate the activation of coagulation or thrombocytosis-related disease [7,9].

Due to alterations in coagulation, the PDW has an important role in the progression of PE: therefore, not only the platelet count but also the platelet function should be carefully assessed. Considering the role of the PDW and platelet indices during the disease as well as the alteration of coagulation, we aimed to evaluate the feasibility of using platelet indices as a severity marker for PE in the present study.

2. Materials and methods

2.1. Participants

This study included 935 women with a singleton pregnancy over 20 weeks of gestation who received continuous prenatal care and underwent delivery at the Konkuk University Medical Center, Seoul, Korea, between January 2009 and December 2012. All study participants were classified into three groups: healthy pregnant women ($n = 816$), pregnant women with mild PE ($n = 59$), and pregnant women with severe PE ($n = 60$). The diagnosis of PE was made using the definitions described by the American College of Obstetricians and Gynecologists [4]. PE was defined as the presence of hypertension and proteinuria after 20 weeks of pregnancy. Severe PE was diagnosed using the following: a blood pressure elevation with a systolic blood pressure of ≥160 mm Hg or a diastolic blood pressure of ≥110 mm Hg and proteinuria >3+ on a urine dipstick. For the diagnosis of mild PE, a systolic blood pressure between 140 and 160 mmHg and a diastolic blood pressure between 90 and 110 mmHg, and proteinuria >1+ or 2+ on a urine dipstick was considered significant. A minimum of two consecutive positive measurements was required for the diagnosis.

Women with a history of diabetes, renal disease, hypertension, cardiovascular illness, symptomatic infectious diseases, chronic medical disorders, a history of smoking, or those with a fetal structural or genetic anomaly were excluded from the study. Women with complete HELLP syndrome and low platelet PE were excluded from the study to evaluate platelet indices in non-thrombocytopenic PE.

This clinical cohort study was approved by the Institutional Internal Review Board.

2.2. Blood sampling and analysis

Blood samples from the healthy pregnant women were collected during a routine antenatal care visit or when they were admitted for delivery. For women in the PE group, blood and urine samples were collected when the patient was admitted at the time of delivery. Blood samples were collected in tubes containing EDTA and in tubes without an anticoagulant. The platelet count and platelet indices were estimated using the Sysmex Xe-2100 automated quantitative hematology analyzer (Sysmex Corp., Kobe, Japan). The mean arterial pressure (MAP) was used as an indicator of the severity of PE and was calculated using the following formula: MAP = [(2 × diastolic blood pressure) + systolic blood pressure]/3 [14]. All blood pressure measurements were confirmed by two readings taken 4–6 h apart. For all the sample data, we compared the platelet indices between healthy pregnant women and the pregnant women with mild and severe PE.

2.3. Statistical analysis

The median was used to express the data values. A one-way analysis of variance (ANOVA) was used to compare the characteristics between healthy pregnant women and pregnant women with PE. Statistical significance was determined using multiple comparisons between the groups performed by a one-way ANOVA

Table 1
Demographic and clinical data of healthy pregnant women and pregnant women with mild to severe preeclampsia.

	Healthy pregnancy ($n = 816$)	Preeclamptic pregnancy ($n = 119$)		p-Value
		Mild preeclampsia ($n = 59$)	Severe preeclampsia ($n = 60$)	
Nulliparity (n, %)	396 (48.5%)	79 (66.4%)		0.031[a]
Maternal age (y)	32 (26–43)	35 (23–49)	35 (19–45)	<0.001[b]
BMI (kg/m^2)	26 (21–35)	27 (20–43)	27 (17–38)	0.026[b]
Pregnancy duration (weeks)	37 (32–38)	36 (27–40)	34 (23–41)	<0.001[b]
Birth weight (kg)	3.2 (2.4–4.1)	2.4 (0.6–3.7)	2.0 (0.5–3.6)	<0.001[b]
Blood pressure (mmHg)				
Systolic	112 (92–136)	148 (130–158)	167 (143–196)	<0.001[b]
Diastolic	67 (49–82)	96 (67–109)	106 (80–131)	<0.001[b]
MAP	97 (78–117)	131 (117–139)	147 (127–163)	<0.001[b]
Blood laboratory value				
Creatinine (mg/dL)	0.5 (0.3–0.7)	0.78 (0.5–1.2)	0.8 (0.4–1.2)	<0.001[b]
AST (IU/L)	20 (12–39)	23 (13–58)	35 (14–151)	<0.001[b]
ALT (IU/L)	11 (3–34)	16 (5–75)	27 (4–175)	<0.001[b]
Platelets (x10^3/L)	228 (140–354)	211 (141–352)	180 (140–303)	<0.001[b]
Albumin (g/dL)	3.2 (2.6–3.7)	3.0 (2.4–3.6)	2.8 (1.6–3.5)	<0.001[b]

Values are given as the median (range) unless otherwise indicated. A p-value of <0.05 with a 95% confidence interval was considered significant. *Abbreviations*: BMI, body mass index; ALT, alanine aminotransferase; AST, aspartate aminotransferase; MAP, mean arterial pressure.

[a] Nulliparity was compared using the Pearson chi-squared (χ^2) test.

[b] Statistical significance was tested by one-way ANOVA, except for nulliparity.