Relationship between Age, Parity and Body Mass Index in Pregnant Women with the Incidence of Preeclampsia at Prof. Dr. Margono Soekardjo Hospital Purwokerto

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Abstract
Background: Preeclampsia is a crucial problem in developing country and contributes 9% of maternal mortality in Asia. Moreover it has been the second main cause of maternal death in Indonesia and the leading cause of maternal death in Central Java since 2019. This study aims to determine the relationship between age, parity and BMI in pregnant women with the incidence of preeclampsia.
Methods: This study is a retrospective analytic observational study with a case control design. The research subjects were all cases of vaginal delivery and cesarean section from July to December 2022.
Results: There were 200 women as subjects consisting of 100 women with preeclampsia and 100 women without preeclampsia. Most of the research subjects were aged <35 years (71.5%). It was found that preeclampsia was significantly associated with age ≥35 years (p=0.019), BMI ≥30 (p=0.008) and primiparity (p=0.006). On bivariate analysis, women with age ≥35 years (OR 2.1; 95% CI; 1.12-3.97), BMI ≥30 (OR 2.4; 95% CI; 1.25-4.87) and primiparity (OR 2.2; 95% CI; 1.2- 3.92) are at increased risk of developing preeclampsia.
Conclusion: The results of this study indicate that age ≥ 35 years, BMI ≥30 and primiparity are associated with the occurrence of preeclampsia.

Key words: preeclampsia, age, parity, body mass index

Hubungan Usia, Paritas dan Indeks Masa Tubuh pada Ibu Hamil dengan Kejadian Preeklamsia di RSUD Prof. Dr. Margono Soekardjo Purwokerto

Abstrak
Pendahuluan: Preeklamsia masih menjadi masalah kesehatan ibu yang krusial di negara berkembang dan berkontribusi sebanyak 9% mortalitas maternal di Asia. Preeklamsia menempati urutan ke-2 kematian ibu di Indonesia dan menjadi penyebab utama kematian ibu di Jawa Tengah sejak tahun 2019. Penelitian ini bertujuan untuk mengetahui hubungan antara usia, paritas, dan IMT pada ibu hamil dengan kejadian preeklamsia.
Metode: Penelitian ini merupakan penelitian observasional analitik retrospektif dengan desain case control. Subjek penelitian adalah seluruh kasus persalinan pervaginam dan seksio sesarea pada bulan Juli sampai Desember 2022.
Hasil: Diperoleh subjek sebanyak 200 wanita yang terdiri atas 100 wanita dengan preeklampsia dan 100 wanita tanpa preeklampsia. Sebagian besar subjek penelitian berusia <35 tahun (71.5%). Ditemukan bahwa preeklamsia secara signifikan berhubungan dengan usia ≥35 tahun (p=0.019), IMT ≥30 (p=0.008) dan primiparitas (p=0.006). Pada analisis bivariat, wanita dengan usia ≥35 tahun (OR 2.1; 95%CI; 1.12 - 3.97), IMT ≥30 (OR 2.4; 95%CI; 1.25 - 4.87) dan primipara (OR 2.2; 95%CI; 1.2 - 3.92) berada dalam peningkatan risiko terjadi preeklamsia.
Kesimpulan: Hasil penelitian ini menunjukkan bahwa usia ≥35 tahun, IMT ≥30 dan primiparitas berhubungan dengan terjadinya preeklampsia.

Kata kunci: preeklamsia, usia, paritas, indeks masa tubuh

Introduction

The World Health Organization (WHO) states that the maternal mortality rate (MMR) is a measure of the country's quality of life. Data retrieved from WHO show that the maternal mortality rate reached 462 per 100,000 live births, with a total of 295,000 maternal deaths in 2017. Most maternal deaths (94%) occur in low- to moderate-income countries, including Africa and Asia.[1] Meanwhile, in Indonesia, the MMR was stated to have decreased from 390 to 305 between 1991 and 2015. However, judging from the number of maternal deaths in Indonesia from 2018 to 2021, there was an increase in the number from 4,225 to 7,389 deaths in 2021, with the most common cause in 2021 being COVID-19, followed by hemorrhage and hypertension in pregnancy.[2] This makes MMR an unfinished problem; therefore, reducing MMR is one of the Sustainable Development Goals (SDGs), with a target of less than 70 per 100,000 live births by 2030.

The results of the national health research from the Agency of Health Research and Development in 2016 show that the causes of maternal deaths are hypertension (33.07%) and hemorrhage (27%). In 2021, the number of maternal deaths due to hypertension in pregnancy was 1,077 out of a total of 7,389 maternal deaths. This illustrates that hypertension in pregnancy is still a crucial risk factor for maternal death.[2,3]

Hypertension in pregnancy includes gestational hypertension, chronic hypertension, preeclampsia, eclampsia, and superimposed preeclampsia. Preeclampsia is a disease of pregnancy associated with new-onset hypertension occurring at more than 20 weeks of gestation and often near-term characterized by the presence of urinary protein. Hemolysis, thrombocytopenia, liver damage, and impaired renal function can be found in severe cases. Preeclampsia is considered a cause of poor perinatal outcomes and, if left untreated, can progress to eclampsia. It can result in acute and long-term complications for both the mother and the baby. Maternal complications could be pulmonary edema, myocardial infarction, stroke, acute respiratory distress syndrome, coagulopathy, renal failure, and retinal injury. Whereas fetal growth restriction, oligohydramnios, placental abruption, and non-reassuring fetal status are the result of impaired uteroplacental blood flow due to preeclampsia. Consequently, pregnancy with preeclampsia increases the risk of indicated preterm delivery.[4,5] Preeclampsia is estimated to complicate 2-8% of all pregnancies worldwide and contribute to 9% of maternal deaths in Africa and Asia. In 2019, in Indonesia, preeclampsia was the second leading cause of maternal death after hemorrhage, with 1066 cases.[2] In Central Java province, preeclampsia was the leading cause of maternal death, with 123 cases (29.6%) of all maternal deaths in 2019. RSUD Prof. Dr. Margono Soekardjo Purwokerto is a referral hospital with the Comprehensive Obstetrics and Neonatal Unit in Banyumas Regency. Data retrieved from the Maternal Perinatal Installation found that preeclampsia cases from 2017 to 2018 still increased from 359 to 443 cases and are still increasing.[6,7]

The mechanism of how pregnancy triggers or aggravates hypertension remains unknown. Some theories explaining the onset of preeclampsia consider that hypertension occurring in pregnancy may be based on the following: (1) Placental implantation with abnormal trophoblast invasion of uterine blood vessels, (2) abnormal immune tolerance of maternal, placental, and fetal tissues, (3) maternal maladaptation to cardiovascular and inflammatory changes in normal pregnancy, and (4) genetic factors. Preeclampsia is classified based on the onset of symptoms, namely early-onset and late-onset preeclampsia. Late-onset preeclampsia reflects maternal (non-placental) etiology,

with an incidence of 80% of preeclampsia cases.[8]

Previous studies show there is an association between age, BMI, and parity in the incidence of preeclampsia in pregnancy. Other risk factors associated with preeclampsia include diabetes mellitus, heart disease, autoimmune disease, and a previous history of preeclampsia.[9,10]

Due to the increasing cases of preeclampsia in Central Java, especially in Purwokerto, and limited research on the relationship between maternal characteristics and neonate outcomes in patients with preeclampsia in Central Java, this study aims to find the relationship between preeclampsia with age, parity, and BMI in mothers who were giving birth at Prof. Dr. Margono Soekardjo Hospital from October to December 2022.

Methods

The population in this study were all patients who underwent delivery with gestational age ≥20 weeks at Prof. Dr. Margono Soekardjo Hospital, Purwokerto, from October to December 2022. The research design of this study is an analytical observational study (non-experimental) with a case-control approach. This study is retrospective because it determines the affected group (case group) and the group that is not affected (control group) first. Furthermore, the risk factors of each group were traced retrospectively.

The sampling technique used in this study is purposive sampling technique, in which the samples selected were patients who met the inclusion and exclusion criteria. Inclusion criteria for the case group are pregnant women with a diagnosis of preeclampsia, age 16-45 years, and gestational age of 20-42 weeks. Meanwhile, the control group is normotensive pregnancy. All samples in the inclusion criteria are singleton pregnancies and had complete medical records. The exclusion criteria used are mothers with a history of hypertension before pregnancy, a history of diabetes mellitus, diseases such as gestational diabetes, kidney, heart/ blood vessels, multifetal pregnancies, and incomplete medical records. The independent variables of this study are age, parity, and body mass index (BMI), while the dependent variable is preeclampsia.

This study uses secondary data obtained from medical records and delivery registers at Prof. Dr. Margono Soekardjo Hospital from October to December 2022. The secondary data used is delivery data registered from 1 October 2022 to 31 December 2022. Secondary data were collected in January 2023 at Prof. Dr. Margono Soekardjo Hospital by compiling tables made by researchers based on existing medical record data.

The samples taken were those who fulfilled the inclusion and exclusion criteria. Then, the data were recorded and tabulated according to the variables studied. Univariate and bivariate analyses were carried out using the *Chi-Square* test. In this study, univariate and bivariate correlation analyses were performed using the IBS SPSS 26 application.

Results

The secondary data retrieved from medical records at Prof. Dr. Margono Soekarjdo Hospital from October to December 2022 obtained a total of 200 research subjects.

Table 1 shows that the respondents were mostly aged <35 years, with a total 143 people (71.5%). Moreover, the respondents mostly had BMI <30 kg/m^2, with a total of 152 people (76%).Table 2 found that preeclampsia was significantly associated with age ≥35 years (p=0.019), BMI ≥30 (p=0.008) and primiparity (*p=0.*006). On bivariate analysis, women aged ≥35 years (OR 2.1; 95%CI; 1.12 - 3.97), BMI ≥30 (OR 2.4; 95%CI; 1.25 - 4.87), and primiparity (OR 2.2; 95%CI; 1.2 - 3.92) were at increased risk of developing preeclampsia.

Table 1 Characteristics of Research Subjects

Variables	Total (n = 200)	Percentage (%)
Mother's age		
<35 years	143	71.5
≥35 years	57	28.5
IMT		
<30 kg/m^2	152	76
≥30 kg/m^2	48	24
Parity		
Primiparity	66	33
Multiparity	134	67

Table 2 Analysis of the Association Between Age, BMI, and Parity with Incidence of Preeclampsia

Variables	Preeclampsia				*p-value*	OR	95%CI
	Available		None				
	n=100	%	n=100	%			
Mother's age							
<35 years old	64	64	79	79	0.019	2.1	1.12-3.97
≥35 years old	36	36	21	21			
IMT							
<30 kg/m^2	68	68	84	84	0.008	2.4	1.25-4.87
≥30 kg/m^2	32	32	16	16			
Parity							
Primiparity	51	51	32	32	0.006	2.2	1.2-3.97
Multiparity	49	49	68	68			

Significance determined at $p < 0.05$ (Chi-Square Test)

Discussion

The study results are in accordance with Cunningham's theory and a study by Ray *et al*. (2019) stating that maternal age over 35 years increases the risk of preeclampsia (RR 1.2). It is explained that, at that age, there begins a decline in organ function and becomes a risk of obesity, hypertension, and gestational diabetes, which are also risk factors for preeclampsia.[8]

Other studies have found that preeclampsia is related to age. Because the size of the uterus has not reached the average size for pregnancy and the age of the mother is >35 years, blood vessels experience peripheral dysfunction and structural changes in the degenerative phase. Therefore, pregnancies of women aged <20 years are vulnerable to preeclampsia. This study is in accordance with the research of Bilano, Ganchimeg, Mori, and Souza stating that there is a relationship between preeclampsia among women aged ≥35 years with a risk of 1.95 times to experience preeclampsia.[9] Noa Rymer-Haskel *et al*. (2018) stated that advanced maternal age (≥40 years old) carries a similar rate of severe preeclampsia and complications as in young women (20 - 34 years old).[14]

Furthermore, this study shows that primiparity status was significantly associated with the incidence of preeclampsia. This is in line with Rafida (2020) and Pogačnik (2018), stating that preeclampsia increases in the first pregnancy. The underlying cause of this event is immunological maladaptation.[5,15] However, the results of this analysis are not in line with the research of Asmana et al., stating that there is no relationship between gravid and preeclampsia; instead, nulliparity is a risk factor for severe preeclampsia. There are differences between the results of this study and the various factors included. The study sample with more than one parity is not a risk factor group but has an age risk factor, i.e., age over 35 years.[9] Besides, Lin et al. in their population-based study in China, found that nulliparity became a significant risk factor for PE in adjusted analysis (aOR: 1.73, 95% CI: 1.32 – 2.25, P<0.001). In addition, they found that nulliparous women had a two-fold increased risk for late-onset preeclampsia.[15]

Obesity triggers preeclampsia through several mechanisms of pro-inflammatory cytokine release, including oxidative stress. The results of this study are in line with Rafida (2020) and Pogačnik (2018), mentioning that obese mothers are at risk of preeclampsia.[5,9] Moreover, Lin et al. (2021) found that high BMI considered overweight (aOR 1.54) and obesity (aOR 2.15) were associated with increased risk for preeclampsia.[15] At higher BMI, where there is excess energy storage, the sympathetic nervous system is activated, which causes lipolysis and increased release of free fatty acids into the circulation. The accumulation of poorly utilized lipids in tissues such as the liver, heart, and skeletal muscle, among others, increases lipo-toxicity and tissue damage.[11] Several studies have shown a direct relationship between BMI and the risk of preeclampsia, gestational hypertension, and gestational diabetes. The relevance of excessive gestational weight gain as a risk factor for preeclampsia is further strengthened by reports showing that the presence of pre-pregnancy obesity and excessive gestational weight gain results in the highest risk for the onset and progression of preeclampsia. It is imperative that this is clearly and timely communicated to pre-pregnant and pregnant women and that risk reduction measures are taken in all pregnancies involving women with high BMI values.[12]

Some hypothesized mechanisms thought to cause preeclampsia are the chronic uteroplacental ischemia, immune maladaptation, very low-density lipoprotein toxicity, genetics, increased trophoblast apoptosis or necrosis, and excessive

maternal inflammatory response to depleted trophoblasts. Recent mechanisms suggest a possible role of angiogenic factor imbalance in the pathogenesis of preeclampsia. A combination of some of these claimed mechanisms may be responsible for triggering the clinical spectrum of preeclampsia.[4]

According to the study, women with one of the high-risk factors for preeclampsia (previous pregnancy with preeclampsia, multifetal pregnancy, renal disease, autoimmune disease, type 1 or type 2 diabetes mellitus, and chronic hypertension) and women with more than one moderate risk factor (first pregnancy, maternal age >35 years or older, BMI >30, family history of preeclampsia, sociodemographic characteristics, and personal history factors) should receive low-dose aspirin (81 mg/ day) for preeclampsia prophylaxis. The dose can be given starting between 12 weeks and 28 weeks of pregnancy (optimal before 16 weeks of pregnancy) and continuing until delivery.[4,13]

The limitations of this study are the lack of comorbid variables, such as diabetes mellitus, and a history of preeclampsia on previous pregnancy, which also contribute to incidence of preeclampsia. Meanwhile, this study could represent various preeclampsia cases in Banyumas because Margono Hospital is one of the tertiary referral health centers in Central Java. Further study based on demographic factors is needed to corroborate the causal relationship between risk factors and the incidence of preeclampsia.

Conclusion

The results of this study showed that age ≥35 years, BMI ≥30, and primiparity were associated with preeclampsia.

Conflict of Interest

The authors have no relevant conflicts of interest in writing this article.

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