PROFESIONAL HEALTH JOURNAL
Volume 6, No. 2, June 2025 (Page. 741-752)
Available Online at https://www.ojsstikesbanyuwangi.com/index.php/PHJ/index
E-ISSN 2715-6249
DOI: https://doi.org/10.54832/phj.v6i2.1147

DIFFERENCES IN HEMATOCRIT AND LEUKOCYTE LEVELS IN PREECLAMPSIA AND SEVERE PREECLAMPSIA

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ARTICLE INFORMATION

Article history
Received (26 February 2025)
Revised (8 March 2025)
Accepted (10 March 2025)

Keywords
Keywords must contain at least three to five keywords representing the main content of the article

ABSTRACT

Introduction: *Preeclampsia is a serious pregnancy complication characterized by hypertension occurring at a gestational age of ≥ 20 weeks. In preeclampsia, hematological changes occur due to vasospasm. Vasospasm leads to endothelial damage of blood vessels, marked by an increase in hematocrit and leukocyte levels.*
Objectives: *This study was conducted to determine whether there is a difference in hematocrit and leukocyte levels between pregnant women with preeclampsia and severe preeclampsia.*
Methods: *A cross-sectional, comparative study strategy was employed in this investigation. The sample for this study included all 76 pregnant patients at Genteng Regional Hospital who had preeclampsia or severe preeclampsia in 2023. 38 pregnant women with preeclampsia and 38 pregnant women with severe preeclampsia made up the two groups into which the sample was split.*
Results: *The findings of the study indicated that there is a significant difference in hematocrit levels between preeclampsia and severe preeclampsia, with the p-value = 0.001 being less than α = 0.05. Furthermore, the findings revealed a significant difference in leukocyte counts between preeclampsia and severe preeclampsia, with a p-value = 0.003, which is likewise less than α = 0.05.*
Conclusions: *There is a significant difference in hematocrit and leukocytes in pregnant women with PE and PEB at Genteng Regional Hospital in 2024.*

Introduction

Preeclampsia is a serious complication in pregnancy characterized by hypertension occurring at a gestational age of ≥ 20 weeks. It is a syndrome that manifests in the second trimester and is marked by elevated blood pressure and the presence of protein in the urine. Preeclampsia is one of the major complications of pregnancy, leading to morbidity, long-term disabilities, and even mortality in mothers, fetuses, and neonates (Dwi Saputri dan Precelia Fransiska 2023; Zainiyah dan Harahap 2023).

The prevalence of preeclampsia is around 5-7% of all pregnancies. However, globally, it contributes to approximately 70,000 maternal deaths and 500,000 neonatal deaths each year. In 2020, Indonesia recorded 4,627 cases of maternal mortality, with hypertensive disorders in pregnancy (HDP) being the second leading cause, accounting for 1,110 cases. In East Java, the maternal mortality rate (MMR) in 2020 was 98.39 per 100,000 live births, with HDP being the leading cause of maternal deaths (152 cases, 26.90%). In Banyuwangi, the MMR in 2023 was 143.6 per 100,000 live births, with preeclampsia and eclampsia being the second most significant contributors to maternal mortality, accounting for 14% of cases (Rana *et al.* 2019; Kementerian Kesehatan Republik Indonesia, 2021; Profil Kesehatan Provinsi Jawa Timur, 2021; Profil Kesehatan Kabupaten Banyuwangi, 2023).

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The exact cause of preeclampsia remains unclear. However, incomplete trophoblast invasion is suspected to be a contributing factor. This incomplete invasion leads to the failure of spiral artery remodeling, resulting in suboptimal blood flow to the hematochorial endothelial lacuna, causing hypoxia. Hypoxia, in turn, leads to endothelial damage in the placenta, exacerbating the condition. If prolonged, this can impair multiple organ functions due to vasospasms and endothelial dysfunction in blood vessels (Asie *et al.* 2022).

Approximately 3-8% of pregnancies are complicated by preeclampsia, increasing the risk of complications for both mother and baby. In affected mothers, complications may include pulmonary edema, acute kidney failure, liver dysfunction, heart attacks, excessive blood clotting, cerebral hemorrhage, placental abruption, and eclampsia. Meanwhile, fetal and neonatal complications include placental insufficiency, neonatal asphyxia, and intrauterine growth restriction (Ambarwati *et al*. 2009; Bokslag *et al*. 2016; Bouter *et al*. 2019; Hartati *et al*. 2018; Rana *et al*. 2019).

Previous studies highlight the importance of preventive measures to address preeclampsia in pregnant women. Midwives, as the frontliners in maternal and child healthcare services, play a crucial role in reducing maternal and neonatal mortality rates. They are expected to conduct preeclampsia screenings through anamnesis, physical examinations, and medical history assessments as part of comprehensive antenatal care. Additionally, collaboration with other healthcare professionals is essential in providing appropriate therapy for pregnant women with preeclampsia. Several studies have shown that hematological profiles including erythrocyte count, hemoglobin levels, hematocrit, leukocyte count, mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), and platelet count can be used to assess the severity of preeclampsia (Amelia *et al.* 2022; Asie *et al.* 2022; Dharagita *et al.* 2022; Marbun dan Irnawati Irnawati 2023; Annisa *et al.* 2024).

Leukocytes are mobile units of the body's immune defense system. Certain conditions can lead to an increase in leukocyte count (leukocytosis). Metabolic disorders such as preeclampsia can cause leukocytosis due to vasospasms, hypoalbuminemia, and microangiopathic hemolysis resulting from arteriole spasms and endothelial damage. In addition to leukocytosis, prolonged vasospasms increase capillary permeability, causing plasma volume depletion and hemoconcentration, which can be reflected in elevated hematocrit levels (Kibas *et al.* 2021; Asie *et al.* 2022).

Kibas et al., (2021) analyzed the relationship between leukocyte count and preeclampsia incidence but did not specifically examine the differences in hematocrit and leukocyte levels between mild and severe preeclampsia. The objective of this study is to bridge this research gap by identifying and proving whether there are significant differences in hematocrit and leukocyte levels in pregnant women with mild and severe preeclampsia. This study is expected to provide additional knowledge for healthcare professionals, particularly midwives and obstetricians, regarding the importance of hematocrit and leukocyte assessments in evaluating the severity of preeclampsia.

Methods

The design used in this study is a comparative study with a cross-sectional approach. The study population consists of pregnant women diagnosed with preeclampsia (PE) and severe preeclampsia (PEB) at RSUD Genteng in 2023, totaling 76 cases. The sampling method applied in this study is total sampling. The sample is divided into two groups: 38 pregnant women with preeclampsia and 38 pregnant women with severe preeclampsia.

The inclusion criteria for this study are as follows: pregnant women with PE and PEB who visited and/or were hospitalized at RSUD Genteng in 2023, those confirmed with PE and PEB

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diagnosed by an Obstetrics and Gynecology specialist, pregnant women with PE and PEB recorded in the medical records of RSUD Genteng in 2023, and those with available hematocrit and leukocyte blood profile data. The exclusion criterion for this study is pregnant women with PE and PEB who have anemia (Hb ≤11 g/dL) based on medical record data.

The study was conducted from September 2 to September 30, 2024. Data collection tools in this study include medical records and observation sheets. Data analysis was performed using the Chi-square test with the assistance of SPSS 25 software.

Results

The basic characteristics of pregnant women with preeclampsia (PE) and severe preeclampsia (PEB) at RSUD Genteng in 2023 can be seen in Table 1

Table 1: Essential Features of Expectant Mothers at RSUD Genteng with Preeclampsia and Severe Preeclampsia in 2023

Variable	Category	Preeclampsia n= 38 (N%)	Severe Preeclampsia n= 38 (N%)
Age	20-35 years	8 (21,1%)	11 (28,9%)
	<20 years and >35 years	30 (78,9%)	27 (71,1%)
BMI	Severely Underweight	0	0
	Underweight	0	0
	Normal	1 (2,6%)	0
	Overweight	14 (36,8%)	9 (23,7%)
	Obese	23 (60,5%)	29 (76,3%)
Education	Elementary School	33 (43,4%)	30 (39,5%)
	Junior High School	2 (2,6%)	5 (6,6%)
	Senior High School	1 (1,3%)	3 (3,9%)
	Diploma	2 (2,6%)	0
	Bachelor's Degree	0	0
	Master's Degree	0	0

Table 2 shows the results of a comparison test of the hematocrit and leukocyte levels in pregnant women with PE and PEB at RSUD Genteng in 2023.

Table 2. Comparative Test of Hematocrit and Leukocyte Levels in Pregnant Women with PE and PEB at RSUD Genteng in 2023

Variable	Category	Preeclampsia n= 38 (N%)	Severe Preeclampsia n= 38 (N%)	Comparative Test
Hematocrit	Low	6 (15,8%)	1 (2,6%)	0,001
	Normal	1 (2,6%)	2 (5,3%)	
	High	31 (81,6%)	35 (92,1%)	
Leukocytes	Low	7 (18.4%)	1 (2,6%)	0,003
	Normal	5 (13,2%)	9 (23,7%)	
	High	26 (68,4%)	28 (73,7%)	

Discussion

Basic Characteristics of Pregnant Women with PE and PEB at RSUD Genteng in 2023

a. Maternal Age

Based on Table 1, the highest age group affected by preeclampsia at RSUD Genteng Banyuwangi was <20 years and >35 years, with 30 respondents (78.9%) experiencing

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preeclampsia. Meanwhile, the highest age group affected by severe preeclampsia at RSUD Genteng Banyuwangi was 35 years, with 27 respondents (71.1%) experiencing severe preeclampsia.

The findings of this study align with previous research conducted at RSUD Ulin Banjarmasin, which reported that the highest age groups affected by preeclampsia (PE) and severe preeclampsia (PEB) were >30 years and 18–25 years. Maternal age <20 years and >30 years is considered a risk factor for preeclampsia. This is because, at <20 years of age, the reproductive organs are not yet fully matured for pregnancy. Additionally, women under 20 years old tend to have unstable emotional stability, making them more prone to stress, which can lead to increased blood pressure. On the other hand, women over 30 years old experience a decline in reproductive readiness, which reduces the quality of reproductive cells and increases the risk of medical complications during pregnancy and childbirth (Asie *et al.* 2022).

The findings of this study are corroborated by earlier studies that linked the incidence of preeclampsia to maternal age. Women aged >35 years are more likely to experience pregnancy complications, including preeclampsia. This may occur due to physical decline at this age. Furthermore, women over 35 years old are more prone to health issues such as hypertension (Aziz *et al.* 2022).

This study supports that of Hermawati (2020), who discovered that 13 respondents in the high-risk age group had mild preeclampsia and 37 respondents had severe preeclampsia. At a hospital in Banda Aceh, statistical analysis revealed a strong correlation between maternal age and the frequency of preeclampsia, with a p-value of 0.036. Hermawati (2020) explained that maternal age plays a crucial role in the improvement and decline of maternal body functions, particularly in the cardiovascular system, which leads to increased oxidative stress and can affect maternal health by triggering preeclampsia (Hermawati 2020).

This study is supported by research conducted by Kusumaningtyas & Dharmayani (2023), which explains that mothers at risky ages, namely those under 20 and over 35 years old, have a higher likelihood of experiencing preeclampsia compared to mothers of non-risky ages. This occurs due to changes in tissue and body functions. Mothers under 20 years old are vulnerable to preeclampsia because their uterus and pelvis are not yet fully mature. Additionally, psychological aspects and significant hormonal changes facilitate an increase in blood pressure. Meanwhile, mothers over 35 years old are categorized as being at an advanced maternal age, particularly in older primiparous women, making them at high risk for preeclampsia. This is associated with reduced flexibility of the birth canal and, theoretically, linked to endothelial pathology due to cardiovascular changes and a decreased ability to adapt to hormonal changes (Kusumaningtyas dan Dharmayani 2023).

Walle & Azagew (2019) state that with increasing maternal age, there is an increased reaction of the villi, leading to the occurrence of preeclampsia, as well as degenerative processes that elevate the risk of chronic hypertension. Women with chronic hypertension are at a greater risk of developing preeclampsia. Degenerative processes also cause structural and functional changes in peripheral blood vessels, which contribute to alterations in blood pressure. Additionally, increasing age leads to a decline in pancreatic beta-cell function and insulin sensitivity, resulting in glucose intolerance, as well as affecting triglyceride and cholesterol levels, which heighten oxidative stress. On the other hand, research by Bere found that preeclampsia was more frequently observed in women of normal reproductive age (20–35 years). However, the study still concluded that there is a significant relationship between maternal age as a risk factor and the incidence of preeclampsia (Walle dan Azagew 2019).

According to researchers, women under 20 years old and over 35 years old are at high risk of experiencing pregnancy complications. Additionally, being within this risk age range can be

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detrimental to maternal health as well as fetal growth and development. In women under 20 years old, the reproductive organs are not yet fully mature to support pregnancy, increasing the likelihood of preeclampsia. Meanwhile, as a woman ages beyond 35 years, the risk of preeclampsia further increases due to the decline in the maternal reproductive system. In Indonesia, early marriage remains prevalent. As part of their responsibilities, midwives must work to reduce maternal and infant morbidity and mortality rates by educating the community about the dangers of pregnancy at ages under 20 and over 35.

b. Body Mass Index (BMI)

Based on Table 5.2, the highest BMI group suffering from severe preeclampsia at RSUD Genteng Banyuwangi was the obese category, with 23 respondents (60.5%). Meanwhile, the highest BMI group suffering from preeclampsia at RSUD Genteng Banyuwangi was also the obese category, with 29 respondents (76.3%).

Pratamaningtyas & Kristianti (2019) explains that uncontrolled or excessive weight gain in pregnant women can lead to a high risk of pregnancy complications, such as preeclampsia, postmature pregnancy, gestational diabetes, emergency cesarean section, elective cesarean section, pelvic infection, postpartum hemorrhage, wound infection, macrosomia, urinary tract infection, and stillbirth. Weight gain during pregnancy varies greatly and can be influenced by several factors, including maternal age, parity, basal metabolic rate (BMR), diet, smoking, pre-pregnancy weight, fetal size, and maternal diseases such as diabetes (Pratamaningtyas dan Kristianti 2019).

A previous study conducted at RSUD Kota Mataram found a data analysis result with a p-value of 0.034 (p-value <0.05), indicating a significant relationship between BMI and the incidence of preeclampsia at RSUD Kota Mataram. This study explains that there is a link between BMI and the occurrence of preeclampsia. Before pregnancy, a BMI in the obese range causes the heart to work harder to warm the blood. Obesity is a cause of endothelial dysfunction in both pregnant and non-pregnant individuals. This condition damages the endothelium and accelerates the progression of preeclampsia. Individuals with excess weight require more blood to supply nutrients and oxygen to body tissues. As a result, there is an increased blood volume flowing through the arteries, leading to elevated cardiac output and increased blood pressure (Pramesti *et al.* 2024).

One risk factor for preeclampsia is obesity, and the risk rises with an elevated BMI. Obesity is a major risk factor for preeclampsia and is closely linked to insulin resistance. Pregnant women with obesity may develop preeclampsia through mechanisms such as metabolic syndrome, hyperleptinemia, increased oxidative stress, inflammatory reactions, and mediated by cytokines, as well as the direct hemodynamic effects of hyperinsulinemia (increased sympathetic activity and enhanced tubular sodium reabsorption). These processes ultimately lead to endothelial damage and dysfunction. The exact cause of preeclampsia remains unknown; however, several studies suggest that various factors contribute to its development, including excessive weight gain or obesity during pregnancy. Obesity during pregnancy has detrimental health effects, particularly for pregnant women, as it can lead to hypertension, hypercholesterolemia, and hyperglycemia—commonly known as the "3H" conditions (Zainiyah dan Harahap 2023).

Findings from this study indicate that as a woman's weight increases, lipid peroxides also rise, while antioxidant levels decline. Consequently, relatively high concentrations of lipid peroxide oxidants become more prevalent during pregnancy. Lipid peroxides are highly harmful oxidants that circulate throughout the body, damaging endothelial cell membranes. Because endothelial cell membranes are directly exposed to circulation, which is rich in unsaturated fatty acids, they are more vulnerable to lipid peroxide-induced damage. Hydroxyl radical oxidants have the ability to rapidly convert unsaturated fatty acids into lipid peroxides (Arief dan Widodo 2018).

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Lipid peroxides can spread throughout the body via the bloodstream, leading to endothelial cell membrane damage. This endothelial cell membrane damage disrupts endothelial function and destroys the entire endothelial cell structure, a condition known as "endothelial dysfunction." One of the key functions of endothelial cells is to produce prostaglandins. If endothelial cells are impaired, prostaglandin metabolism is disrupted, resulting in decreased prostacyclin production. A reduction in prostacyclin production leads to higher thromboxane levels, causing vasoconstriction and increased blood pressure (Prawirohardjo 2017).

This study is supported by research conducted by Nadiro et al., (2024), which states that being overweight during pregnancy is a nutritional issue in pregnant women and can be a risk factor for preeclampsia. Excessive body mass index (BMI) (obesity) leads to an imbalance between intake and output, resulting in fat accumulation, particularly in the glomerulus. Disruptions in the glomerulus can increase levels of Low-Density Lipoprotein (LDL) and triglycerides. Hypertriglyceridemia causes vascular abnormalities in the placenta, triggering endothelial dysfunction, atherosclerosis, and thrombosis, which stimulate arteriolar vasospasm. Arteriolar vasospasm leads to increased blood pressure, which can result in preeclampsia (Nadiro *et al.* 2024).

According to researchers, nutritional status is a measure of the success of the balance between nutrient intake and requirements in meeting nutritional needs during pregnancy. To determine nutritional status, BMI measurement is performed by measuring maternal height and weighing body weight, allowing the classification of maternal nutritional status into normal, underweight, overweight, or obese categories. Maternal dietary intake and physical activity significantly influence nutritional status. A BMI categorized as overweight or obese is one of the risk factors for preeclampsia. This occurs through the release of inflammatory cytokines from fat tissue cells, which subsequently cause endothelial inflammation, triggering the onset of preeclampsia.

c. Education

Based on Table 5.3, the highest education level group suffering from severe preeclampsia at RSUD Genteng Banyuwangi was elementary school or equivalent, with 33 respondents (43.3%). Similarly, the highest education level group experiencing preeclampsia at RSUD Genteng Banyuwangi was also elementary school or equivalent, with 30 respondents (39.5%).

Education is one of the benchmarks for determining a person's socioeconomic status and knowledge of a particular subject. It also influences how easily someone can absorb and understand acquired knowledge. Individuals with a higher level of education generally have better knowledge about health (Suryatini *et al.* 2022).

This finding aligns with previous studies, which reported that the incidence of preeclampsia was 77.4%, while severe preeclampsia accounted for 22.6%. Furthermore, 58.1% of cases were in the high-risk age group, whereas 32.1% were in the non-risk age group. Regarding education level, 43.5% had higher education, while 66.5% had lower education. The research identified a significant association between the level of education and severe preeclampsia ($\rho = 0.03$), as well as between age and the occurrence of severe preeclampsia (p-value = 0.03).

Previous studies indicate that low education levels may contribute to the incidence of severe preeclampsia. Individuals with higher education are generally more knowledgeable about severe preeclampsia than those with lower educational attainment. Consequently, severe preeclampsia is more prevalent among those with lower education. Theoretically, mothers with lower education levels are less likely to pay attention to their health, which increases their risk of developing severe preeclampsia (Permadi dan Deliana 2018).

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In order to help people achieve or experience the best possible social and personal development, education is the process by which they are exposed to specific and regulated environmental influences, especially from schools. The relationship between education level and severe preeclampsia is attributed to lower education levels, which result in a lack of knowledge about proper nutritional intake, thereby increasing the risk of severe (Permadi dan Deliana 2018).

Education is a significant risk factor for the incidence of preeclampsia in pregnant women, with a p-value of 0.001. Pregnant women with low education levels are 2.265 times more likely to experience severe preeclampsia compared to those with higher education. Educational theory states that education is an activity or effort to enhance personality and maturity. The more education a person receives, the more mature they become, making it easier for them to accept and understand positive information. This is consistent with research conducted by Suryatini et al., (2022), which indicates that low education levels are associated with a higher risk of preeclampsia compared to higher education levels. This finding suggests that respondents with higher education are better able to absorb information (Darmawan 2021; Suryatini *et al.* 2022).

According to researchers, low education levels or lack of schooling significantly influence the response to the process of severe preeclampsia. This is associated with maternal education levels, as lower education can contribute to the occurrence of severe preeclampsia. Individuals with higher education tend to have a better understanding compared to those with lower education levels, leading to a higher incidence of preeclampsia among less-educated individuals. Mothers with low education levels are less likely to pay attention to their health, which increases the risk of developing preeclampsia.

Comparative Test of Hematocrit and Leukocyte Levels in Pregnant Women with PE and PEB at RSUD Genteng in 2023

a. Hematocrit

Based on Table 5.4, the Chi-Square test results showed a p-value of 0.001, which is lower than the significance level (α = 0.05). Therefore, the alternative hypothesis (Ha) is accepted, and the null hypothesis (Ho) is rejected. These results support the research hypothesis, demonstrating a significant difference in hematocrit levels between preeclampsia (PE) and severe preeclampsia (PEB) at RSUD Genteng in 2023.

This finding is consistent with previous studies that have demonstrated a significant difference in hematocrit levels among pregnant women with PE and PEB. The study reveals that changes in hematocrit levels in pregnant women result from hemoconcentration occurring in preeclampsia. Vasoconstriction due to endothelial activation and plasma leakage into the interstitial space caused by increased capillary permeability leads to hemoconcentration. This hemoconcentration is associated with changes in blood viscosity, as peripheral blood flow resistance is influenced by both blood viscosity and vascular resistance (Asie *et al.* 2022).

Hematocrit levels in PEB are higher than in PE due to plasma extravasation into tissues following neutrophil activation. Neutrophil activation occurs in response to cytokines (TNF-α) and chemoattractants released during inflammation. When neutrophil activation occurs, neutrophils are released and undergo metabolic activation, entering the bloodstream and tissues. This process contributes to increased oxidative stress and inflammatory responses, leading to increased vascular permeability and, consequently, a higher risk of preeclampsia (Asie *et al.* 2022).

The severity of PE can be assessed using several hematological profile parameters, including hematocrit, MCV, and MCHC. Over time, prolonged vasospasm can compromise vascular endothelial integrity, leading to increased capillary permeability and the shift of blood into the

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extravascular space. Plasma volume decreases, resulting in hemoconcentration, which can be identified by elevated hematocrit levels. Hemoconcentration subsequently reduces organ perfusion, exacerbating the severity of PE itself (Chandra *et al.* 2012; Khoigani *et al.* 2012).

In early-onset preeclampsia, the disorder is caused by placental dysfunction, which leads to incomplete remodeling of the spiral arteries, resulting in malperfusion and stress on the syncytiotrophoblast. This stress triggers the release of pro-inflammatory factors into circulation. These pro-inflammatory factors subsequently cause endothelial dysfunction, leading to plasma leakage. Due to plasma leakage, plasma seeps out of the blood vessels, potentially causing hemoconcentration or an increase in the number of erythrocytes relative to blood volume, thereby elevating hematocrit levels. High hematocrit is associated with increased blood viscosity, leading to elevated peripheral vascular resistance, which can impede oxygen exchange in tissues. Additionally, high hematocrit levels are suspected to be a contributing factor to vascular dysfunction (Kishimoto *et al.* 2020).

A study by Dai et al. (2017) supports these findings, stating that the dysfunction of the renin-angiotensin-aldosterone system and the vasodilator system contributes to increased peripheral vascular resistance, reduced cardiac output, limited blood volume expansion, and heightened blood pressure in individuals with preeclampsia. Vasomotor dysfunction and endothelial damage in preeclampsia patients result in increased vascular permeability, which limits blood volume amplification. This condition worsens when patients experience hypoalbuminemia. In preeclampsia patients, damage to capillary endothelial cells and albumin leakage into the interstitial space lead to hemoconcentration, hypoalbuminemia, and edema, ultimately increasing hematocrit (HCT) levels and decreasing albumin (ALB) levels, resulting in a higher HCT-ALB difference (Dai *et al.* 2017).

According to researchers, widespread endothelial damage in individuals with preeclampsia leads to numerous changes, system dysfunction, and organ failure. One of the changes occurring in preeclampsia is a decrease in plasma volume. This reduction in plasma volume results in increased hemoconcentration, followed by an increase in blood viscosity, which can be identified by elevated hemoglobin and hematocrit levels. Endothelial damage causes an imbalance in the production of substances that act as vasodilators, leading to vasospasm that further damages endothelial integrity. As a result, blood plasma shifts into the interstitial space, reducing plasma volume and increasing hematocrit levels.

b. Leukocytes

The Chi-Square test results reveal a p-value of 0.003, which is lower than the significance level ($\alpha = 0.05$), as presented in Table 5.4. This indicates that the null hypothesis (Ho) is rejected, while the alternative hypothesis (Ha) is accepted. These findings suggest a significant difference in leukocyte levels among cases of preeclampsia and severe preeclampsia at RSUD Genteng in 2023.

This result aligns with previous studies, which reported that the serum leukocyte levels of mothers with preeclampsia were statistically higher than those in normal pregnancies ($p = 0.001$). Elevated maternal leukocyte levels have been identified as a risk factor for preeclampsia, increasing the likelihood by nine times (OR = 9.04, 95% CI = 2.80–29.13, $p = 0.001$). A common test to determine the body's inflammatory levels and immune system is the leukocyte count evaluation. Infections, inflammation, and tissue necrosis are typically linked to an increase in the leukocyte count. Numerous studies have extensively examined the role that inflammatory processes play in the pathophysiology of preeclampsia. The inflammatory response involves the activation and increased number of leukocytes as a reaction to inflammatory signals, making elevated leukocyte levels a potential predictor of preeclampsia.

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Previous research has explained that leukocyte function undergoes changes during pregnancy. Polymorphonuclear leukocyte chemotaxis adhesion decreases in early pregnancy and may persist throughout gestation. The leukocyte count may increase due to physiological stress induced by pregnancy (Angelina *et al.* 2019; Santoso 2019).

The placenta has been identified as a key factor in the development of preeclampsia. Impaired trophoblast invasion remodeling, commonly found in preeclampsia, leads to placental insufficiency. In preeclampsia, placental hypoperfusion and ischemia serve as potential sources of reactive oxygen species (ROS) and cytokines, which subsequently induce oxidative stress and endothelial dysfunction. In maternal circulation, the inflammatory response produces C-reactive protein (CRP), tumor necrosis factor-alpha (TNF-α), pro-inflammatory cytokines, including interleukin-6 (IL-6). These inflammatory markers increase as endothelial damage progresses. Conversely, the inflammatory reaction triggers leukocyte activation in the bloodstream, further exacerbating endothelial injury. The hypoperfused placenta in preeclampsia serves as a source of inflammatory cytokines and reactive oxygen species such as TNF-α, IL-6 and CRP, which are believed to induce oxidative stress and endothelial cell dysfunction. Another common inflammatory response observed is an elevated circulating leukocyte count. Leukocytes produce L-selectin, which facilitates adhesion to the endothelium, reinforced by vascular cell adhesion molecules. Cytokines activate neutrophils, leading to the production of chemoattractants that intensify the inflammatory response (Angelina *et al.* 2019).

Leukocytes, also known as white blood cells, serve as the mobile components of the body's immune defense mechanism. The primary function of leukocytes is to protect the body from microorganisms that cause diseases or serve as part of the immune defense system (immunity). Under certain conditions, although the number of leukocytes in the body varies depending on the body's needs, abnormalities in leukocyte production can occur. These abnormalities include a decrease in leukocyte count (leukopenia) or an increase in leukocyte count (leukocytosis). Conditions that may lead to leukocytosis include bacterial infections, particularly pyogenic bacteria, inflammation and necrosis (e.g., vasculitis), metabolic disorders during pregnancy, all types of neoplasms, acute bleeding or hemolysis, and medications (e.g., corticosteroid therapy). Oxidative stress is elevated in patients with preeclampsia, triggered by an increase in trophoblast debris and necrotic trophoblast products. This condition stimulates a strong inflammatory response. The inflammatory response activates endothelial cells and increases the number of macrophages/granulocytes, which subsequently produce an inflammatory reaction (Kibas *et al.* 2021; Tutik Nushah dan Yuly Peristiowati 2022).

In pregnant women with preeclampsia, metabolic imbalances arise due to endothelial dysfunction, which subsequently causes an increase in leukocyte levels. This leukocyte elevation is part of a cascade triggered by placental hypoxia, leading to the activation and upregulation of P38 MAPK, thereby inducing an inflammatory response. As a result, the equilibrium between angiogenic and anti-angiogenic factors is disrupted, further exacerbating endothelial dysfunction. This dysfunction increases vascular permeability, promoting blood vessel vasoconstriction, which ultimately contributes to the development of preeclampsia. This result is consistent with studies conducted by Kibas et al., (2021), which explains that the narrowing of the spiral arteriole lumen disrupts blood flow to the placenta, triggering an increase in leukocyte levels. Reduced perfusion and a hypoxic environment lead to the release of placental debris, causing systemic inflammation. These foreign substances stimulate the inflammatory process, resulting in an elevated leukocyte count. In contrast, under normal conditions, trophoblast debris remains within normal limits, ensuring that the inflammatory response remains regulated (Kibas *et al.* 2021; Tutik Nushah dan Yuly Peristiowati 2022).

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DOI: https://doi.org/10.54832/phj.v6i2.1147

According to researchers, preeclampsia is caused by impaired spiral artery remodeling, leading to decreased uteroplacental perfusion and subsequent placental ischemia. This condition triggers oxidative stress, which induces an inflammatory response involving TNF-α, IL-6, and CRP. The increased inflammatory response contributes to endothelial dysfunction, resulting in various symptoms of preeclampsia. Additionally, leukocyte levels in the blood increase as part of the inflammatory response. Therefore, hematocrit and leukocyte level assessments may be considered as supportive examinations in diagnosing preeclampsia in pregnant women.

Conclusion

There is a notable distinction in hematocrit and leukocyte levels among pregnant women with PE and PEB at RSUD Genteng in 2024. Future research may explore factors influencing hematocrit and leukocyte levels in patients with preeclampsia and severe preeclampsia.

Acknowledgments

We express our gratitude to Genteng Regional Hospital and STIKES RUSTIDA for providing the necessary facilities for this research.

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