

## Accuracy of Platelet Parameters (PC, MPV, and PDW) as A Predictor of The Severity of Preeclampsia

Heru Maranata Nababan,<sup>1,2</sup> Donel Suhaimi,<sup>1</sup> Arfianti,<sup>2</sup> Arya Marganda Simanjuntak<sup>3</sup>

<sup>1</sup> Department of Obstetric – Gynecology, Faculty of Medicine, Universitas Riau, Arifin Achmad General Hospital, Pekanbaru, Riau

<sup>2</sup> Department of Biomedicine, Faculty of Medicine, Universitas Riau, Pekanbaru, Riau

<sup>3</sup> Research Assistant, Department of Internal Medicine, Faculty of Medicine, Universitas Riau, Arifin Achmad General Hospital, Pekanbaru, Indonesia

Correspondence: Heru Maranata Nababan, Email: Herunababan20@gmail.com

### Abstract

**Objective:** To evaluate the accuracy of platelet parameters—platelet count (PC), mean platelet volume (MPV), and platelet distribution width (PDW)—as predictors of preeclampsia severity.

**Methods:** A case-control study was conducted on 153 pregnant women with preeclampsia at Arifin Achmad Hospital from January 2019 to December 2020. Platelet indices (PC, MPV, PDW) were compared between 61 patients with severe preeclampsia and 92 with non-severe preeclampsia. ROC analysis determined predictive accuracy, with sensitivity and specificity calculated for selected cut-off values.

**Results:** Significant differences were found in PC ( $p=0.000$ ), PDW ( $p=0.049$ ), and MPV ( $p=0.012$ ) between groups. ROC analysis showed PDW  $>12.3\%$  had a sensitivity of 60.7% and specificity of 59.8%, while MPV  $>10.65$  fL had a sensitivity of 62.3% and specificity of 64.1%. AUC values for PDW and MPV were 0.62 and 0.66, respectively, indicating weak predictive accuracy.

**Conclusion:** Although platelet parameters differ significantly between preeclampsia severity groups, their predictive value is limited. They should not be solely relied upon for assessing preeclampsia severity.

**Keywords:** Preeclampsia, Platelet Count, Platelet Distribution Width, Mean Platelet Volume, Predictive Biomarkers

## Akurasi Parameter Trombosit (PC, MPV, dan PDW) sebagai Prediktor Tingkat Keparahan Preeklampsia

### Abstrak

**Tujuan:** Penelitian ini dilaksanakan pada pasien preeklampsia untuk mengevaluasi akurasi parameter trombosit—jumlah trombosit (PC), volume trombosit rata-rata (MPV), dan lebar distribusi trombosit (PDW)—sebagai prediktor tingkat keparahan.

**Metode:** Studi kasus-kontrol dilakukan pada 153 ibu hamil dengan preeklampsia di Rumah Sakit Arifin Achmad dari Januari 2019 hingga Desember 2020. Indeks trombosit (PC, MPV, PDW) dibandingkan antara 61 pasien dengan preeklampsia berat dan 92 pasien dengan preeklampsia tanpa gejala berat. Analisis ROC digunakan untuk menentukan akurasi prediktif, dengan perhitungan sensitivitas dan spesifisitas berdasarkan nilai cut-off tertentu.

**Hasil:** Terdapat perbedaan signifikan pada PC ( $p=0.000$ ), PDW ( $p=0,049$ ), dan MPV ( $p=0.012$ ) antara kedua kelompok. Analisis ROC menunjukkan bahwa PDW  $>12.3\%$  memiliki sensitivitas 60.7% dan spesifisitas 59.8%, sedangkan MPV  $>10.65$  fL memiliki sensitivitas 62.3% dan spesifisitas 64.1%. Nilai AUC untuk PDW dan MPV adalah 0.62 dan 0.66, menunjukkan akurasi prediktif yang lemah.

**Kesimpulan:** Meskipun parameter trombosit menunjukkan perbedaan signifikan antara kelompok preeklampsia berat dan tidak berat, nilai prediktifnya terbatas. Parameter ini tidak dapat digunakan secara mandiri untuk menilai tingkat keparahan preeklampsia.

**Kata kunci:** Preeklampsia, Jumlah Trombosit, Lebar Distribusi Trombosit, Volume Trombosit Rata-rata, Biomarker Prediktif

## Introduction

Preeclampsia is a pregnancy-specific syndrome that often manifests after 20 weeks of gestation and is linked to acute-onset hypertension. Preeclampsia is a significant pregnancy concern and is the primary cause of maternal and neonatal mortality. Worldwide, between 3 and 8% of pregnant women develop preeclampsia.<sup>1</sup> The three leading causes of maternal death are infection, bleeding, and preeclampsia. In the United States, the prevalence of preeclampsia rose from 3.4% in 1980 to 3.8% in 2010. Preeclampsia-eclampsia incidence data are very scarce in Indonesia, particularly at the national level.<sup>2</sup> According to National Research in 2018, 3.3% of pregnant Indonesian women have hypertension. The prevalence of pregnancy-related hypertension in Riau Province is somewhat lower than the 2.9% national incidence rate.<sup>3</sup> The number of preeclampsia cases treated in 2019 was 99 out of 624 total instances of obstetric patients treated in the Obstetrics Ward of Arifin Achmad Hospital, Riau Province, or 15.8%, according to statistics from the Department of Obstetrics and Gynecology at the Arifin Achmad Hospital. Then, in 2020, there were 76 cases of preeclampsia out of 411 cases of obstetric patients treated in the same ward, or 18.5% of all cases. A clinical syndrome that can impact several organ systems is preeclampsia. Hematological abnormalities are among the alterations frequently brought on by preeclampsia. Thrombocytopenia is a common feature of preeclampsia in women, particularly in those with severe preeclampsia. The severity of preeclampsia can be predicted by thrombocytopenia, which is caused by increased platelet activation, aggregation, and consumption.<sup>4</sup>

The clinical syndrome begins with abnormal placentation with subsequent release of antiangiogenic markers, mediated primarily by soluble fms-like tyrosine

kinase-1 (sFlt-1). The typical platelet characteristics that are analyzed in a complete blood count include platelet count (PC), mean platelet volume (MPV), platelet distribution width (PDW), and PCT. Previous research on preeclamptic women by Alsheeha et al. found no appreciable variation in PDW and MPV between preeclamptic and control women with regard to platelet count and platelet properties. However, this study demonstrated that preeclampsia patients had lower platelet counts and platelet/MPV ratios than control women. The PC/MPV cut-off was 31.2, with an AUC of 0.622, for the diagnosis of preeclampsia, with a 71% sensitivity and a 49% specificity.<sup>5</sup>

The production of cytokines and chemokines that draw leukocytes and encourage adherence to the injured endothelium is also linked to platelets' role in the inflammatory response. Platelets and leukocytes interact during the inflammatory process to generate platelet-leukocyte aggregation. Through direct contact, bacterial encapsulation, reactive oxygen release, and platelet microbicidal protein (PMP), platelets also assist leukocytes in combating bacterial infections.<sup>6,7</sup> Women with severe preeclampsia had lower PC than women with preeclampsia without severe characteristics and women with normal blood pressure, according to a similar study by Alsheeha et al. and Tesfay et al. that was previously carried out in Ethiopia on 219 pregnant women. Platelet features including mean platelet volume (MPV), platelet distribution width (PDW), and platelet large cell ratio (PCLR) were positively connected with the severity of preeclampsia. Furthermore, this study showed that the MPV value  $>9.45$  fL had a sensitivity of 83.5%, a specificity of 86.4%, a negative predictive value of 90.3%, and a positive predictive value of 77.6% for the diagnosis of preeclampsia.<sup>8</sup> One of the most frequent hematological alterations seen in preeclampsia is a shift in platelet properties.

Platelet parameter analysis has the potential to be developed as a predictor to identify the prognosis of pregnant women with preeclampsia because it is reasonably priced and accessible in practically all Indonesian healthcare facilities. The tendency of Arifin Achmad Hospital Riau Province, a referral hospital, to see a rise in preeclampsia cases (15.8% in 2019 to 18.5% in 2020) suggests that preeclampsia cases are on the rise in the community. Therefore, it is crucial to do research on creating laboratory measures that can be utilized as predictors for preeclampsia screening in order to lower the mortality rate among preeclampsia patients.

## Method

Using a cross-sectional design from April to May 2021, the study was carried out at the Arifin Achmad Hospital in the Medical Faculty of Riau University's Department of Obstetrics and Gynecology in the province of Riau. All pregnant patients with preeclampsia who received care at the Arifin Achmad Hospital between January 2019 and December 2020 made up the study's population. Based on data from the Department of Obstetrics and Gynecology at Arifin Achmad Hospital from January 2019 to December 2020, the study's sample consisted of all pregnant women with preeclampsia who met the following requirements: The case group was all preeclampsia patients with severe features who had met the ACOG diagnostic criteria who were treated at the Department of Obstetrics and Gynecology Arifin Achmad Hospital. Systolic blood pressure of 160 mmHg or diastolic blood pressure of 110 mmHg with proteinuria with one of the following conditions diagnosed: thrombocytopenia (<100,000/uL); pulmonary edema, neurological symptoms like stroke, headache, or visual disturbances, uteroplacental circulation disorders like oligohydramnios, fetal growth restriction

(FGR), or absent or reversed end diastolic velocity (ARDV), renal impairment with elevated serum creatinine above 1.1 mg/dL, and liver disorders with an increase in transaminases concentration twice the normal limit or right upper abdominal pain.

Patients with preeclampsia without severe symptoms who received treatment at the Arifin Achmad Hospital's Department of Obstetrics and Gynecology made up the control group. If the blood pressure is at least 140 mmHg systolic or 90 mmHg diastolic on two tests 15 minutes apart and the urine protein is more than 300 mg in a 24-hour period or the urine dipstick test is more than positive 1, preeclampsia without severe characteristics is diagnosed. Exclusion criteria of this study were pregnant women with chronic hypertension, diabetes mellitus, gestational diabetes, liver disease, heart disease, and infections. In addition, pregnant women taking routine drugs such as glucocorticoids, antiplatelets, and anticoagulants based on the results of the anamnesis listed in the medical record were also excluded. The medical records of the selected patients were the medical records of preeclampsia patients who were hospitalized according to the criteria for cases and controls and selection was made of the medical records of preeclampsia patients who met the inclusion criteria and identified samples with the exclusion criteria. Medical records that passed the selection were then opened to view and record the necessary data in the form of anamnesis, diagnostic physical examinations and complete laboratory examinations to support diagnosis. Furthermore, laboratory results in the form of PC, PDW, and MPV in case and control medical records and the degree of preeclampsia in case samples were inputted into the SPSS version 23 program for statistical analysis.

To do the statistical analysis, we used IBM's Statistical Package for Social Sciences (SPSS) v.23 (Chicago, IL, USA). Initially,

the Shapiro-Wilk test was used to analyze the data distribution. Data that are normally distributed are assessed using the independent t-test, whereas data that are not normally distributed were analyzed using the Mann-Whitney test. The degree to which the platelet index accurately predicted the severity of preeclampsia patients was evaluated using the area under the curve (AUC) of the receiver-operating characteristic (ROC), which is a trade-off between sensitivity and specificity at various cut-off points. AUC = 1 indicates an accurate diagnostic test, whereas AUC = 0.5 indicates a diagnostic test with no discriminating power.<sup>9</sup> markers, or features as potential predictors in binary problems. We distinguish raw ROC diagnostics and ROC curves, elucidate the special role of concavity in interpreting and modelling ROC curves, and establish an equivalence between ROC curves and cumulative distribution functions (CDFs). Moreover, positive predictive values,

negative predictive values, and sensitivity and specificity were computed for every cut-off for the platelet index. It was deemed statistically significant when the P value was less than 0.05. This research received ethical clearance from Ethical Board, Faculty of Medicine, Universitas Riau by number: B/160/UN19.5.1.1.8/UEPKK/202

### Result

At the Arifin Achmad Hospital, 91 pregnant women with preeclampsia without severe symptoms and 61 pregnant women with severe features received treatment. Table 1 shows the baseline for this study, which included a sample of all preeclampsia patients treated at the Arifin Achmad Hospital. The characteristics of 153 individuals with severe symptoms and those without severe indications of preeclampsia are compared in Table 1. A statistically significant difference

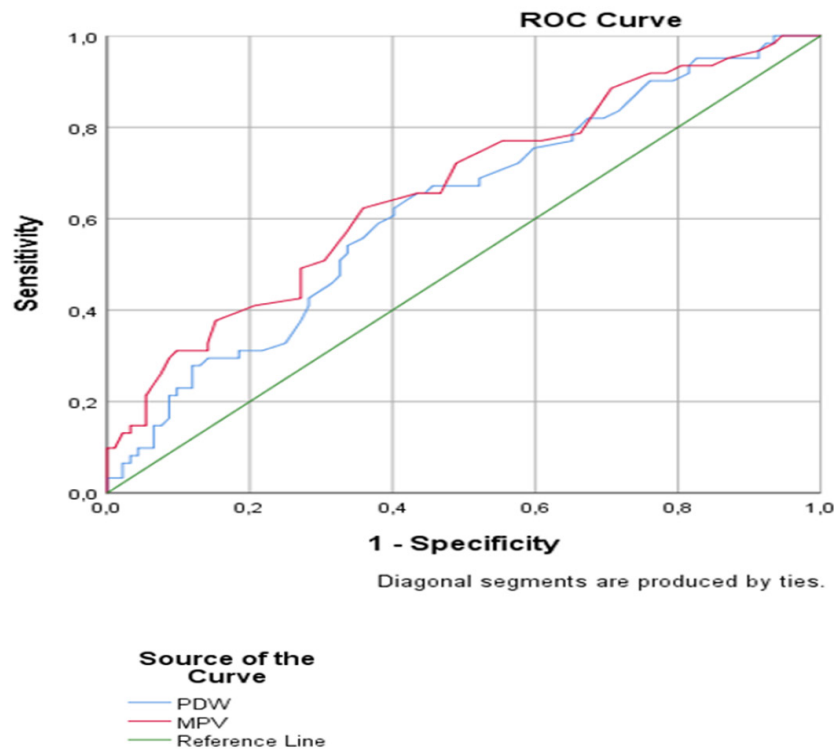


Figure 1 ROC curves for mean platelet volume (MPV) and platelet distribution width (PDW)

**Table 1 Comparison of characteristics of preeclampsia with severe features and preeclampsia without severe features**

Variable	Pre-eclampsia		<i>p-value</i>
	Severe Feature* (n = 62)	Non-Severe Feature* (n = 62)	
Age	30.46 (6.19)	31.87 (6.10)	0.186
Parity	1.31 (1.40)	1.50 (1.44)	0.378
Gestational age, week	33.69 (4.00)	34.78 (4.10)	0.096
Body Mass Index, kg/m <sup>2</sup>	25.14 (4.07)	23.91 (4.21)	0.024

\*Mean ± SD

**Table 2 Comparison of platelet parameters of preeclampsia with severe features and preeclampsia without severe features**

Variable	Pre-Eclampsia		<i>p-value</i>
	Severe Feature* (n = 62)	Non Severe Feature* (n = 62)	
PC, x10 <sup>3</sup> uL	182.49 (103.36)	256.14 (74.84)	0.000
PDW, %	13.51 (3.31)	12.22 (2.56)	0.049
MPV, fL	11.06 (1.15)	10.41 (0.91)	0.012

\*Mean ± SD

( $p=0.024$ ) was found between the BMIs of the preeclampsia with severe characteristics group and the preeclampsia without severe features group. The comparison of platelet parameters between the groups receiving treatment for severe symptoms of preeclampsia and those not receiving treatment is displayed in Table 2. There were statistically significant variations in PC ( $P=0.00$ ), PDW ( $P=0.049$ ), and MPV ( $P=0.012$ ) between the groups with and without severe preeclampsia symptoms.

Furthermore, platelet parameters in the form of PDW and MPV were included in the ROC analysis for the preeclampsia group with severe features and the preeclampsia group without severe features in order to establish the cut-off point for enforcing the severity of preeclampsia based on the platelet index, which is displayed in Figure 1. A PDW result of greater than 12.35% exhibited a sensitivity of 60.7%, a specificity of 59.8%, a positive predictive value of 50.6%, and a negative predictive value of 70.5% for diagnosing severe preeclampsia. The AUC for the PDW

parameter was 0.62. The MPV parameter yielded an AUC (area under the curve) of 0.66 (Fig. 1), while MPV results exceeding 10.65 had a 62.3% sensitivity, a 64.1% specificity, a 50.6% positive predictive value, and a 71.2% negative predictive value.

### Discussion

A substantial difference was detected in the body mass index (BMI) of patients with severe preeclampsia compared to those without severe symptoms in a study involving 153 preeclampsia patients, 62 of whom had severe features and 91 of whom did not. Patients with severe preeclampsia had an average BMI of 25.14 kg/m<sup>2</sup> (obesity), whereas those without severe characteristics had an average BMI of 23.91 kg/m<sup>2</sup> (overweight). The majority of preeclampsia patients treated at the Arifin Achmad Hospital are overweight or obese according to the Asia-Pacific BMI criteria. 10. This study is not consistent with the meta-analysis conducted by Motedayen

et al. Patients with severe signs of preeclampsia had an average BMI of 26.33 kg/m<sup>2</sup>, which is deemed overweight based on the WHO body mass index standards. This suggests that preeclampsia patients without severe symptoms had a higher mean BMI than those with severe features.<sup>10,11</sup> According to Shao et al.'s research, patients who were fat or overweight were more likely to get preeclampsia. According to their research, women who are overweight or obese have a 1.76-fold increased risk of preeclampsia without severe symptoms and a 1.79-fold increased risk of preeclampsia with severe characteristics when compared to women of normal weight.<sup>12</sup> China. Three hundred forty seven pregnant women with preeclampsia and 9516 normotensive women at Gansu Provincial Maternity and Child Care Hospital were included in the present study. Unconditional logistic regression models were used to evaluate the associations between pre-pregnancy BMI, GWG, and risk of preeclampsia and its subtypes. Results: Compared to women with normal pre-pregnancy BMI, those who were overweight/obese had an increased risk of preeclampsia (OR=1.81; 95%CI: 1.37-2.39). Insulin resistance, which can result in low-grade inflammation and endothelial activation, is a characteristic of obesity and metabolic syndrome. Vasoconstriction brought on by endothelial activation raises vascular pressure, which in turn leads to hypertension. Platelets and fibrinogen, among other blood components, will leak through the interstitial space as a result of endothelial cell injury, building up in the subendothelium. Pregnant obese women had decreased endothelial function and markedly elevated blood levels of C-reactive protein and IL-6. The fundamental hypothesis is that pregnant women who are overweight or obese are more likely than normoweight women to experience severe symptoms of preeclampsia.<sup>13</sup> Thus, the researchers came to the conclusion that endothelial activation increases with a person's

BMI, resulting in hypertension and interstitial leakage, particularly platelets, as well as elevated serum levels of pro-inflammatory cytokines like IL-6 and C-reactive protein triggering the endothelium.

Preeclampsia patients with severe characteristics and those without showed a significant difference in PC, according to this study. Compared to preeclampsia patients without severe symptoms, those with severe features had a lower mean PC. There appears to be a substantial difference between PC in preeclampsia patients with severe characteristics and those without, according to numerous prior research.<sup>14-17</sup> the most common of hypertensive disorders of pregnancy is an idiopathic multisystem disorder affecting 2 – 10% of all pregnancies and together they form one member of the deadly triad, along with hemorrhage and infection that contribute greatly to the maternal morbidity and mortality rates. The identification of this clinical entity and effective management play a significant role in the outcome of pregnancy. Platelet count is emphasized to play a significant role in hemostasis mechanism of preeclampsia and the degree of thrombocytopenia increases with severity of preeclampsia. This study was conducted to find correlation of platelet count in severe preeclampsia, mild preeclampsia and normal subjects. Methods: Total 140 subjects, 70 control and 70 cases were enrolled in the study. Samples for platelet count were collected and estimation was carried out by the auto-analyzers. The statistical evaluation is done using SPSS version 22 along with Anova and student t-test. Results: The mean platelet count was significantly lower ( $p < 0.05$ ). However, prior research just looked at variations in PC; it didn't look at the size and shape of these platelets. Reddy et al. conducted a recent study that was comparable to this one and found a statistically significant difference ( $p$  value 0.001) between PC in

patients with preeclampsia without severe characteristics vs preeclampsia with severe features. Additionally, according to Reddy et al., the mean PC was lower in preeclampsia patients with severe symptoms ( $181 \pm 38.9$ ) than in those without severe features ( $210 \pm 47$ ).<sup>18</sup> and hence, its detection depends on signs or investigations. The platelet (PLT) The preeclampsia syndrome was linked to a number of hematological disorders, with thrombocytopenia being one of the most common observed in patients with preeclampsia. Each preeclamptic patient experiences preeclampsia at a different frequency and intensity, which frequently varies depending on the severity and length of preeclampsia. Generally speaking, the incidence of maternal and fetal morbidity and mortality increases with decreasing platelet counts. Because thrombocytopenia tends to worsen, it is usually advised to terminate a pregnancy in these patients. The platelet count may decrease on the first day following pregnancy termination, but it will gradually rise again to return to normal levels in three to five days.<sup>13</sup> When platelets come into contact with exposed subendothelium as a result of vascular injury, they might become activated and aggregate to form a thrombus. Normally, platelets are inactive in the bloodstream. The fundamental pathophysiology of preeclampsia is endothelial damage. Glycoprotein Iib/IIIa (GP Iib/IIIa) (CD41) and P-selectin (CD 62P) are indicators of platelet activation. CD 63, or glycoprotein 53. Platelets seem to be circulating in a highly active state in preeclamptic patients. P-selectin (CD62P), CD63, plasmatic thromboglobulin, and platelet endothelial cell adhesion molecule 1 (PECAM-1) were all found to be elevated in preeclamptic women in the third trimester, indicating more widespread platelet activation, according to flowcytometry. If CD63 is linked to diastolic hypertension during the first trimester of pregnancy, it may be helpful in identifying a

subgroup of patients who are at a high risk of developing preeclampsia.<sup>19</sup> Because of the greater platelet activation in the preeclampsia group, poor platelet values were achieved, particularly in this group with severe characteristics. The significant endothelial damage present in severe preeclampsia is the cause of this increased platelet activation. These platelets' activation will require blood platelets to cover endothelial damage; hence, the more activated platelets are, the more blood platelets will be used. This is why individuals with severe preeclampsia are reported to have low platelet counts.

The PDW value of preeclampsia patients with severe symptoms was higher than that of the preeclampsia group without severe features, according to this study. PDW was higher in preeclampsia patients with severe symptoms than in those without severe features ( $p$  value  $< 0.001$ ), according to a study by Reddy et al. that is comparable to this one.<sup>18</sup> and hence, its detection depends on signs or investigations. The platelet (PLT) PDW displayed platelet reactivation and morphological alterations. When platelets are activated, they will undergo morphological changes, such as becoming more spherical and developing pseudopodia. Changes in morphology are the cause of the variation in platelet size, which raises PDW.<sup>20</sup> According to this study, preeclamptic patients with severe features had higher PDW values than preeclampsia patients without severe features. This could be because the patients with severe features had higher platelet activation, which results in variations in platelet size.

Patients with severe signs of preeclampsia and those without severe characteristics showed significantly different MPV. The studies by Reddy et al. and Karateke et al., which demonstrated a statistically significant difference between the MPV of preeclamptic patients with severe symptoms and those without severe features, are comparable to this one.<sup>18,20</sup> platelet distribution width (PDW

MPV displays platelet size in relation to platelet activation. A number of disorders are linked to MPV, a measure of platelet activation. While small platelets are linked to chronic illnesses like rheumatoid arthritis and systemic lupus erythematosus, large platelets indicate platelet activation, as seen in cardiovascular disease and prothrombic or hypercoagulable states (conditions in which bloodstream components tend to cause thrombosis). MPV levels are higher in preeclampsia patients, according to numerous research.<sup>20</sup> According to this study, patients with severe preeclampsia had a higher MPV rate than those without such symptoms. The activation of a large number of platelets, which raises platelet production, is most likely the cause of the increase in MPV. Compared to the older platelets, the newly formed platelets are bigger and more active. Additionally, this study discovered that platelet measures including PDW and MPV exhibited inadequate diagnostic accuracy, with an AUC of 0.62 on PDW and 0.66 on MPV. With a cut-off for PDW of 12.3% and MPV of 10.65 to predict the severity of preeclampsia, PDW and MPV in this study exhibited low sensitivity and specificity. This study differs from that of Reddy et al., who reported that their discrimination was very good with an AUC on MPV of 0.78 and a PDW of 0.742. According to Reddy et al.'s research, the PDW cut-off of >17.75 had a sensitivity of 66% and a specificity of 62%, while the MPV cut-off of >10.95 had a sensitivity of 80% and a specificity of 75%.<sup>18</sup> Because platelet measures like PDW and MPV have poor specificity and sensitivity as well as a weaker discriminatory power, they cannot be used as diagnostic tools to assess the severity of preeclampsia.

### Conclusion

Severe preeclampsia patients have significant variations in BMI, platelet count, PDW, and

MPV. A PDW of 12.3% or higher has a higher sensitivity and specificity for assessing severity.

### Conflict of Interest (if any)

None to Declare

### Funding

None to Declare

**Ethics Approval and Consent To Participate**  
This research has the ethical review of the Medical and Health Research Ethics Unit, Faculty of Medicine, Riau University and received a research permit at the Arifin Achmad Hospital, Riau Province

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