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Original Research Article

Association between anemia and preeclampsia: a case control study in Gorontalo region, Indonesia

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ABSTRACT

Background: Preeclampsia is one of the most common health problems in pregnancy that relates to several risk factors leading to an increase in maternal and perinatal mortality. The risk factors for preeclampsia include maternal age ≥35 years old, primigravida, chronic hypertension, obesity, and history of preeclampsia. However, studies investigating anemia as a risk factor for preeclampsia were still limited and showed conflicting results. This study aims to investigate the association between anemia and preeclampsia.
Methods: A case-control study was conducted in the department of obstetrics and gynecology Dr. M. M. Dunda public hospital, Indonesia, from December 2020 to May 2021. Secondary data was collected in singleton pregnancy patients aged <35 years, admitted from 2016 to 2020. The number of patients used in this study was 264 consisting of 132 preeclampsia and 132 healthy women. Patient basic characteristics, obstetrics status, urinalysis, and complete blood count were collected and analysed using SPSS 25 for Mac. Kolmogorov-Smirnov test was done to examine data distribution. Chi-square was used to analyse the association between anemia and preeclampsia, $p<0.05$ is considered to be statistically significant.
Results: BMI was found significantly higher in preeclampsia group ($p<0.000$), and infants born to mothers with preeclampsia had lower birth weight and height compared to the control group with p-value respectively $p<0.032$ and $p<0.001$. There was no significant association between anemia and pre-eclampsia ($p=0.712$; $p>0.05$).
Conclusions: Preeclampsia is significantly associated with higher maternal BMI and lower birth weight/height. However, no association was identified between anemia and preeclampsia.

Keywords: Anemia, Preeclampsia, BMI, Low birth weight

INTRODUCTION

Preeclampsia is one of the most common health problems in pregnancy. Preeclampsia is defined as systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg, along with proteinuria occurring after 20 weeks of gestation.[1] Preeclampsia affects 2-8% of pregnant women and accounts for 9% of maternal deaths, particularly in Africa and Asia.[2] WHO estimated the incidence of preeclampsia in developing countries is 2.8% compared to 0.4% in developed countries.[3] Maternal mortality rate in Indonesia increased from 228 cases per 100.000 live births in 2007 to 359 cases per 100.000 live births in 2012.[4] In 2019, hypertension in pregnancy was the second leading cause of maternal mortality with 1.066 cases after antepartum hemorrhage with 1.280 cases.[4] The high maternal mortality rate due to preeclampsia shows the need to understand the cause of preeclampsia to set effective health programs and policies. The risk factors for preeclampsia include history of preeclampsia in previous pregnancy, multiple pregnancy, chronic hypertension, renal disorders, diabetes mellitus, first pregnancy, obesity, family history of preeclampsia, and age ≥35 years old.[5]

Preeclampsia with anemia is often found in pregnant women visiting health facilities for antenatal care. Anemia in pregnancy is a physiologic response because the plasma volume expansion is greater than the rate of erythrocyte production, which results in hemodilution. Various studies showed a relation between anemia and preeclampsia. Study by Ali et al found that severe anemia during pregnancy can increase the risk of preeclampsia, eclampsia, premature birth, low birth weight, and neonatal death.[6] A study by Getu et al reported association between anemia and preeclampsia with AOR 1.49.[7] Similar study by Gupta et al found that the severity of anemia had a positive correlation with preeclampsia, maternal and perinatal mortality and morbidity.[8] According to WHO, the prevalence of anemia in pregnancy was 40% globally. In Indonesia, the number of iron deficiency anemia in pregnancy was 48.9%.[9] Due to the high maternal mortality rate related to preeclampsia and anemia in pregnancy in Indonesia, modifiable risk factor identification is necessary to decrease preeclampsia. Research on anemia and preeclampsia at Dr. M. M. Dunda Limboto regional general hospital has not been conducted yet. Therefore, a study to explore the association between anemia and preeclampsia is needed to help in establishing effective clinical intervention and policy.

METHODOS

A case-control study was conducted in obstetrics and gynecology department Dr. M. M. Dunda Limboto regional general hospital, Indonesia, from December 2020 to May 2021. Secondary data was collected from patient registry data that admitted from 2016 to 2020. The number of patients used in this study was 264 consisting of 132 preeclamptic women (case group) and 132 healthy women (control group). Preeclampsia is defined as systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg, documented on two occasions for at least four hours apart, along with proteinuria ≥300 mg on a 24-hours urine test or +2 by protein dipstick test occurring after 20 weeks of gestation. Anemia is defined as hemoglobin level <11 g/dl.

Inclusion and exclusion criteria

Inclusion criteria of this study were new-onset preeclampsia patients aged <35 years with singleton pregnancy. Exclusion criteria were patients aged >35 years, chronic hypertension, previous history of preeclampsia, multiple pregnancy, chronic renal disorder, diabetes mellitus, autoimmune disease, and pre-pregnancy obesity.

Procedure

Patient age, gestational age, parity, education level, work, delivery method, body mass index, blood pressure, urinalysis, complete blood count, and past medical history were recorded as maternal data. Birth weight and length were recorded as neonatal data. Data were analyzed by using SPSS 25 for Mac. We used Kolmogorov-Smirnov test to examine data distribution. Chi-square was used to analyze the significant association between preeclampsia and anemia in pregnancy, $p<0.05$ was considered to be statistically significant.

RESULTS

This study involved 264 pregnant women consisting of 132 preeclampsia and 132 healthy women. Patient basic characteristics between two groups was shown in (Table 1). There was no statistically significant difference between patient age, gestational age, parity, delivery method, education level, and occupation. Vaginal delivery was higher in healthy women (69) while most preeclamptic women undergo caesarean delivery (75), however, the difference was statistically insignificant. A significantly higher body mass index in the preeclamptic women than in the healthy women (30.8 vs. 28.8; p=0.000) is depicted in (Table 1). Moreover, the differences in birth weight and height between the two groups were statistically significant. Infants born to mothers with preeclampsia had lower birth weight and height. Table 2 showed insignificant association between anemia and preeclampsia (p=0.712). Similar result was presented in Table 3 that there were no statistically significant differences in hemoglobin, hematocrit, leukocyte, and thrombocyte level between two groups.

Table 1: Basic characteristics of pregnant women and newborns (n=132).

Parameters		Preeclampsia	Non Preeclampsia	P value
Age		27 (18-34)	25 (17-34)	0.060[a]
Parity	Primiparity	53 (20)	58 (22)	0.618[b]
	Multiparity	79 (29)	74 (28)	
Gestational age		38 (33-41)	38 (33-42)	0.062[a]
Education level	Elemetary school	42 (16)	32 (12)	0.279[b]
	Junior high school	19 (7.1)	25 (9.5)	
	Senior high school	56 (21.2)	65 (24.6)	
	University	15 (5.9)	10 (3.8)	
Work	Housewife	121 (45.8)	118 (44.7)	0.674[b]

Continued.

Parameters		Preeclampsia	Non Preeclampsia	P value
	Employee	11 (4.17)	14 (5.3)	
Delivery method	Vaginal delivery	57 (21.6)	69 (26.1)	0.175[b]
	Caesarean delivery	75 (28.4)	63 (23.9)	
Body mass index		30.8(24.7-39)	28.8(22-38)	0.000[a]
Birth weight		2950 (1900-4300)	3025 (2100-4200)	0.032[a]
Birth height		48 (39-52)	49 (39-55)	0.001[a]

[a]Data were shown as median (minimum-maximum) and P value is acquired using Mann-Whitney U test
[b]Data were shown as n (%) and P value is acquired using Chi-square test

Table 2: Anemia and pre-eclampsia cross tabulation.

Parameter		Preeclampsia	Non-Preeclampsia	P value
Anemia status	Anemia	68 (25.7)	64 (24.2)	0.712[b]
	Non-anemia	64 (24.2)	68 (25.7)	-

[b]Data were shown as n (%) and P value is acquired using Chi-square test

Table 3: Number of patients based on severity of anemia.

Severity	Preeclampsia N (%)	Non-preeclampsia N (%)
No anemia	64 (24.2)	68 (25.7)
Mild anemia	28 (10.6)	38 (14.4)
Moderate anemia	32 (12.1)	20 (7.6)
Severe anemia	8 (3)	6 (2.3)

Table 4: Hemoglobin, hematocrite, leukocyte, dan thrombocyte levels.

Parameters	Preeclampsia	Non-Preeclampsia	P value
Hemoglobin	10.8 (5.7-14)	11 (6.7-16.5)	0.547
Hematocrit	31.8 (17.2-40)	32.5 (22.8-48.9)	0.390
Leukocyte	13.8 (6.7-36.9)	12.7 (3.1-34.1)	0.085
Thrombocyte	283 (32-790)	285 (143-551)	0.769

*Data were shown as median (minimum-maximum) and p value is acquired using Mann-Whitney U test

DISCUSSION

This study shows no significant difference in maternal age between the two groups. This finding may be due to the sample population aged 20-34 years old. According to study by Laminpaa and associates, the number of preeclampsia cases increased significantly in patients aged 35 years or above.[10] A retrospective study by Das et al in Nepal found similar result that pregnancy at 35 years or above had threefold more significant risks of developing preeclampsia than those aged 20-34 years.[11] The considerable increase of preeclampsia in pregnancy at 35 years or above is suspected to be due to uterine artery aging and increased arterial wall stiffness resulting in vascular tone regulation disorder and gradual loss of compliance of the cardiovascular vessels which leads to endothelial dysfunction.[12,13] Preeclampsia cases in primigravida and multigravida have relatively the same proportion is shown in (Table 1). Studies conducted in Ethiopia showed similar results that no significant differences in the risk of preeclampsia between primigravida and multigravida.[13,14] Conversely, a study in Indonesia and a systematic review by Luo et al. stated that preeclampsia was higher in primigravida due to immune maladaptation of the first chorionic implantation within the endometrium.[15,16] These different results might be due to the difference in sample basic characteristics and the study design.

The number of preeclampsia most commonly found in the high school education group is shown in (Table 1). However, there is no significant difference in education level between the two groups. A study conducted in Netherlands found that women with lower education levels have a fivefold greater risk of developing preeclampsia.[17] This might be due to the association between education level and the use of health services. Women with lower education levels tend to have more difficulty getting health information such as antenatal care, signs of complications, and nutrition during pregnancy.[18] Moreover, (Table 1) also shows there is no significant difference in patient occupation between the two groups. This result is similar to a cohort study by Lawlor and associates that stated no significant

association between socioeconomic status and preeclampsia or gestational hypertension.[19] A study in Egypt also showed no significant relationship between non-working women and women with physical or stressful work in preeclampsia incidence.[20] In contrast, a meta-analysis by Mozurkewich and associates found an increase in preeclampsia and gestational hypertension in patients doing a lot of physical activity[21]. A cohort study in South Korea (2016) stated that low income is an independent risk factor of preeclampsia with odds ratio (OR) 1.26.[22] It was presumably due to the association between low income with lower education level, unhealthy lifestyle, stressful environment, limited access to health facilities or information, risk of infection, and unwanted pregnancy.[23]

In this study, body mass index was found higher in the preeclampsia group. This result is similar to a meta-analysis based on 16 studies by Motedayen which found a positive correlation between body mass index and preeclampsia.[24] Obesity with metabolic syndrome patient usually has insulin resistance with an excessive flux of fatty acids and a proinflammatory state leading to imbalance disorder of immunology, metabolic changes, and systemic inflammation needed for a healthy pregnancy.[25] Infants born to preeclamptic women have lower birth weight compared to healthy women is shown in (Table 1). A study in Uganda and cohort study in Sweden also found a correlation between preeclampsia and lower birth weight/height.[26,27] These findings might be due to inadequate maternal perfusion of placental villi, local placental hypoxia, and impaired fetal growth resulted from shallow cytotrophoblast invasion of the uterus in preeclamptic women.[28] An insignificant association between anemia and preeclampsia using the Chi-square test method (p=0.712) is shown in (Table 2). This result is similar to a study done in Indonesia (2019) which reported an insignificant association between anemia and preeclampsia.[29] In contrast, a case-control study in Ethiopia found that women with anemia have higher risk to develop preeclampsia.[7] As exhibited in (Table 3) descriptively a greater number of preeclampsia cases in women with moderate-severe anemia. This result is coherent with a study in Sudan that found a significant association between severe anemia and preeclampsia.[6] That study stated that women with severe anemia have 3.6 times more risk of developing preeclampsia than non-anemic women. The susceptibility of severely anemic women to preeclampsia is perhaps due to micronutrients and antioxidants deficiency and an increase in pro-inflammatory cytokines and acute-phase protein lactoferrin systemically.[6,30] It is thought that the different results between this study and other previous studies might be due to most samples in this study diagnosed with mild-moderate anemia with median of hemoglobin levels 10.8 g/dl in preeclampsia group and 11 g/dl in non-preeclampsia group (Table 4). This study has some limitations so that the result should be interpreted carefully. First, this study did not have the same number of patients for each category of anemia (mild-moderate-severe). Most of the patients were classified in mild-moderate anemia. The result of this study may be limited to the association between preelamptic patients with mild-to-moderate anemia. Study with sufficient number of severe anemia patients should be conducted to obtain more meaningful results. Second, the diagnosis of anemia in this study was obtained at patient admission. The one-time blood examination made this study difficult to determine whether anemia is a cause or a result of preeclampsia. A prospective cohort study with a large number of patients is still further needed to investigate anemia as the cause or a result of preeclampsia.

CONCLUSION

Preeclampsia is significantly associated with higher maternal body mass index and lower birth weight/height. However, no association was identified between anemia and preeclampsia.

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