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by Faizah Fulyani

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The difference of platelet-white blood cell ratio in severe preeclampsia and normotensive pregnancy



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Nisrina Aisyah Nur Safirani¹, Faizah Fulyani², Putri Sekar Wiyati³,
Besari Adi Pramono^{3*}

¹Undergraduate Program, Faculty of Medicine, Universitas Diponegoro;

²Department of Biology and Biochemistry, Faculty of Medicine, Universitas Diponegoro;

³Department of Obstetrics and Gynecology, Faculty of Medicine, Universitas Diponegoro;

*Corresponding author:

Besari Adi Pramono;
Department of Obstetrics and Gynecology, Faculty of Medicine, Universitas Diponegoro;
babas1504@yahoo.com

¹⁰
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ABSTRACT

Background: Inflammation is believed to play a role in preeclampsia. Leukocytes increase due to inflammatory response. Endothelial damage in preeclampsia induces platelet aggregation, triggers platelet consumption, and decreases platelet. Therefore, preeclampsia could alter the platelet-white blood cell ratio, which can be used as a marker for preeclampsia. This study examines the difference of platelet-white blood cell ratio in severe preeclampsia and normotensive pregnancy.

Methods: This study used the medical records of pregnant women in Dr. Kariadi General Hospital Semarang from 2019 to 2020. Samples were collected using a consecutive sampling method. Data were analyzed using an independent t-test and Mann-Whitney.

Results: There was a significant difference in platelet count ($p=0.011$) and leukocyte count ($p=0.018$) between severe preeclampsia and normotensive pregnancy. Therefore, a difference ($p<0.01$) in platelet-white blood cell ratio between severe preeclampsia and normotensive pregnancy was observed.

Conclusion: Platelet-white blood cell ratio in severe preeclampsia is 0.7 times lower than in normotensive pregnancy.

Keywords: inflammation, severe preeclampsia, platelet-white blood cell ratio.

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INTRODUCTION

According to World Health Organization (WHO), Global Maternal Mortality Rate in 2017 reached 211 per 100,000 live births.¹ In Indonesia, Maternal Mortality Rate in 2019 called 305 per 100,000 live births.² Direct obstetric causes of maternal death in Indonesia are bleeding (28%), preeclampsia/eclampsia (24%), and infection (11%).³ It should be noted that preeclampsia incidence in developing countries is seven times higher than in developed countries, with the number of preeclampsia found in Indonesia to be 7-10% of all pregnancies.⁴

The etiology and mechanism of preeclampsia are still unknown up to this day, making this disease "the disease of theories".⁵ One of the theories states that preeclampsia is caused by the failure of the trophoblast invasion process, which leads to hypoperfusion and ischemic of the placenta.

This, in turn, will create destruction of endothelial cells and induce vasospasm, thrombocytes aggregation, and thrombocytes usage.⁶ Angiogenesis

imbalance and systemic inflammation are believed to play a role in the etiopathogenesis of preeclampsia.⁷ The inflammatory response in preeclampsia involves leukocyte activation, and leukocytes are found to be increased due to the inflammatory response.⁸

Platelet-Lymphocyte Ratio (PLR) and Neutrophil-Lymphocyte Ratio (NLR) are potential markers for predicting inflammation. Research conducted in Boston reported that PLR has a crucial role in inflammation.⁹ Another study in Antwerp University Hospital found that PLR levels are lower while NLR levels are higher in preeclampsia.¹⁰

Platelet-white blood cell ratio (PWR) refers to the hematologic marker of systemic inflammatory response.¹¹ Other research reported the potential of PWR as an additional test for preeclampsia screening and adjuvant fetal health test during antepartum due to its simplicity and convenience.¹² Therefore, this study's objective was to confirm the difference between PWR in preeclampsia and normotensive birth, especially among Indonesian pregnant women.

METHODS

Study Design

This research is an observational analytic study with a cross-sectional approach. Data collected in this research are secondary data from medical records of pregnant patients in Dr. Kariadi General Hospital. The sample was chosen through consecutive sampling. The inclusion criteria were pregnant patients admitted to Dr. Kariadi General Hospital during 2019-2020, preeclampsia with severe features, gestational age above 20 weeks, and single pregnancy. Exclusion criteria of this research are incomplete or unreadable medical records, history of diabetes mellitus, Coronavirus Disease 2019 (COVID-19), autoimmune, renal, heart, liver, and infectious disease. In total, 45 patients with severe preeclampsia and 45 control patients were analyzed. The Independent variable in this study is severe preeclampsia, while the dependent variable is the platelet-white blood cell ratio.

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Statistical analysis

Data were analyzed using the Statistical Package of Social Science (SPSS) Software version 26. The normality test was assessed using Saphiro-Wilk. Data were analyzed using an Independent t-Test and Mann-Whitney. The difference of haemoglobin, trombocyte and platelet-white blood cell ratio between two groups was assessed using Independent t-Test, while the difference of leukocyte in two groups was assessed using Mann-Whitney. P-value <0.05 is considered statistically significant.

RESULTS

Based on table 1, severe preeclampsia patients are primarily found in the age group of 20-35 years old, with 26 patients (57.8%). Twenty-four patients with severe preeclampsia (53.3%) do not have an occupation. Twenty patients with severe preeclampsia (44.4%) were senior high school graduates. Patients with severe preeclampsia were mainly on multigravida (84.4%). Most parity statuses found were primipara with (44.4%). Half of the preeclampsia patients (55.6 %) were hospitalized for more than three days, and one patient required treatment in the Intensive Care Unit (ICU).

Table 2 shows the hemoglobin, leukocyte, and thrombocyte levels of patients with severe preeclampsia and normotensive pregnancy. Compared with normotensive pregnancy, patients in the severe preeclampsia group have significantly higher hemoglobin ($p < 0.001$), higher leukocyte ($p = 0.018$), and lower thrombocyte counts ($p = 0.011$).

Data of platelet-white blood cell ratio is tested using an independent t-test. Based on table 3, there is a significant difference in platelet-white blood cell ratio ($p < 0.001$) between the severe preeclampsia group and the normotensive pregnancy group. The mean platelet-white blood cell ratio in severe preeclampsia is lower (21.37 ± 7.97 vs. 28.77 ± 8.34) than in normotensive pregnancy.

DISCUSSION

This study primarily observed severe preeclampsia in 20-35 years old. The result is consistent with a previous study.¹³ This may be due to that particular age being

Table 1. Characteristics of Research Subject.

Variable	Severe Preeclampsia (%)	Normotensive Pregnancy (%)
Age		
<20	0 (0)	1 (2.2)
20-35	26 (57.8)	41 (91.1)
>35	19 (42.2)	3 (6.7)
Place of Origin		
Semarang	28 (62.2)	29 (64.4)
Others	17 (37.8)	16 (35.6)
Occupation		
Working	21 (46.7)	20 (44.4)
Not Working	24 (53.3)	25 (55.6)
Education		
Elementary School	6 (1)	1 (2.2)
Junior High School	9 (20)	4 (8.9)
Senior High School	20 (44.4)	20 (44.4)
Bachelor	10 (22.2)	20 (44.4)
Admission		
Individual Visit	33 (73.3)	44 (97.8)
Private Hospital	6 (13.3)	0 (0)
Public Hospital	6 (13.3)	1 (2.2)
Gravida		
Primigravida	7 (15.6)	21 (46.7)
Multigravida	38 (84.4)	24 (53.3)
Parity		
Nullipara	9 (20)	25 (55.6)
Primipara	20 (44.4)	10 (22.2)
Multipara	16 (35.6)	10 (22.2)
Gestational Age		
Preterm	25 (55.6)	2 (4.4)
Aterm	20 (44.4)	43 (95.6)
Treatment		
Ward	43 (95.6)	45 (100)
ICU	1 (2.2)	0 (0)
HCU	1 (2.2)	0 (0)
Length Of Stay		
One day	0 (0)	20 (44.4)
Two days	2 (4.4)	18 (40)
Three days	18 (40)	6 (13.3)
>Three days	25 (55.6)	1 (2.2)
Labor Type		
Caesarean Section	32 (71.1)	6 (13.3)
Spontaneous Vaginal	11 (24.4)	39 (86.7)
Vacuum	1 (2.2)	0 (0)
Hysterectomy	1 (2.2)	0 (0)
Sex of Infant		
Male	25 (55.6)	20 (44.4)
Female	20 (44.4)	25 (55.6)
Condition of Infant		
Alive	43 (95.6)	45 (100)
Dead	2 (4.4)	0 (0)

Table 2. The difference in laboratory results.

Variable	Severe Preeclampsia	Normotensive Pregnancy	p
Hemoglobin (g/dL)	12.16 ± 1.64	10.83 ± 1.44	<0.001 ^a
Leukocyte (10 ³ /μL)	12.51 ± 4.11	10.86 ± 3.20	0.018 ^b
Thrombocyte (10 ³ /μL)	251.48 ± 89.41	295.22 ± 69.51	0.011 ^a

Data were shown as mean ± SD; ^aIndependent t-Test; ^bMann-Whitney

Table 3. The difference in Platelet-White Blood Cell Ratio.

Group	Platelet-White Blood Cell Ratio	p
Severe Preeclampsia	21.37 ± 7.97	<0.001 ^a
Normotensive	28.77 ± 8.34	

Data were shown as mean ± SD; ^aIndependent t-Test.

the ideal and healthy age for reproduction, making pregnancy and birth common.¹⁴ Through this study, we found that 53.5% of severe preeclampsia patients were unemployed. Research in Majalengka showed that employment status was a risk factor for preeclampsia.¹⁴ Stay-at-home pregnant women tend to get stressed due to a lack of outdoor activities.¹⁵ This study also found 44.4% of severe preeclampsia patients have a senior high school diploma. This result matches prior research that showed preeclampsia is mainly found in pregnant females with an old high school diploma.¹⁴ Patients with high education show a better understanding of pregnancy problems and have increased interest in seeking further professional help.

It was found that most severe preeclampsia patients are multigravida. This result is consistent with research conducted in Ethiopia in 2015, which shows that preeclampsia/eclampsia patients are commonly found in the multigravida group.¹⁶ In this study, 44.4% are primipara. This result is in line with a 2018 study in India which found that primipara is commonly found in the severe preeclampsia group.¹⁷ This contradicts the existing theory, most likely due to other factors, such as the history of prior pregnancies.

Severe preeclampsia may cause various complications which require special treatment. One severe preeclampsia patient underwent treatment in the Intensive Care Unit (ICU) in this study. Our result supports prior research that shows one severe preeclampsia patient being treated in the ICU.¹⁸ Most lengths of stay of severe preeclampsia patients

in this study are above three days. A prior study found that most severe preeclampsia/eclampsia patients were hospitalized for 5-10 days.¹⁶ This duration is the recommended treatment for severe preeclampsia, hospitalization during expectative treatment.

There is a significant difference in hemoglobin levels between severe preeclampsia and normotensive pregnancy, with higher mean hemoglobin in severe preeclampsia, consistent with other research.¹⁹ Hemoglobin increase in severe preeclampsia is predicted to be caused by hematologic disorders and endothelial dysfunction. This condition could create hemoconcentration and increase erythrocyte production, increasing hemoglobin levels.²⁰ Furthermore, the increase in hemoglobin level could be from the consumption of iron supplements to prevent anemia.

There is a significant difference in leukocyte levels between severe preeclampsia and normotensive pregnancy, where a higher leukocyte level is found in severe preeclampsia. This supports a previous study stating a significant difference in leukocyte levels, more elevated in severe preeclampsia.^{19,21} During pregnancy, leukocyte levels will rise due to the ongoing physiological stress and inflammation.^{22,23} Leukocyte level increase may describe the severity degree of inflammation response in preeclampsia, especially in severe preeclampsia.¹⁹

It is found that thrombocyte count in severe preeclampsia is significantly lower than in normotensive pregnancy. Similar research conducted in Semarang in 2019 also showed thrombocyte levels in severe

preeclampsia to be lower than in normal pregnancy and preeclampsia without severe features.²⁴ Decrease in thrombocyte levels in preeclampsia is related to the process of endothelial inflammation, and the occurrence of endothelial dysfunction, increase of thrombocyte activation and consumption, and hemodilution process will cause a decrease in thrombocyte level.^{6,22,25}

Platelet-white blood cell ratio is obtained from the platelet count divided by leukocyte count. This study has a significantly lower platelet-white blood cell ratio between severe preeclampsia and normotensive pregnancy. This result aligns with a previous study showing a significant difference in platelet-white blood cell ratio in the pregnancy age of 34 weeks in normotensive pregnancy, preeclampsia without IUGR, and preeclampsia with IUGR. A previous study found that the platelet-white blood cell ratio is lower in preeclampsia with and without IUGR than in normotensive pregnancy at 34 weeks.¹² This is related to the low amount of thrombocytes and high leukocytes in severe preeclampsia obtained in this research.

According to one the research, preeclampsia is an inflammatory disease.²¹ Whether in normal pregnancy or preeclampsia, the number of leukocytes experiences an increase due to inflammation. In severe preeclampsia, severe destruction of endothelial cells causes thrombocyte aggregation and induces a higher usage of thrombocytes, decreasing the number of thrombocytes.^{6,22} These processes will influence the platelet-white blood cell ratio, lower in severe preeclampsia than in normotensive pregnancy.

This research is not without its limits. This research does not include a cut-off value of platelet-white blood cell ratio between severe preeclampsia and normotensive pregnancy. Besides

that, severe preeclampsia patients are not divided into those with or without HELLP syndrome, where one of the characteristics of severe preeclampsia is thrombocytopenia. The gestational age of the samples is not the same from one to another. This factor may influence leukocyte levels, thrombocyte levels, and platelet-white blood cell ratio.

CONCLUSION

Platelet-white blood cell ratio in severe preeclampsia is lower than in normotensive pregnancy. Future researchers are advised to study the relationship between platelet-white blood cell ratio and severity degree of preeclampsia or other burdening factors. Moreover, a cut-off value of the platelet-white blood cell ratio should be studied. The subject used in future research should be differentiated between those with and without HELLP Syndrome and have the same gestational age.

ETHICAL APPROVAL

This study has been approved by the Health Research Ethics Committee Faculty of Medicine, Universitas Diponegoro, with ethical clearance reference number: No.152/EC/KEPK/FK-UNDIP/V/2021.

CONFLICT OF INTEREST

There is no conflict of interest in this research.

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None.

AUTHOR'S CONTRIBUTION

NANS and BAP developed the concept and the design of the study. NANS contributed to literature research, collected and analyzed the data, and analyzed statistical data, manuscript preparation, editing, and finalization. BAP contributed to manuscript preparation, editing, review, supervising, and approval for finalization. PSW contributed to the editing and completion of the manuscripts. FF contributed to the editing, review, and completion of the manuscript.

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