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Original Article

Increased Hematocrit Levels in Third Trimester Pregnant Women as a Predictor of Preeclampsia

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ABSTRACT

Background: Preeclampsia is a high blood pressure disorder diagnosed during pregnancy which is known to be characterized by the sudden onset of hypertension, proteinuria, and other organ failures at 20 weeks of gestational age. Hematocrit levels in pregnant women have been speculated to be a predictor parameter for the incidence of preeclampsia in pregnancy. One of the mechanisms associated as a predictor of preeclampsia is the blood volume ratio which does not increase simultaneously as in pregnant women with normal blood pressure, thereby producing hematocrit levels (HCT) that are relatively greater than the established standards.
Methods: The research method used was case-control, with the primary sample data being the patient's venous blood sample and the secondary data being the patient's medical records. The data collected was a total of 20 samples with a control population of 10 samples of normal pregnant women and a case population of 10 samples of preeclamptic pregnant women. Bivariate analysis uses the Non-Parametric Mann-Whitney Test.
Results: The research showed that the case group had higher hematocrit levels with Asymp. Sig. (2-tailed) which has a value greater than the Mann-Whitney Test significance level ($\alpha = 0.05$), namely $0.001 > \alpha = 0.05$.
Conclusions: This research concluded that there is a significant difference between the hematocrit levels in preeclamptic pregnant women, which are higher when compared to the hematocrit levels in normal pregnant women.

Key Words: *Hematocrit, pregnancy, preeclampsia*

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INTRODUCTION

Maternal Mortality Rate (MMR) can be defined as a comparison of maternal mortality rates during pregnancy, childbirth, and postpartum periods which can be caused by the pregnancy process, childbirth, postpartum, and their management for every 100,000 births. MMR has been identified as one of the main indicators in evaluating and maintaining the health of pregnant women [1]. MMR due to bleeding and circulatory dysfunction is observed at the value of 28% and infection due to anemia and chronic energy deficiency in the mother also plays a huge role [2].

Indonesia is one of the examples representing developing countries, that have quite high levels of both maternal and perinatal mortality. Specifically, it is ranked third in ASEAN and number one in Southeast Asia. The MMR that occurs in Indonesia continues to increase quite drastically every year [3]. In the year 2019, MMR in Indonesia was recorded at 4,221 deaths and this figure continued to increase to 4,627 in 2020. Based on etiology, the majority of MMR in 2020 were caused by bleeding, namely, 1,330 cases were recorded, 1,110 cases of high blood pressure in pregnancy, and 230 cases were caused by circulatory system disorders [1]. The Province of East Java itself has the highest number of maternal deaths, namely 91.45 out of every 100,000 births [3].

High blood pressure during pregnancy is the second largest cause of MMR in the world and accounts for around 192 deaths per day [4]. In 2019, there were 4,226 maternal deaths in Indonesia, and around 1,066 cases of maternal death, that year were a result of hypertension in pregnancy [1]. Hypertension during pregnancy itself can be categorized into four types, namely chronic hypertension, preeclampsia, chronic hypertension superimposed preeclampsia, eclampsia, and gestational hypertension [5]. Preeclampsia is a high blood pressure disorder that impacts pregnancy and affects an average of 2-8% pregnancies worldwide, causing high maternal mortality rates [6].

Preeclampsia is a pregnancy disorder that is associated with hypertension in pregnancy, which often occurs after 20 weeks of gestation [7]. Preeclampsia can cause multi-organ failure, affect fetal growth, and have fatal consequences for

the mother and the baby itself; thus, preeclampsia can be categorized as the main factor causing MMR, especially in developing countries [8]. Preeclampsia affects 3-5% of all pregnancies and results in more than 60,000 MMR and 500,000 fetal deaths every year in the world, therefore, both preeclampsia and eclampsia can be defined as blood pressure disorders that cause the most significant health complications in pregnant women and fetuses [9].

In 2020, Indonesia's preeclampsia rate was recorded at 9.4%, and specifically in East Java, the prevalence of preeclampsia was recorded at 30.88% from 568,295 deliveries. This figure has increased compared to the data from 2019 which was at 27.27% out of 575,485 deliveries [1]. A diagnosis of preeclampsia can be made if a pregnant woman has a systolic blood pressure of > 140 mmHg or a diastolic blood pressure of >90 mmHg with a gestational age of 20 weeks, accompanied by proteinuria (>300 mg of protein in urine for 1 day) or a protein/creatinine ratio ≥ 0.3 in urine [9].

There are several speculations about laboratory hematology tests, especially hemoglobin and hematocrit levels, as predictors of patients with preeclampsia and patients without preeclampsia. This theory is based on physiological changes that can be observed during normal pregnancy to accommodate the growth and development of the fetoplacental unit [10]. Low blood hematological levels are significant risk factors as predictors of hypertensive disorders in pregnancy. This has encouraged the expansion of the old diagnostic criteria also to include other changes as predictors of preeclampsia, one of which is changes in hematological parameters [7]. Hematological parameters indicate immunological, nutritional, and hemostatic conditions and are considered the main factors influencing pregnancy [11]. Normal hematologic changes in pregnancy include an increase in plasma volume that exceeds the pregnancy-associated increase in red blood cell mass creating a "physiological anemia state." This physiological anemia predisposes women to lower hemoglobin and hematocrit values during pregnancy [12]. Hematocrit levels decrease during pregnancy compared to normal women [13].

One of the mechanisms used as a predictor of preeclampsia is the blood volume ratio which does not increase simultaneously as in pregnant women with normal blood pressure, thereby producing hemoglobin (Hb) levels and hematocrit levels (HCT) that are relatively greater than the established standards, so that many studies have evaluated hematocrit levels in pregnant women to predict the onset of preeclampsia. This relationship between hematocrit levels and the diagnosis of preeclampsia provides a basis and guideline in providing further evaluation and may be valuable as a screening test for early diagnosis of preeclampsia in pregnant women[6]. Based on the data above, the author wants to know the truth of the predictive formula which explains that increasing hematocrit levels in the blood of pregnant women can be evaluated as an early diagnosis of preeclampsia in pregnant women.

METHODS

This observational-analytic and case-control study was performed from August 2023 to November 2023 at Bhakti Dharma Husada (BDH) Regional Hospital in the city of Surabaya, Indonesia. The sample size was assessed as 20 cases with a 95% confidence interval and 10% dropout criteria. The sample size in this research was calculated using the Lemeshow formula. With a total sample of 20 individuals, the participants were then divided into 2 groups, 10 samples from preeclamptic women as the case group and 10 samples from normal pregnant women as the control group. The sampling technique applied in this study was random sampling.

Obtaining BDH Regional Hospital ethics committee permission and consent for each case, utilizing a population of pregnant women with a gestational age of over 20 weeks who were treated as an inpatient or outpatient at BDH Regional Hospital. The respondents were then screened further according to this study's research inclusion, as follows: (1) multigravida pregnancy, (2) a single fetus pregnancy, (3) women diagnosed with mild preeclampsia, severe preeclampsia, and chronic hypertension superimposed preeclampsia, (4) complete medical record document data.

They were then eliminated according to this study's research exclusion, as follows: (1) incomplete medical records, (2) not registered at BDH Regional Hospital, (3) If comorbidities or other organ disorders before the onset of pregnancy were found. Data recapitulation is then carried out which includes data such as name, age, height, weight, BMI, systolic blood pressure, diastolic blood pressure, and hematocrit levels.

Before advancing further to the procedures, informed consent must be given to the participants regarding the purpose of this study, the procedures taken, the health benefits from this procedure, as well as potential risks that could happen during or after the procedure is done. Venous blood samples were then collected as the main sample of this study. The samples were then taken to the laboratory facility to be examined. The hematocrit levels between the two groups are examined and distinguished from each other.

Univariate analysis was first conducted to determine the frequency of each affecting variable, which are hematocrit levels elevation and the occurrence of preeclampsia. Bivariate analysis was then performed by SPSS, utilizing the normality test, and the Mann-Whitney test which were performed on the two main variables suspected to be related. A

confidence interval level of 95% (α = 0,05) is used to conclude the presence of a significant difference between the two variables utilized in this study.

RESULTS

There are several factors differentiating both the case and control group. The mean age was 32.60 ± 4.142 for preeclamptic women, which is higher than those found in non-preeclamptic women, which is 26.80 ± 5.5538. The mean systolic blood pressure for preeclamptic women was 156.10 ± 16.482, significantly higher than 102.60 ± 8.1268 found in non-preeclamptic women. The mean diastolic blood pressure for preeclamptic women is 99.20 ± 5.903, which is also higher than 62.50 ± 3.4721 in non-preeclamptic women. The mean weight differs greatly between the two, 81.300 ± 7.1188 for preeclamptic women and 46.60 ± 4. 9933 for non-preeclamptic women. The mean height shows a little difference between the two, 158.700 ± 6.6508 in preeclamptic women and 152.20 ± 6.5328 in non-preeclamptic women. The BMI also shows a significant difference between the two groups, with values of 32.400 ± 3.7644 in preeclamptic women and 20.196 ± 2.0971 in non-preeclamptic women. Finally, the hematocrit levels found in preeclamptic women are much higher than those in non-preeclamptic women, estimated in 39.800 ± 1.9551 for preeclamptic women and 32.300 ± 2.1628 for non-preeclamptic women. After data analysis was done, it can be concluded that the average values of demographic characteristics such as age, systolic and diastolic blood pressure, weight, height, and body mass index, as well as hematocrit levels, showed higher levels in the case group (preeclamptic pregnant women) than those in the control group (non-preeclamptic pregnant women) (Table 1).

As for the analysis of the hematocrit levels, normality tests should first be conducted as our number of samples does not meet the requirement of 50 data (N = 20). The normality test used is the Shapiro-Wilk test, in which a significant value can be determined based on the p-value, and normal distribution must meet the requirement of $p > 0.05$. The significance values obtained in this study are 0.693 in preeclamptic women and 0.458 in non-preeclamptic women (Table 2). Therefore, the data obtained can be categorized as abnormally distributed ($p < 0.05$). Consequently, the consequent non-parametric test used in this study will be the Mann-Whitney test. Given two abnormally distributed independent samples, the purpose of the Mann-Whitney test is whether one variable tends to have values higher than the other. Data obtained from the consequent non-parametric test which utilized the Mann-Whitney test (Table 3). Based on the results, the Asymp Sig. (2-tailed) obtained. has a greater value than the significance level, namely (α = 0.05), $p = 0.001 > 0.05$.

DISCUSSION

The mean age was 32.60 ± 4.142 for preeclamptic women, which is higher than those found in non-preeclamptic women, which is 26.80 ± 5.5538. The results of this study also proved to be in line with previous research, which concluded that there was a relationship between maternal age and the incidence of preeclampsia in pregnant women ($p = 0.001 < 0.05$). In this study, it was found that pregnant women whose age was classified as high risk (age < 20 years or > 35 years) were mostly diagnosed with preeclampsia when compared to pregnant women whose age was not at risk [14].

The mean systolic blood pressure for preeclamptic women was 156.10 ± 16.482, significantly higher than 102.60 ± 8.1268 found in non-preeclamptic women. The results of this study were also proven to be in line with previous research done in 2019, which stated that the frequency of pregnant women with high systolic blood pressure were more at risk of experiencing preeclampsia during pregnancy (37.5%) than pregnant women with normal blood pressure (7.5%) [15].

The mean diastolic blood pressure for preeclamptic women is 99.20 ± 5.903, which is also higher than 62.50 ± 3.4721 in non-preeclamptic women. The results of this study are in line with a previous research in 2019, which states that diastolic blood pressure is the most serious risk factor as a cause of preeclampsia. This is supported by evidence that from a total of 120 respondents, there were 60 respondents (50%) of pregnant women with normal diastolic blood pressure and not experiencing preeclampsia, 19 respondents (15.8%) of pregnant women with normal diastolic blood pressure but are diagnosed with preeclampsia and 41 respondents (34,2%) of those with high diastolic blood pressure with preeclampsia. This data concludes that the highest frequency of pregnant women experiencing preeclampsia is among those who have high blood pressure [16].

The mean weight differs greatly between the two, 81.300 ± 7.1188 for preeclamptic women and 46.60 ± 4. 9933 for non-preeclamptic women. The results of this research are also in line with a previous research from 2020, which concluded from the results of the chi-square statistical test analysis, it was found that $p = 0.001 < 0.05$, which states that there is a relationship between excess body weight (obesity) and the incidence of preeclampsia [17]. The mean height shows a little difference between the two, 158.700 ± 6.6508 in preeclamptic women and 152.20 ± 6.5328 in non-preeclamptic women. The results of this study are also in line with previous research which stated that of the 327 respondents from pregnant women with preeclampsia, 53 respondents (16.2%) had a shorter stature compared to 274 respondents (83.8%) of pregnant women with taller stature [18].

The BMI also shows a significant difference between the two groups, with values of 32.400 ± 3.7644 in preeclamptic women and 20.196 ± 2.0971 in non-preeclamptic women. The results of this research are also supported by a previous conducted in 2019, which states that through the results of the Chi-Square test, a p-value = 0.000 < 0.05 with an Odds Ratio value of 5.923 was obtained. This concludes that there is a relationship between BMI values and preeclampsia incidence [16].

Finally, the hematocrit levels found in preeclamptic women are much higher than those in non-preeclamptic women, estimated in 39.800 ± 1.9551 for preeclamptic women and 32.300 ± 2.1628 for non-preeclamptic women. Based on the results of the Mann-Whitney test, the Asymp Sig. (2-tailed) obtained. has a greater value than the significance level, namely ($\alpha = 0.05$), $p = 0.001 > 0.05$. Thus, it can be concluded that there is a significant difference between the hematocrit level in preeclamptic pregnant women compared to normal pregnant women. This value concludes that there is a significant difference in the value of hematocrit levels, which increases in normal pregnant women and preeclamptic pregnant women, and based on the average results, it was found that patients with preeclamptic pregnant women had higher hematocrit values compared to normal pregnant women.

Similar to the conclusions of this research, the same conclusion is also found in a previous study, which was expressed with the p-value = 0.004 < 0.05 and an odds ratio value of 15.556, which can conclude that pregnant women who have high hematocrit levels have a 15 times risk of experiencing severe preeclampsia during pregnancy(Elgari M., 2013). Furthermore, these results are also in line with a previous study, which stated that the results of plasma hematocrit levels in pregnant women could predict 26 (4.6%) patients, and the incidence of preeclampsia occurred in 35 (6.2%) patients. This study can also conclude that plasma hematocrit findings show 60% sensitivity, 99% specificity, and 97% diagnostic accuracy, ($p<0.001$) in the diagnosis of preeclampsia [19].

CONCLUSIONS

Based on the results of this study, it is proven that preeclamptic pregnant women have higher hematocrit levels compared to normal pregnant women, namely with a mean + SD value of 38,900 + 1.9551 compared to 32,300 + 2.1628. This research proves that hematocrit can be useful as a useful screening biomarker to predict the diagnosis of preeclampsia in pregnant women. This study also discovered the significance of age, blood pressure, weight, height, and BMI as risk factors for preeclampsia.

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Table 1: Demographic Characteristics of the Study Population

Variables	**Preeclampsia N = 10 (50%)**	**Non-Preeclampsia N = 10% (50%)**
Age	32.60 ± 4.142	26.80 ± 5.5538
Systolic BP	156.10 ± 16.482	102.60 ± 8.1268
Diastolic BP	99.20 ± 5.903	62.50 ± 3.4721
Weight	81.300 ± 7.1188	46.60 ± 4. 9933
Height	158.700 ± 6.6508	152.20 ± 6.5328
BMI	32.400 ± 3.7644	20.196 ± 2.0971
Hematocrit	39.800 ± 1.9551	32.300 ± 2.1628

Table 2: Hematocrit Normality Test

	Preeclampsia N = 10 (50%)	**Non-Preeclampsia N = 10% (50%)**
Statistic	,181	,174
Sig.	.693	.458

Table 3: *Mann - Whitney* Test

	Results
Mann – Whitney	0.000
Asymp. Sig. (2-tailed)	0.001