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Differences Hematology Profiles between Preeclampsia Patient with Normotensive Pregnancy in Dumai Hospital

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Abstract

Introduction: Preeclampsia is hypertension after 20 weeks gestation, characterized by systolic ≥140 mmHg or diastolic ≥90 mmHg in 2 examinations with an interval at least 4 hours in women whose blood pressure was previously normal, accompanied by proteinuria. Preeclampsia is the highest cause of maternal mortality in Indonesia. Changes in the hematological profile in preeclampsia occur due to hemoconcentration, inflammatory processes, thrombocyte activation, and thrombocyte coagulation. **Objective**: This research aims to determine the difference in hematological profile between preeclampsia patients and normotensive pregnancy at dr. Suhatman MARS Dumai Hospital. **Method**: This study was analytic observational research with a cross sectional approach, which conducted at dr. Suhatman MARS Dumai Hospital in January – June 2024. The sample of this study is all preeclampsia patients (mild and severe preeclampsia) and normotensive pregnancy recorded in medical records for the 2022-2023 period, who meet the inclusion and exclusion criteria. Hematology profile data (hemoglobin, hematocrit, erythrocyte, leukocyte, and thrombocyte) were tested for normality and homogeneity. The difference in hematology profile between mild preeclampsia, severe preeclampsia, and normotensive pregnancy were analyzed by the ANOVA one-way test. **Results:** Mild preeclampsia group had the lowest mean hemoglobin level, which was 11.43 gr/dl. Severe preeclampsia group had the lowest mean hematocrit levels and erythrocyte count with values of 32.30% and 3.91 million/mm3, respectively. The highest mean leukocyte count and the lowest mean thrombocyte count were found in normotensive group among which 12,778/mm3 and 232,565/mm3, respectively. Statistical test showed there was no significant difference between mild preeclampsia, severe preeclampsia, and normotensive group in hemoglobin levels (p=0.864), hematocrit levels (p=0.326), erythrocytes count (p=0.191), leukocytes count (p=0.422), and thrombocyte count (p=0.287). **Conclusion:** There was no significant difference in hematology profile (hemoglobin, hematocrit, erythrocytes, leukocytes, and thrombocyte) between preeclampsia patient and normotensive pregnancy at dr. Suhatman MARS Dumai Hospital.

Keywords: Hematology profile, Mild preeclampsia, Normotensive pregnancy, Severe preeclampsia

Abstrak

Pendahuluan: *Preeklampsia adalah hipertensi setelah usia kehamilan 20 minggu ditandai dengan sistolik >140 mmHg atau diastolik >90 mmHg pada 2 kali pemeriksaan dengan selang waktu minimal 4 jam pada wanita yang tekanan darah sebelumnya normal, yang disertai proteinuria. Preeklampsia merupakan penyebab mortalitas maternal tertinggi di Indonesia. Perubahan profil hematologi pada preeklampsia terjadi karena hemokonsentrasi, proses inflamasi, aktivasi platelet, dan koagulasi platelet.* ***Tujuan penelitian:*** *untuk mengetahui adanya perbedaan profil hematologi antara Pasien Preeklampsia dengan Kehamilan Normotensi di RSUD dr. Suhatman MARS Kota Dumai.* ***Metode:*** *Penelitian ini bersifat observasional analitik dengan*

pendekatan cross sectional, yang dilakukan di RSUD dr. Suhatman MARS Kota Dumai pada Januari – Juni tahun 2024. Sampel penelitian ini adalah semua pasien preeklampsia dan ibu hamil normotensi yang tercatat di rekam medis periode tahun 2022-2023, yang memenuhi kriteria inklusi dan eksklusi. Data profil hematologi, dilakukan uji normalitas dengan menggunakan uji Saphiro-Wilk. Perbedaan profil hematologi antara pasien preeklampsia dengan kehamilan normotensi dianalisis dengan uji one-way. ***Hasil:*** *Hasil penelitian ini menunjukkan Rerata kadar hemoglobin terendah pada kelompok preeklampsia ringan yaitu 11,43 gr/dl. Rerata kadar hematokrit dan jumlah eritrosit menunjukkan nilai yang terendah pada kelompok preeklampsia berat dengan masing-masing nilai yaitu 32,30% dan 3,91 juta/mm3. Rerata jumlah leukosit tertinggi dan trombosit terendah terdapat pada kelompok normotensi yaitu masing-masing 12.778/mm3 dan 232.565/mm3 Hasil uji statistik menunjukkan bahwa tidak terdapat perbedaan yang bermakna antara kelompok preeklampsia ringan, preeklampsia berat, dan normotensi pada kadar hemoglobin dengan nilai p=0,864, kadar hematokrit dengan nilai p=0,326, jumlah eritrosit dengan nilai p=0,191, jumlah leukosit dengan nilai p=0,422, dan jumlah trombosit dengan nilai p=0,287.* ***Kesimpulan:*** *tidak terdapat perbedaan yang bermakna pada profil hematologi (kadar hemoglobin, kadar hematokrit, jumlah eritrosit, jumlah leukosit, dan jumlah trombosit) antara pasien preeklampsia dengan kehamilan normotensi di RSUD dr. Suhatman MARS Kota Dumai.*

Kata kunci: *Kehamilan normotensi, Preeklampsia ringan, Preeklampsia berat, Profil hematologi*

I. INTRODUCTION

Preeclampsia is determined as new-onset hypertension and end-organ damage, including proteinuria, after 20 weeks gestation characterized by systolic blood pressure >140 mmHg or diastolic blood pressure >90 mmHg at two examinations at least 4 hours apart, in women who previously had normal blood pressure.[1] Normotensive patients were defined as patients who had maximum blood pressure <130/80 mmHg before 20 weeks of gestation and no previous diagnosis of chronic hypertension.[2]

Karrar et al (2024) stated that preeclampsia is a hypertensive disorder of pregnancy that is associated with 2-8% of pregnancy-related complications worldwide.[3] The World Health Organization (WHO) estimates that cases of preeclampsia are 7 times higher in developing countries than in developed countries.[4] Preeclampsia is also one of the highest causes of maternal mortality in Indonesia. Most maternal deaths in 2020 were caused by hypertension in pregnancy, totaling 1,110 cases.[5] The incidence of preeclampsia in Indonesia is 128,273 cases per year or about 5.3% of all pregnant women. In the last 2 decades, there has been no significant decrease in the incidence of preeclampsia in Indonesia.[6] Data on maternal mortality in Riau Province itself in 2022 showed that the three biggest causes of maternal death were bleeding 43%, hypertensive disorders 24%, and other causes 30%.[7] Based on data from Dr. Suhatman MARS Dumai Hospital in 2022-2023, mild preeclampsia patients occupied the top 10 with a total number of 117 patients, while severe preeclampsia patients occupied the top 15 with a total number of 76 patients.

According to Cunningham et al (2022) the decreased function of a number of organs and systems in preeclampsia is due to vascular endothelial dysfunction and vasospasm.[8] The decrease in organ function causes various changes in pregnancy, including in hematological profile of pregnant women.[9] Hematology profile consist of hemoglobin level, hematocrit level, erythrocyte count, leukocyte count, and thrombocyte count.[10] The decrease in thrombocyte count can occur due to increased thrombocyte activation and thrombocyte coagulation due to blood vessel injury. This also facilitates hemolysis and fragmentation of erythrocytes so that the number of erythrocytes also changes.[9] The number of leukocytes, especially neutrophils, increases because it indicates the inflammatory process that occurs in preeclampsia. The increase in neutrophil count can also suggest the severity of the inflammatory response in severe preeclampsia.[11]

A number of studies have been conducted to determine the association of hematological parameters with preeclampsia. Bellos et al (2020) stated that hemoglobin in preeclampsia can increase significantly due to hemoconcentration, or could be secondary anemia due to hemolysis.[12] Aisagbonhi and Morris (2022) and Kibas et al (2021) said that there was no significant association between leukocyte counts and preeclampsia patients.[13,14] Wu et al (2022) also revealed the same that there was no significant association between leukocyte count and preeclampsia patients.[15] In contrast to Hayuningsih et al (2023), found that there is a significant difference in thrombocyte count between preeclampsia and normotensive pregnancy.[16]

Because the incidence of preeclampsia in dr. Suhatman MARS Dumai Hospital is relatively high and the differences in the results of previous studies regarding hematological profiles due to preeclampsia conditions, this study aims to determine the differences in hematological profiles between preeclampsia patients and

normotensive pregnancies at dr. Suhatman MARS Dumai Hospital.

II. METHOD

This study was analytic observational research with a cross sectional approach. This research was conducted in the Medical Record Department at dr. Suhatman MARS Dumai Hospital from January to June 2024. The research has passed ethical review by the Abdurrab University Research Ethics Committee with letter No.276/KEP-UNIVRAB/VI/2024.

The samples in this study were preeclampsia patients and normotensive pregnant women who were treated at dr. Suhatman MARS Dumai Hospital in the period of 2022 and 2023, whose medical records contained hematological examination results, which met the inclusion and exclusion criteria. The inclusion criteria included pregnant women over 17 years of age and single pregnant women >20 weeks. Exclusion criteria included pregnant women with a history of chronic inflammatory diseases such as autoimmune, diabetes mellitus, chronic hypertension, pregnant women with a history of kidney, heart and liver disease, pregnant women with a history of blood disorders, pregnant women with infectious diseases, incomplete medical records of pregnant women. This study used purposive sampling technique. The number of samples was at least 30 for each of mild preeclampsia, severe preeclampsia, and normotensive pregnancy.

Independent variables in this study were mild preeclampsia, severe preeclampsia and normotension. Mild preeclampsia is a patient >20 weeks gestation with blood pressure >140/90mmHg, proteinuria: >300 mg/24 hours or >1+ dipsticks. Severe preeclampsia is a patient >20 weeks gestation with one or more of the following symptoms: blood pressure >160/110 mmHg; proteinuria >5g/24 hours or 4+ dipsticks; severe thrombocytopenia: <100,000 cells/mm^3; oliguria, which is urine production less than 500 cc/24 hours; visual and cerebral disturbances; epigastric pain or pain in the right upper quadrant of the abdomen; and impaired hepatic function. Normotensive pregnancy is a pregnant patient with systolic blood pressure <140 mmHg and diastolic blood pressure <90 mmHg without comorbidities.

Dependent variable in this study is hematology examination performed on patients with pre-eclampsia and normotensive pregnancy where the hemoglobin level, hematocrit level, erythrocyte count, leukocyte count, and thrombocyte count are tested. Patients from each category (mild preeclampsia, severe preeclampsia, and normotension) will be grouped based on hematological profiles, namely anemia <10 g/dl; no anemia >10g/dl; leukocytosis >15,000/mm^3; normal leukocytes 5,000-15,000/mm^3; leukopenia <5,000/mm^3; thrombocytosis >400,000/mm^3; normal thrombocytes 150,000-400,000/mm^3; and thrombocytopenia <150,000/mm^3.[8,9]

We conducted univariate and bivariate analysis using the Statistical Package for Social Science (SPSS). Univariate analysis described the frequency distribution and percentage of each variable studied for both the dependent variable and independent variable. Bivariate analysis was conducted to determine the association between independent variable and dependent variable. Normality and homogeneity tests were performed on dependent variable of hematological profile (hemoglobin, hematocrit, erythrocytes, leukocytes, thrombocytes). Data were normally distributed and or homogeneous if the p-value >0.05. One-way ANOVA test was performed if the data were normally distributed, if data were not normally distributed, the Kruskal-Wallis test is performed. When the results of ANOVA or

Kruskal-Wallis test showed p-value <0.05, it will be followed by Post-Hoc test, to find which group was most significantly different among the three groups.

III. RESULT

This study analyzed differences in hematological profiles, namely hemoglobin level, hematocrit level, erythrocyte count, leukocyte count and thrombocyte count in mild preeclampsia, severe preeclampsia and normotensive groups. In this study, the number of respondents studied was 95 samples consisting of 30 respondents for mild preeclampsia, 30 respondents for severe preeclampsia, and 35 respondents for normotensive. Distribution and characteristics of subjects are shown in Table 1.

TABLE 1. BASIC CHARACTERISTICS OF RESPONDENTS WITH MILD PREECLAMPSIA, SEVERE PREECLAMPSIA AND NORMOTENSIVE PREGNANCY

Variable	Mild Preeclampsia		Severe Preeclampsia		Normotensive Pregnancy	
	Range (min-max)	(Mean±SD)	Range (min-max)	(Mean±SD)	Range (min-max)	(Mean±SD)
Maternal age (years)	20-41	30.07±6.475	22-44	33.33±5.339	21-42	29.89±6.397
Gestational age (weeks)	36- 41	38.40±1.653	31-41	36.87±2.285	28-40	37.91±2.356
Gravida (times)	1-6	2.70±1.725	1-7	3.20±1.518	1-7	2.60±1.649
Parity(times)	0-5	1.70±1.725	0-6	2.20±1.518	0-6	1.60±1.649
Systolic Blood Pressure (SBP) (mmHg)	140-158	147.00±5.925	136-218	169.00±20.081	110-139	124.26±6.959
Diastolic Blood Pressure (DBP) (mmHg)	80-144	99.23±12.221	90-148	104.80±10.842	70-100	81.51±6.823

Table 1 showed the mean maternal age was highest in the severe preeclampsia at 33.33 years. The mean gestational age in the mild preeclampsia was slightly higher than severe preeclampsia and normotensive at 38.40 weeks. The mean number of pregnancies (gravida) and maternal parity in severe preeclampsia were slightly higher than those in the mild preeclampsia and normotensive at 3.20 and 2.20 times, respectively. The mean

systolic blood pressure was highest in severe preeclampsia at 169.00 mmHg. The mean diastolic blood pressure in severe preeclampsia was slightly higher than mild preeclampsia at 104.80 mmHg. Characteristics of subject based on hematological profile are shown in Table 2

TABLE 2. CHARACTERISTICS OF SUBJECTS BASED ON HEMATOLOGICAL PROFILE IN MILD PREECLAMPSIA, SEVERE PREECLAMPSIA AND NORMOTENSIVE PREGNANCY

No	Variable	Mild Preeclampsia			Severe Preeclampsia			Normotensive Pregnancy		
		N (%)	Range (min-max)	Mean±SD	N (%)	Range (min-max)	Mean±SD	N (%)	Range (min-max)	Mean±SD
1.	Anemia	4(13.3)	8.7-9.8	9.1±0.49	5(16.6)	7.90-9.8	9.26±0.83	0	0	0
	Normal hemoglobin	26(86.6)	10.0-13.2	11.81±2.71	25(83.3)	10.4-13.40	12.0±0.68	35(100)	10.1-14.7	11.24±1.15
2.	Leukocyosis	5(16.6)	15,800-19,200	17,270±1,66	2(6.67)	16,400-23,300	11,443±7,52	8(22.8)	16,500-26,000	20,288±3,25
	Normal Leukocyte	25(83.33)	5,200-14,900	10,144±2,01	28(93.3)	7,000-13,200	10,114±2,15	27(77.1)	5,760-15,270	10,323±3,05
	Leukopenia	0	-	-	0	-	-	0	-	-
3.	Trombocytosis	0	-	-	0	-	-	0	-	-
	Normal thrombocyte	28(93.3)	159,000-378,400	259,857±687,3	29(96.6)	159,000-340,000	249,133±199,05	32(91.4)	160,000-357,000	234,430±72,79
	Trombocytopenia	2(6.6)	106,000-139,000	122,500±23,33	1(3.33)	128,000	128,000±0	3(8.57)	121,000-134,000	129,000±7,00

The table above showed most subjects were not anemic in all three groups. Mean of haemoglobin in non-anemia was similar in the three groups, but the lowest was in the normotensive, which was 11.24. Subject experienced anemia insevere preeclampsia, namely 5 respondents (16.6%), followed by mild preeclampsia with 4 respondents (13.3%). These results were same with Giyanto and Pramono (2015) which showed anemia in severe preeclampsia was slightly higher than mild preeclampsia.[10]

Most subjects had normal leukocyte and thrombocyte counts in all three groups. In normal leukocyte variable showed the mean in the three groups was not different, but normotensive group was the highest, which is 10,323/mm^3. This study is consistent with Kibas et al (2021) which found that most preeclampsia patients have normal leukocytes.[14] In normal thrombocyte variable showed the mean in the three groups was similar, but normotensive group was the lowest, namely 234,430/mm^3.

Each hematological profile in the three groups was tested for normality and homogeneity which continued to the One Way Anova and Kruskal Walis tests. Bivariate analysis of hematological profile between mild preeclampsia, severe preeclampsia, and normotensive groups is shown in Table 3.

TABLE 3. BIVARIATE ANALYSIS OF HEMATOLOGY PROFILE BETWEEN MILD PREECLAMPSIA, SEVERE PREECLAMPSIA, AND NORMOTENSIVE PREGNANCY GROUPS

Variable	Mild Preeclampsia n=30 mean (SD)		Severe Preeclampsia n=30 mean (SD)		Normotensive pregnancy n=35 mean (SD)		P-value
	Range (min-max)	Mean (SD)	Range (min-max)	Mean (SD)	Range (min-max)	Mean (SD)	
Hemoglobin (g/dl)	8.70-13.20	11.43 (1.32)	7.90-13.40	11.54 (1.30)	10.10-14.70	11.81 (1.24)	0.864[B]
Hematokrit (%)	24-39	33.03 (3.98)	22-40	32.30 (3.89)	28-44	33.74 (3.69)	0.326[A]
Eritrosit (juta/mm^3)	3.20-5.27	4.12 (0.43)	2.95-4.84	3.91 (0.43)	3.35-5.16	4.05 (0.48)	0.191[A]
Leukosit (/mm^3)	5,200-19,200	11,475.67 (36.83)	7,000-23,300	11,043.33 (30.17)	5,760-26,000	12,778.00 (49.31)	0.422[B]
Trombosit (/mm^3)	106,000-378,400	249,333.33 (603.17)	128,000-340,000	253,800.00 (610.69)	121,000-357,000	232,565.71 (532.51)	0.294[A]

[A] One-Way ANOVA
[B] Uji Kruskal-Walis

Based on table 3, mean hemoglobin level was lowest in mild preeclampsia group at 11.43 gr/dl. Mean hematocrit level and erythrocyte count showed the lowest value in severe preeclampsia with 32.30% and 3.91 million/mm^3, respectively. The highest mean leukocyte count and the lowest thrombocyte count were in the normotensive group, which were 12,778/mm3 and 232,565/mm^3, respectively.

IV. DISCUSSION

This study found that there was no significant difference in hemoglobin levels between mild preeclampsia, severe preeclampsia and normotensive groups (p=0.864). These results were in accordance with Astuti and Suparni (2018), who found

that there was no significant difference in hemoglobin levels between severe preeclampsia and mild preeclampsia (p=0.102) with mean hemoglobin level in mild preeclampsia was 12.6 gr/dl and in severe preeclampsia was 13.19 gr/dl.[17] Normala et al (2023) also supported this study with their findings that there was no significant difference in hemoglobin levels between eclampsia, mild preeclampsia and severe preeclampsia (p=0.235) with mean hemoglobin in mild preeclampsia was 11.20 gr/dl and severe preeclampsia was 10.90 gr/dl.[18] This can be caused by other factors that affect the hemoglobin levels of pregnant women including nutritional intake during pregnancy, maternal age, maternal education level, family income, and consumption of blood supplement tablet.[19]

There was no significant difference in hematocrit levels between mild preeclampsia, severe preeclampsia, and normotensive groups in this study (p=0.326). Parralel with Eko Martanti et al (2020) that found there was no difference in hematocrit levels between preeclampsia and normal pregnant women (p=0.163) with mean hematocrit in preeclampsia was 34.85% and in normal pregnant women was 33.10%.[20] In contrast to research conducted by Giyanto and Pramono (2015), obtained mean hematocrit levels of severe preeclampsia significantly higher (p=0.001) that was 36.94% when compared to mild preeclampsia and normotensive, which mean hematocrit of mild preeclampsia was 33.40% and normotensive pregnancy was 34.20%.[10] This study also found number of erythrocytes between mild preeclampsia, severe preeclampsia, and normotensive groups had no significant difference (p=0.191). This study was different with Giyanto and Pramono (2015), which found significant difference in erythrocyte count between preeclampsia and normotension (p=0.001) and the mean respectively in mild

preeclampsia and severe preeclampsia were 3.87 million/mm^3 and 4.45 million/mm^3 while in normotensive pregnancy was 4.09 million/mm^3.[10] The difference in research results can be caused by confounding variables such as bleeding due to unknown causes, medication, and differences in inclusion/exclusion criteria between studies. The higher erythrocyte levels in preeclampsia than normotensive pregnancies may also be due to the consumption of iron supplements which in Indonesia are given to pregnant women in anticipation of iron deficiency anemia.

No significant difference in the number of leukocytes between mild preeclampsia, severe preeclampsia, and normotensive groups (p=0.422), found in this study. In line with Toptas et al (2016), where the number of leukocytes was not significantly difference (p=0.214) between preeclampsia with mean of 13,643.4/mm^3 and normal pregnancy with mean of 12,793.4/mm^3.[21] However, these results are not concordance with Örgül et al., (2019), which stated that there was significant differences (p<0.05) in the total number of leukocytes between the early onset preeclampsia with mean of 10,470/mm^3, late onset preeclampsia with mean of 9,730/mm^3, and normotensive pregnancy with mean of 8,420/mm^3.[22]

This study also found no significant difference in thrombocyte counts between mild preeclampsia, severe preeclampsia, and normotensive pregnancy groups (p=0.294). These results are supported by several previous studies. Giyanto and Pramono (2015) in their research found that there was no significant difference in thrombocyte counts (p=0.452) between mild preeclampsia with mean of 248,560/mm^3, severe preeclampsia with mean of 223,780/mm^3 and normotensive pregnancy with mean of 254,120/mm^3.[10] In contrast to Hayuningsih et al (2023), which mean of thrombocyte counts in preeclampsia lower (256,400/mm^3) than normotensive pregnancy (306,400/mm^3) with p value =0.003, so there was significant difference in thrombocyte counts between preeclampsia and normotension.[16]

The differences results in leukocyte and thrombocyte counts might be due to confounding variables such as infection or inflammation due to other unknown causes, administration of drugs, and differences in inclusion/exclusion criteria between studies. In severe preeclampsia, leukocytosis is common as this condition is associated with systemic inflammation that can increase leukocyte count. However, normal leukocyte can be caused by infection that suppressed the leukocytosis response that should occur. Hidayat et al., (2021) said infection can affect leukocyte counts in various ways, depending on the type of pathogen or the patient's immune response.[23] A decrease in the number of granulocytes in the blood is known as neutropenia. Neutropenia can be caused by inadequate granulopoiesis or accelerated neutrophil destruction. Decreased neutrophil counts are present in viral infections, leukemia, iron deficiency anemia, and others.

V. CONCLUSION

There was no significant difference in hemoglobin concentration, hematocrit level, erythrocyte count, leukocyte count and thrombocyte count between mild preeclampsia, severe preeclampsia and normotensive groups with p=0.864; p=0.326; p=0.191; p=0.422; and p=0.294, respectively.

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