

RISK FACTORS ASSOCIATED WITH SEVERE PRE-ECLAMPSIA

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ABSTRACT

PEB (severe pre-eclampsia) is influenced by several variables, including maternal age during pregnancy, parity, gestational age, number of fetuses, frequency of antenatal care (ANC) appointments, and any history of hypertension. Identifying these elements among particular groups helps to direct successful therapeutic interventions and inform public health policies. This study was designed as a case-control study and used analytic observational techniques. Data were collected from the medical records of women giving birth and without preeclampsia at the obstetrics and gynecology department of Dr. Slamet General Hospital in Garut. The results of bivariate analysis using the chi-square test showed that there was no significant relationship between risk factors, including maternal age, parity, gestational age, number of fetuses, and ANC visits, with p-values greater than 0.05. based on multivariate analysis using logistic regression testing, it was found that pregnant women over the age of 35 had a higher risk of developing severe preeclampsia, with a significance value of $p = 0.034$. these findings indicate that maternal age over 35 and a history of hypertension play a role in increasing the likelihood of PEB.

Keywords: hypertension; hospital; maternal, risk factors, severe pre eklampsia

INTRODUCTION

It should be emphasized that although data shows a downward trend over the past 15 years, maternal mortality rates in Indonesia remain quite high. Further reductions can be achieved through improved access to quality health services, increased early detection, equitable distribution of health workers, and social interventions that support pregnant women. Although maternal mortality rates have declined significantly from 1994 to 2017, Indonesia still has highest maternal mortality ration (MMR) in Asia. The main causes of maternal mortality has shifted. Previously, it was predominantly caused by hemorrhage and infection, but now pregnancy-induced hypertension such as severe preeclampsia (PEB) has become one of the main causes. If PEB is not treated quickly and appropriately, this condition can develop into eclampsia, which significantly increases. From 2016 to 2020, Indonesia MMR was recorded at around 249 deaths per 100,000 live births, with most deaths due to complications from pregnancy-induced hypertension (Syairaji et al., 2024).

To date, the exact cause of preeclampsia remains unclear, which is why it is often referred to as a “theoretical disease”. However, recent studies have consistently highlighted three main pathways: immunological disorders in the mother and fetus, imbalances in various vascular mediators including prostaglandins, and impaired placental blood flow (uteroplacental ischemia) (Javandoust Gharehbagh F, Soltani-Zangbar MS, 2024). Severe pre-eclampsia in pregnant women does not occur by chance, there are various risk factors that play an important role. Based on recent studies, factors such as maternal age, parity, gestational age, twin or multiple pregnancies, number of ANC visits, and history of chronic hypertension have been shown to be strongly associated with the risk of developing severe pre-eclampsia (Wulandari et al., 2021). The basic mechanism from pre-eclampsia to eclampsia starts with vasospasm, which is the narrowing of blood vessels. This condition causes blood flow to be obstructed, resulting in increased blood pressure in the arteries and hypertension (Retnaningtyas, 2021). Angiotensin II also triggers contraction in endothelia cells. As a result, the structure and function of the endothelium are disrupted, increasing the risk of damage and causing gaps between cells that

allow fluid leakage (Loppies et al., 2024). This condition also occurs along with hypoxia in the blood vessels and surrounding tissues, which is thought to contribute to bleeding, tissue death (necrosis), and damage to other vital organs.

Preeclampsia is a serious complication of pregnancy that can occur during pregnancy (antenatal), during labor (intranatal), or after childbirth (postartum). This condition is individualistic, so the symptoms that appear can vary from one pregnant women to another. Based on recent research, the main clinical signs commonly found in cases of preeclampsia include high blood pressure (hypertension), protein in the urine (proteinuria), and swelling (edema). Although the order in which symptoms appear may vary, edema is often the first sign, followed by hypertension and proteinuria. This understanding is important for detecting preeclampsia early and preventing more severe complications (Tanner MS, Davey MA, Mol BW, 2022).

A diagnosis of severe preeclampsia can be made if a pregnant women at 20 weeks of gestation or older has consistently high blood pressure $\geq 140/90$ mmHg, accompanied by evidence of protein the urine equivalent to ≥ 300 mg per 24 hours or 1 on a dipstick test. These criteria are repeated to confirm the diagnosis, as the combination of hypertension and proteinuria is a key indicator of severe preeclampsia (Karrar SA, Martingano DJ, 2024), (Bisri & Bisri, 2025), (Fishel Bartal et al., 2022), (Stefańska et al., 2020). Several modern studies confirm that risk factors such as first pregnancy (nulliparity) and maternal age above 35 years are strongly associated with severe preeclampsia. Women who have never been pregnant before are known to have nearly three times the risk of developing preeclampsia compared to those who have been pregnant. This study was conducted with the aim of identifying various risk factors associated with severe preeclampsia in pregnant women.

METHOD

This study was conducted at the Medical Records Subdivision of Dr. Slamet General Hospital, Garut Regency, from August 2024 to February 2025. A total of 74 cases and 74 controls were sample in this study. The subjects included mothers with severe preeclampsia who were treated or had undergone treatment, as well as mothers without preeclampsia at Dr. Slamet General Hospital, Garut Regency, who met the inclusion criteria and were not covered by the exclusion criteria. Sampling was conducted using simple random sampling. Every member of the population has an equal opportunity in basic random sampling to be chosen as a participant. The subjects included mothers without preeclampsia as well as mothers with serious preeclampsia who were either treated or had undergone treatment. First, a comprehensive list of all the target group's participants is created. Participants are then chosen at random until the required sample size is reached using a random number generator, lots, or random selection program. This approach guarantees the sample fairly represents the population and helps to lower selection bias. The collected data were processed using computers and analyzed descriptively, followed by bivariate analysis using the chi-square test at a significance level of $p < 0.05$, and multivariate analysis using logistic regression at a significance level of $p < 0.05$.

RESULT

Table 1, it can be seen that the distribution of maternal age, parity, gestational age, number of fetuses, and frequency of ANC visits in the groups of mothers with and without PEB show almost similar figures. However, differences were found in the variable of history of hypertension, which only appeared in mothers with PEB.

Table 1.
Frequency distribution of research subjects according to characteristics

Characteristics	PEB		Without PEB		Total		
	f	%	f	%	f	%	
Mother's age	<20	2	2,7	1	1,4	3	2,1
	20-35	49	66,2	61	82,4	110	74,3
	>35	23	31	12	16,2	35	23,6
	Total	74	100	74	100	148	100
Parity	Primigravida	22	29,8	29	39,2	51	34,5
	Multigravida	52	70,2	45	60,8	97	65,5
	Total	74	100	74	100	148	100
Gestational age	20-36	26	35,2	8	10,8	33	23
	≥35	48	64,8	66	89,2	115	77
	Total	74	100	74	100	148	100
Number of fetuses	Singles	70	94,6	72	97,2	142	95,9
	Twins	4	5,4	2	2,8	6	4,1
	Total	74	100	74	100	148	100
Number of ANC visits	<4	22	29,8	12	16,2	34	23
	≥4	52	70,2	62	83,8	114	77
	Total	74	100	74	100	148	100
History of hypertensoin	Yes	11	14,8	0	0	11	7,4
	No	63	85,2	74	100	137	92,6
	Total	74	100	74	100	148	100

Table 2.

Multivariate analysis using logistic regression on the variable of maternal age, party, number of fetuses, and number of ANC visits.

Variable	PEB				P	95%CI
	Yes		No			
	N	%	N	%		
Mother's age						
<20 years	2	2,7	1	1,4	0,378	2,996 (0,262-34,287)
20-35 years	49	66,2	61	82,4		1
>35 years	24	31	12	16,2	0,034	2,386 (1,069-5,326)
Parity						
Primigravida	22	29,8	29	39,2	0,721	0,872 (0,410-1,852)
Multigravida	52	70,2	70,2	60,8		1
Number of fetuses						
Twins	4	5,4	2	2,8	0,316	2,649 (0,422-14,431)
Single	70	94,6	72	97,2		1
Number of ANC visits						
<4	22	29,8	12	16,2	0,051	2,237 (0,996-5022)
≥4	52	70,2	62	83,8		1

Based on Table 2, it was found that the variables with p-values > 0.05 were maternal age below 20 years, parity, number of fetuses, and number of ANC visits.

DISCUSSION

Table 1, the results of bivariate analysis using the chi-square test showed a p-value of 0.186. since the p-value considered significant is < 0.05, these results indicate that there is no significant relationship between maternal age and severe preeclampsia (PEB). Thus, PEB can occur in various age groups of mothers. However, mothers aged <20 years or >35 years are categorized as having a higher risk of developing severe preeclampsia. In general, the ideal reproductive age for a woman is between 20 and 35 years old. In a retrospective study at Kasma et al., (2024), more than half of severe preeclampsia cases occurred in mothers of extreme age

(< 20 or > 35 years), even though the majority of the sample was within the productive age range (20-35 years). Furthermore, an analytical study at Kusmintarti et al., (2024) confirmed a significant association between maternal age and preeclampsia ($p = 0.001$), with extreme age suspected to be an independent risk factor. At Utari & Hasibuanb, (2022), case-control analysis also concluded that maternal age plays a role in the incidence of preeclampsia ($p < 0.05$), reinforcing the finding that being too young or too old increases the risk. In Malaysia Sutan et al., (2022), discrepancies in the prevalence of preeclampsia between age group show that 19.5% of mothers aged > 35 years experience preeclampsia, which is much higher than mothers under 20 years of age.

The results of the analysis of parity showed an Odds Ratio (OR) of 1.318 with a 95% Confidence Interval (CI). This indicates that primigravida mothers are 1.318 times more likely to experience severe preeclampsia (PEB) than multigravida mothers. However, the chi-square test yielded a p-value of 0.1, indicating no significant association between parity and the occurrence of PEB. Thus, PEB can occur in both primigravida and multigravida mothers. This finding is in line with research conducted by Rospia et al., (2021) at Panembahan Senopati Bantul Regional General Hospital, which reported that parity was not significantly associated with the incidence of preeclampsia ($p > 0.05$). Similar results were obtained in a multicenter study in Ghana (Asare et al., 2023), where primigravida had a relatively higher risk of experiencing PEB (OR = 1.95), but the relationship was not statistically significant in the wider population. On the other hand, some studies show different results. A systematic review by Meazaw et al., (2020) in Sub-Saharan Africa reported that primigravida mothers are 2.5 times more likely to experience preeclampsia than multiparas (OR = 2.52; 95% CI: 1.19-3.86), so parity is considered an important risk factor in the occurrence of preeclampsia. Similar results were found in a study at Muhammad Sani Karimun Regional General Hospital Bratasena & Henriette, (2021), which reported that multiparous women had a 6.875 times higher risk of experiencing PEB (95% CI: 3.318-12.410). The differences in results between studies may be due to variations in population characteristics, sample size, and other risk factors that interact with the occurrence of preeclampsia. Thus, the results of this study indicate that PEB can occur in both primigravida and multigravida mothers, although statistically no significant relationship was found between parity and the incidence of PEB in the study population.

The results of the analysis on the variable of gestational age showed an Odds Ratio (OR) of 1.375 with a 95% Confidence Interval (CI), indicating that mothers with a gestational age of ≥ 37 weeks had a 1.375 times greater chance of experiencing severe preeclampsia (PEB) compared to mothers with a gestational age of 20-36 week. However, the chi-square test yielded a p-value of 0.298, indicating no statistically significant association between gestational age and the occurrence of PEB. These findings suggest that PEB can occur in all gestational age groups above 20 weeks, regardless of specific gestational age categories. Several previous studies have evaluated the relationship between gestational age and the incidence of severe preeclampsia (PEB). A retrospective study in Boadu et al., (2025) reported that the prevalence of PEB varied according to gestational age with a rate of 4.0% at 39-40 weeks of gestation and only 2.3%-2.1% at < 37 weeks and 37-38 weeks. However, these differences did not reach statistical significance, so gestational age cannot be concluded as a major predictor of PEB. Similar findings were reported in a recent meta-analysis (2023) that distinguished between early onset preeclampsia (< 34 weeks) and late onset (> 34 weeks), where gestational age did not have a significant contribution as an independent determinant. These results emphasize that other variables, such as maternal age and medical comorbidities, play a more significant role in the occurrence of PEB (Boadu et al., 2025). In addition, machine learning-based research by (Azhari Fadhilah et al., 2024) also showed similar results, where the gestational age at screening

(around the second trimester) did not differ significantly between the preeclampsia group and the control group ($p = 0.525$). The study emphasized that although gestational age is important for determining the classification of preeclampsia, it is not an independent risk factor in predicting the occurrence of PEB.

The analysis of the number of antenatal care (ANC) visits showed an Odds Ratio (OR) of 0.545 with a 95% confidence interval (CI). This finding indicates that mothers with fewer than 4 ANC visits have a 0.545 times greater likelihood of experiencing severe preeclampsia (PEB) compared to mothers who had ≥ 4 ANC visits. However, the chi-square test yielded a p-value of 0.161, indicating no statistically significant association between the number of ANC visits and the occurrence of PEB. Therefore, the number of ANC visits is not direct factor influencing the occurrence of PEB. A study by (Mardiyah et al., 2022) recorded an average of 7.5 ANC visits but found no significant association with morbidity or maternal mortality due to PEB ($p = 1.000$). In contrast, research in Ethiopia (Tesfa et al., 2023) reported that low frequency of ANC visits (below WHO standards) increased increased the likelihood of developing preeclampsia by 5.43 times (AOR = 5.43; 95% CI: 2.86-10.33). Consistent results are reinforced by research in (Desriva et al., 2023) showing a significant association between ANC compliance and the incidence of pre-eclampsia. This indicates that the quality and intensity of ANC monitoring also influence pregnancy outcomes.

Analysis of the number of fetuses variable showed an Odds Ratio (OR) of 0.500 with a 95% Confidence Interval (CI), indicating that mothers with multiple pregnancies (twins) are 0.500 times more likely to experience severe preeclampsia (PEB) than mothers with single pregnancies. However, the chi-square test yielded a p-value of 0.069, meaning there is no statistically significant association between the number of fetuses and the occurrence of PEB. Therefore, the number of fetuses has not been proven to influence the risk of PEB in the studied population. Similar results were reported in Norway by Laine et al., (2019), where the adjusted OR reached 4.07 (95% CI 3.65-4.54; $p = 0.001$), reinforcing the evidence that multiple pregnancy is n independent risk factor for preeclampsia. Furthermore, a study in Shanghai (Zhu et al., 2023) highlighted that increased fetal growth discordance ($> 25\%$) in multiple pregnancies was associated with a 2.44-fold increased risk of PEB (95% CI 1.74-3.42), confirming that fetal growth dynamics also contribute. On the other hand, research in Ethiopia shows that twin pregnancies with PEB greatly increase the probability of premature birth (adjusted OR 2.58; $p < .05$), indicating that twins worsen pregnancy outcomes when PEB occurs (Sium et al., 2022). The Chinese twin preeclampsia prediction model (2022) also confirmed multiple pregnancy as a significant variable (probability 13.16%), along with other factors (primiparity, pre-eclampsia BMI), supporting the importance of risk monitoring in antenatal care for this group (Han et al., 2022).

The results of the analysis of the hypertension history variable showed that all respondents with a history of hypertension experienced severe preeclampsia (PEB). Based on the data obtained, there were no mothers with a history of hypertension who did not experience PEB. Therefore, statistical analysis using the chi-square test could not performed. Thus, it can be concluded that in the group of mothers who did not experience PEB, there was no previous of hypertension. Analysis of the variable of pre-pregnancy hypertension history shows that no mothers with a history of hypertension were free from severe preeclampsia, so the chi-square test could not be applied. Thus, in the group of mothers without PEB symptoms, no previous history of hypertension was found indicating that chronic hypertension with a certain frequency and duration is a strong predisposing factor for the development of PEB. This is supported by the study by Nie et al., (2024), where 24.7% of women with chronic hypertension developed PEB

compared to only 4% without hypertension; the risk increased in patients with hypertension >3 years and inadequate use of antihypertensive medications.

The selection of candidate variables for multivariate analysis was based on the results of bivariate analysis using the chi-square test, with a criterion value of $p < 0.25$. of the six variable analyzed, four variables met the criteria, namely maternal age ($p = 0.186$), parity ($p=0.1$), number of fetuses ($p = 0.69$), and number of ANC visits ($p = 0.161$). based on these results, variables with p -values > 0.05 , including maternal age < 20 years, parity, number of fetuses, and number of ANC visits, were deemed statistically insignificant because they did not meet the significance threshold of $p < 0.05$. Meanwhile, the only variable that showed statistical significance was maternal age > 35 years with a p -value of 0.034 and a 95% Confidence Interval (CI) of 2.386 (1.069-5.326).

CONCLUSION

The results of this study indicate that maternal age > 35 years and a history hypertension are significant risk factors for severe preeclampsia (PEB). Although other variables such as parity, gestational age, number of fetuses, and frequency of antenatal care (ANC) visits did not show statistically significant associations, these findings emphasize the importance of close monitoring of older pregnant women and those with a history of hypertension as a preventive measure to reduce maternal morbidity and mortality due to PEB.

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