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The incidence of preeclampsia based on maternal characteristics: a cohort study

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ABSTRACT

Preeclampsia is one of the leading causes of maternal mortality. Research on the characteristics of mothers who are at risk for preeclampsia at the first pregnancy visit is important to prevent the incidence of preeclampsia. This study aims to determine the incidence of preeclampsia based on maternal characteristics. A cohort study design was used to determine the effect of maternal characteristics on the incidence of preeclampsia Sample was pregnant women who made their first pregnancy visit. The analysis was chi-square. The results showed that the factors that were significantly associated with the occurrence of preeclampsia were: primigravida (P-value: 0.00), family history of preeclampsia (P-value: 0.00), occupation (P-value:0.04), and insurance ownership (P-value:0.03). A risk assessment of preeclampsia in pregnant women can be carried out at the time of the first antenatal visit.

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INTRODUCTION

The World Health Organization (WHO) estimates that 16% of maternal deaths occur due to hypertensive disorders in pregnancy, where eclampsia is the most common cause (1). The maternal mortality rate due to complications of eclampsia in the last fourteen years is 19.6% - 46% and while fetal death is around 65%.(2),(3) Maternal mortality in Indonesia in 2012, 32.5% was caused by hypertension, preeclampsia, and eclampsia, while in 2015 it was 24.22% and in 2016 it was 26%.(4) Maternal mortality in Central Java in 2015 was 26.34% due to hypertension. Currently, Central Java is one of the provinces with the second highest maternal mortality after West Java.(5) One of the causes of high mortality due to hypertension is the delay in early detection in pregnancy.(6)

Early detection of preeclampsia, and adequate monitoring, can prevent the deterioration of the condition of mothers with preeclampsia, and can even reduce the possibility of recurrent preeclampsia. Pregnancy counseling, the accuracy of the initial visit, and the quality of care for pregnant women at risk of preeclampsia are the keys to the management of appropriate care.(7) The complexity of treatment in early-onset preeclampsia has an impact on the cost and length of treatment time. Often the mother must be referred to a tertiary health facility with intensive care. Not only that, babies also often need an extended period of intensive care.(8,9) Early detection of preeclampsia in Indonesia is by checking blood pressure and urine protein. Currently, preeclampsia

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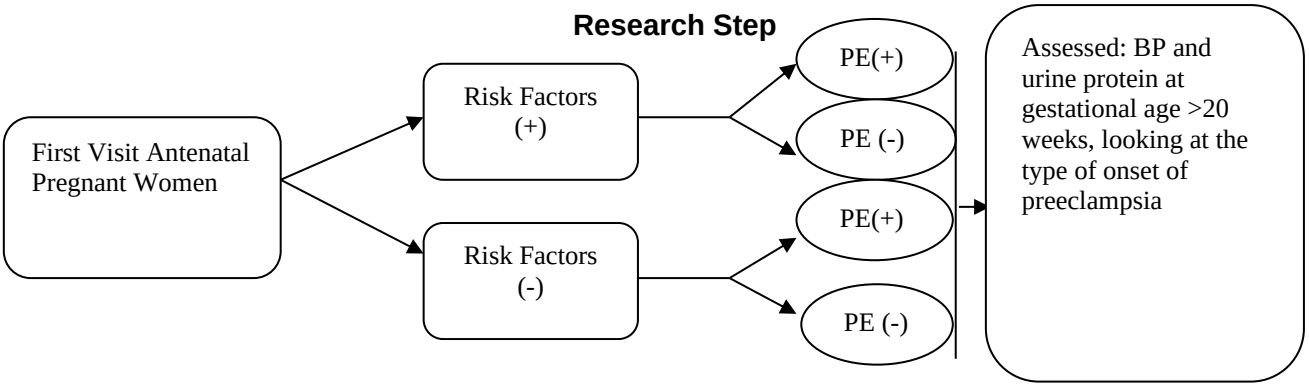
screening based on maternal characteristics has not been carried out during the first visit. Antenatal monitoring was carried out at least four times during pregnancy (K4). Pregnant women with K4 status have received at least 10T services (examination of uterine fundal height, weight, blood pressure measurement, administration of TT immunization, administration of at least 90 tablets of additional blood, tests for sexually transmitted diseases, and interviews in preparation for referrals). Thus, risk factors related to anemia, preeclampsia, bleeding, or other risk factors can be prevented, including referral to a more complete level of service.(4) The midwife's authority in the first visit to carry out antenatal care at the initial visit aims to: detect problems that can be handled before endangering the mother's life, prevent problems such as neonatal tetanus, preeclampsia, anemia, harmful traditional habits, build a trusting relationship, start preparation for birth and face complications.(10)

The number of pregnant women in Cilacap Regency in 2016 reached 32,329 people. Twenty percent of them are high-risk pregnancies. The number of pregnancies with preeclampsia was 7.2%. In 2016 the number of deaths was 25 cases with the cause of bleeding at 28%, preeclampsia at 20%, and other causes: at 52%. In 2015 the number of deaths was 26 cases: bleeding and preeclampsia: 31%, other causes: 31%, infection: 7%. The number of maternal deaths in Cilacap Regency In 2014 as many as 36 cases, the cause of maternal death in Cilacap Regency 3 cases due to bleeding, 8 cases due to preeclampsia and eclampsia, and 25 cases due to other causes.(11)

Until now, the etiology of preeclampsia is unknown, there have been many theories that have tried to explain the causes of the disease, but none have been able to provide a satisfactory answer.(12) Talking about its pathophysiology is nothing more than "collecting" useful phenomena findings. Until now, 3 (three) theories underlie the pathogenesis of preeclampsia, namely: placental ischemia, immunological factors, and genetic factors.(12–15) Based on this, it can be concluded that preeclampsia is currently the highest cause of maternal death in the Cilacap district. Based on the preliminary study, the researcher wanted to know how the influence of maternal characteristics on the incidence of preeclampsia. It is important to make preventive efforts against complications of preeclampsia in pregnant women.

METHOD

This study was conducted with a cohort design, starting from K1 pregnant women until delivery. The sampling technique used was the accidental sampling of pregnant women who made their first pregnancy visit. The number of K1 pregnant women at the Kroya 1 Health Center in 2016 was 1,034 people (with an average of 86 people per month) and at the Adipala 1 Health Center was 1,025 people (with an average of 85 people per month). Based on the calculation of Cohen Manion and Marrion with a 95% confidence degree and an alpha of 0.05, the sample size is 462 people(16). In anticipation of dropping out, 15% was added to 531 people with inclusion criteria: patients with K1 at 16 weeks of gestation. Data collection was carried out by the midwife at the time of K1 of the patient by conducting an assessment of the risk factors for preeclampsia which were maternal factors: age, parity, gestational age, BMI, family history of preeclampsia, marital history, and waist circumference. Furthermore, patients were grouped into risk groups and non-risk groups and followed up until delivery. Data analysis using chi-square. The description of the implementation of the research is as follows:



RESULTS

Maternal Characteristics

An overview of the characteristics of pregnant women can be seen in Table 1.

Table 1. Characteristics of Respondent

Variable	Category	N=549	%
Education level	Low	201	36.6
	Middle/High	348	63.3
Women's job	No working/housewife	367	66.8
	working	182	33.2
Husband's job	Farm workers	153	27.9
	Trade	12	2.6
	Private sector employee	316	57.6
	civil servant	68	11.9
Income	< Regional minimum salary	450	81.9
	≥ Regional minimum salary	99	18.1
insurance ownership	Yes	388	70.8
	No	161	29.2
Parity	Primigravida	96	17.5
	Multigravida	453	82.5
Pregnancy Interval	< 10years	484	88.2
	≥ 10 years	65	11.8
Age	<20 years or >35 yeras	102	18.6
	20-35 years	447	81.4
Body Mass Index	< 35 kg/m^2	508	92.5
	≥ 35 kg/m^2	41	7.5
Family history of preeclampsia	Yes	33	6.0
	No	516	94.0
Marriage History	1	512	93.3
	≥ 2	37	6.7
Waist size	< 80 cm	509	92.7
	≥ 80 cm	40	7.3

Based on the table above, it can be seen that the education level of the mother in the Middle/High category is 63.4%. Based on the wife's occupation, the most in the category of not working / housewives is equal to 66.8%. Most of the respondents' husbands work as private employees 57.6%. As for based income, the most in the < UMR category, which is 81.9%. Health insurance ownership has the most insurance, both insurance in the form of financing by the government (BPJS PBI) / own cost (Non-PBI) and other private insurance, which is 70.8%.

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Screening for preeclampsia risk factors was carried out at the first visit (K1), so the results of the screening carried out were the results at K1. Based on Table 1, it can be concluded that the frequency distribution of the risk of preeclampsia based on the characteristics of the mother in primigravida is 17.5%, gestational interval 10 years is 11.8%, maternal age <20 years and > 35 years is 18.6%, BMI > 35 kg/m2 of 7.5%, family history of preeclampsia 6.0%, history of marriage more than 1 time ≥ 6.7%, waist circumference > 80 cm by 7.3%. The risk factors for preeclampsia in hypertension in pregnancy and previous history of preeclampsia are 0.7%. Meanwhile, the incidence of multiple pregnancies was 0.5%, and diabetes mellitus suffered by pregnant women was 0.2%.

Prevalence of Preeclampsia

The number of occurrences of preeclampsia can be seen in Table 2:

Table 2. Prevalence of Preeclampsia in Cilacap Regency August 2018 to July 2020 (N=549)

Preeclampsia	F	%
Positive	39	7.1
Negative	510	92.9

Based on the table above, it was found that the prevalence of preeclampsia at the Kroya 1 and Adipala 1 health centers was 7.1% during the period from August 2018 to July 2020.

Maternal Characteristics of Preeclampsia

The description of the characteristics of pregnant women with preeclampsia in the period August 2018 to July 2020 is in Table 3:

Table 3 Description of the Characteristics of Mothers with Preeclampsia in Cilacap Regency August 2018 to July 2020

Characteristics	Category	Type of PE	
		Early Onset (n=7) (%)	Late Onset(n=32) (%)
Education level	Low	28.6	41.7
	Middle/High	71.4	58.3
Women's job	No working/housewife	85.7	81.2
	working	14.3	18.8
Husband's job	Farm workers	14.3	37.5
	Trade	0.0	0.0
	Private sector employee	57.2	50.0
	civil servant	28.5	12.5
Income	< Regional minimum salary	85.7	83.3
	≥ Regional minimum salary	14.3	16.7
insurance ownership	Yes	71.5	87.5
	No	28.5	12.5
Parity	Primigravida	57.1	40.6
	Multigravida	42.9	59.4
Pregnancy Interval	< 10years	14.3	3.1
	≥ 10 years	85.7	96.9
Age	<20 years or >35 yeras	0.0	37.5
	20-35 years	100.0	62,5

Characteristics	Category	Type of PE	
		Early Onset (n=7) (%)	Late Onset(n=32) (%)
Body Mass Index	< 35 kg/m^2	42.9	6.2
	≥ 35 kg/m^2	57.1	93.8
Family history of preeclampsia	Yes	57.1	56.2
	No	42.9	43.8
Marriage History	1	0.0	9.4
	≥ 2	100.0	90.6
Waist size	< 80 cm	42.9	6.2
	≥ 80 cm	57.1	93.8

Based on the table above, it can be concluded that the majority of patients with early-onset preeclampsia are in secondary/higher education, which is 71.5%, household work is 86.4%, a private husband is 57.2%, income < UMR is 85.7%, and have insurance that is equal to 71.5%. While the majority of late-onset preeclampsia were at the secondary/higher education level, namely 51.2%, the work as household workers were 79.2%, the husband's occupation was 50%, with income < UMR which was 83.3%, and had insurance of 91, 7%.

As for the risk factors for preeclampsia, the incidence of early-onset preeclampsia in primigravida was 57.1%, gestational distance > 10 years was 14.3%, there were no mothers with age < 20 years and > 35 years, BMI > 35 kg/m2 as many as 42.9%, family history of preeclampsia 57.1%, none had a history of marriage > 2, waist circumference > 80 cm by 42.9%, multiple pregnancies by 14.3%, diabetes mellitus by 14.3 %, hypertension was 28.6% and a history of preeclampsia in a previous pregnancy was 6.2%.

The correlation of maternal characteristics to the incidence of preeclampsia

The relationship between factors and the incidence of preeclampsia is shown in Table 4

Table 4. The relationship between maternal characteristics and the incidence of preeclampsia in Cilacap Regency from August 2018 to July 2020 (N=549)

Variable	Category	Preeclampsia				RR (CI 95%)	P
		Yes (n:39)	%	No (n=510)	%		
Education level	Low	15	38.5	186	36.4	1.1 (0.5-2.0)	0.08
	Middle/High	24	61.5	324	63.6		
Women"s job	No working/ housewife	32	82.1	335	65.7	0.4(0.2-0.9)	0.03
	working	7	17.9	175	34.3		
Husband"s job	Farm workers Trade Private sector employee civil servant	31 8	79.5 20.5	419 91	82.2 17.8	0.9 (0.4–1.7)	0.67
Income	< Regional minimum salary	6	16.7	155	30.4	0.4 (0.2-1.0)	0.04
	≥ Regional minimum salary	33	83.3	355	69.6		
insurance ownership	Yes	17	43.6	79	15.5	3.6 (2.0-6.6)	0.00
	No	22	56.4	431	84.5		
Parity	Primigravida	2	5.1	63	12.4	0.4 (0.0-1.6)	0.18

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Variable	Category	Preeclampsia				RR (CI 95%)	P
		Yes (n:39)	%	No (n=510)	%		
	Multigravida	37	94.9	447	87.6		
Pregnancy Interval	< 10years ≥ 10 years	12 27	30.8 69.2	90 420	17.6 82.4	1.,9 (1.0-3.7)	0.04
Age	<20 years or >35 yeras 20-35 years	5 34	5,6 94,4	36 474	7.1 92.9	1.8 (0.07-4.4)	0.18
Body Mass Index	< 35 kg/m^2 ≥ 35 kg/m^2	22 17	56.4 43.6	11 499	2,2 97,8	20.2 (11.9-34.2)	0.00
Family history of preeclampsia	Yes No	3 36	7.7 92.3	34 476	6.7 93.3	1.2 (0.4-3.6)	0.8
Marriage History	1 ≥ 2	5 34	12.9 87.1	35 475	6.9 93.1	1.8 (0.7-4.5)	0.16

Based on the table above, it is known that the significant factors associated with the occurrence of preeclampsia are: primigravida, family history of preeclampsia, age, occupation, and insurance ownership with a P-value < 0.05. The level of education, income, body mass index, marital history, waist circumference, multiple pregnancies, and gestational spacing showed no significant association with the incidence of preeclampsia with a P-value > 0.05.

DISCUSSION

Based on the results of the study, it was found that the primigravida factor had a significant relationship with the incidence of preeclampsia. This is under the research that Nulliparas have almost 3 times the risk of developing preeclampsia (through cohort studies. And women with preeclampsia are twice as nulliparous as compared to multipara through case-control studies(17–19)

Nulliparous have higher sFlt1 and sFlt1 / PlGF than multiparous which causes an angiogenic imbalance that increases the risk of preeclampsia(20) The risk of preeclampsia in primigravida mothers is possible due to immune maladaptation of the fetus and placenta because pregnancy is an immune challenge between mother and fetus.(21,22) Several factors such as primigravida, multiple pregnancies, having a history of preeclampsia, and drinking alcohol during pregnancy are risk factors for pre-eclampsia/eclampsia, that nutritional counseling during pregnancy in ANC is important and health workers are advised to use factors: primigravida, history of preeclampsia, and Gemelli pregnancy as a screening tool for the prediction of preeclampsia.(23)

It is now found that preeclampsia occurs in two stages: the first stage is placental insufficiency, which results in reduced perfusion, followed by maternal symptoms such as hypertension and urinary protein, both of which cause endothelial dysfunction. For this reason, preeclampsia is common in primigravida.(24)

Based on this, health workers need to prevent preeclampsia in primigravida mothers. Prevention can be done by doing primary prevention through lifestyle settings. In addition, prevention by giving calcium tablets as recommended by WHO can be done if the mother has a low calcium intake. No less important is monitoring the incidence of complications of preeclampsia to prevent complications in the mother and fetus.

Based on the results of the study, it was found that there was no relationship between the distance of pregnancy and the incidence of preeclampsia. This shows that pregnant women with a distance of pregnancy > 10 years have almost the same risk of developing preeclampsia compared to pregnant women with a distance of < 10 years. This result contrasts with the results of a systematic review from a large population-based

cohort that showed evidence: when compared with 2 to 4-year interpregnancy intervals, shorter intervals were not associated with an increased risk of recurrent preeclampsia. However, the risk appears to increase at longer intervals between pregnancies.(25) In line with this study, it was found that the long distance between pregnancies, such as more than ten years, was a high-risk factor for preeclampsia because it was similar to nulliparous.(26) This difference is possible due to the difference in the number of samples taken. In line with this study, it was found that the interval of pregnancy affected changes in the Mean Artery Pressure (MAP) in women whose previous pregnancies had preeclampsia.(27) Although it shows an insignificant relationship if the number of samples is increased, it is possible to see a significant relationship between the distance of pregnancy and the incidence of preeclampsia.(28)

WHO recommends that the safe distance between deliveries is at least 2 years.(29) This is because if the distance is less than 18 months or more than 59 months, there is a risk of low birth weight, IUGR, and premature labor.(30) Meanwhile, the longer delivery distance will increase the risk of preeclampsia.

Pregnancy spacing is a combination of social behavior and physiological factors. A change in a partner is often associated with a longer pregnancy interval. For mothers with long gestation intervals coupled with changing partners, the risk of developing preeclampsia will be greater, compared to mothers with the same partner.(31)

Currently, there is an increase in the interval of pregnancy could be due to long-term use of contraception. This condition has a risk of increasing the occurrence of complications such as postpartum hemorrhage by 17.3% and preeclampsia by 20.4%.(32) The results of the study by Trogstad et al. found that in women whose first pregnancy did not have preeclampsia, the risk of preeclampsia increased as the gestational interval lengthened, whereas, in women with a history of preeclampsia in a previous pregnancy, the risk of preeclampsia in subsequent pregnancies decreased as the gestational interval lengthened.(33)

Based on this study, found that there was a significant relationship between age and the incidence of preeclampsia. This shows that pregnant women aged < 20 years or > 35 years have a nearly doubled risk of developing preeclampsia compared to women at 20-35 years old. Young mothers are associated with poor pregnancy outcomes.(34) This is because young mothers are unprepared for biological and social factors, bad behavior such as smoking, malnutrition, and low antenatal care.(35) This is in line with the results of Lamminpää's (2012) study that preeclampsia is more common than in younger women, and their pregnancies are more likely to be complicated by preterm labor and impaired fetal growth.(36) Chan et al said differently that younger maternal age was consistently associated with a lower risk of preeclampsia by showing an increasing incidence every year from 14 - 25 years old.(37)

The risk of developing preeclampsia is almost twice as high for mothers aged 40 years as for women aged < 30 years (OR 1.87).(38) This is possible because of pre-existing diseases such as diabetes mellitus or chronic hypertension.(39,40) Increasing age during pregnancy has been shown to increase the risk of hypertension by 30% for those aged 35 to 39 years, and almost 80% for those aged > 40 years, and has a 2-3 times risk of developing preeclampsia.(41)

The results of the analysis in this study indicate that there is a relationship between BMI and the incidence of preeclampsia. This is following the results of a study in Tanzania (2018) that overweight pregnant women have a risk of preeclampsia of 1.4 – 1.8 times compared to underweight.(42) The risk of preeclampsia usually increases with every increase in BMI of 5-7 kg/m2 before pregnancy.(43) Obesity is a strong risk factor for preeclampsia, with a variation of 4.3% in mothers with a BMI <19.8 kg/m2 to 13.3% in women with a BMI>25 kg/m2.(44)

The increased risk of preeclampsia in obese women may be due to increased cytokine-mediated inflammation and enhancement, dyslipidemia, and increased

sympathetic activity.(12) Obesity is a risk factor for Late Onset Preeclampsia with 1,056 [1,047–1,064] with *a P value*: <0,001.(45) For this reason, pregnancy planning is quite important, how health workers provide health education to women to regulate their diet to avoid obesity during pregnancy planning.

Increased body fat is associated with increased levels of cytokines. Obese women are more likely to initiate pregnancy with subclinical inflammation than women of normal weight. Studies have shown that BMI is positively correlated with neutrophil infiltration into blood vessels, vascular inflammation, and increased blood pressure in women.(46) Obesity is associated with excessive activation of Endothelin (ET)-1. Overweight and obese humans increase endothelial dysfunction.(47) This proves that obese women have a risk of developing preeclampsia.

Based on the results of the analysis, it was found that there was a significant relationship between family history and preeclampsia and the incidence of preeclampsia. This shows that mothers with families (mothers or siblings) who experience preeclampsia tend to experience preeclampsia. Following the results of research by Boyd (2016) that women with a family history of preeclampsia have a strong risk of up to 150% to get *early-onset preeclampsia.*(48) The existence of familial factors in the risk of preeclampsia is possible because there is a genetic component in the development of severe preeclampsia.(49)

The results of this study are in line with research conducted by Bezzera et al (2010) that women with mothers who have a history of hypertension have an increased risk of preeclampsia (p = 0.003). The presence of preeclampsia in the mother increased the daughter's risk of developing severe preeclampsia (p = 0.007). In addition, a history of maternal eclampsia increased the daughter's risk of developing severe preeclampsia (p = 0.038). The risk of preeclampsia was also higher in women with a sister with a history of systemic hypertension (p < 0.001), preeclampsia (p < 0.001), or eclampsia (p = 0.008).(50)

Based on the results of the analysis, it was found that mothers with a history of marriage > 1 time (change partners) had a risk of experiencing preeclampsia by 1.2 times. This shows that mothers with multiple partners have a 17% higher risk of developing preeclampsia. Preeclampsia is more common in nulliparas but has been shown to increase in multiparous women who change partners.(51) In addition, women who use barrier contraception or who have contact with their husbands have a slightly greater risk of developing preeclampsia than women who do not use barrier contraception or who have longer contact with their husbands.(52) This may be due to a lack of exposure to semen, which could be one of the immunogenic factors in the etiology of preeclampsia. Another possibility is due to genetic factors, where there is a small number of men who cause preeclampsia in their wife's pregnancies.(53) Tubbergen explained that a change in partner may increase the risk of preeclampsia in subsequent pregnancies in Dutch multiparous women. This phenomenon can be explained well through the theory of *immune maladaptation.*(54) In women who change partners not long after their previous pregnancy, where the previous pregnancy did not develop preeclampsia, it is recommended to get pregnant early, so that there is no time to build immunity to paternal antigens. Because some women who wait longer to get pregnant with different partners have a greater risk of developing preeclampsia.(55)

The risk of preeclampsia is genetically attributable to the mother (35%), the fetus (20%), and the partner (13%). A change in partner increases the risk of preeclampsia by 1.6%, and it increases to 2.9% in a woman who is second pregnant with a man who has had a previous partner with preeclampsia.(56) Switching partners play a role in the risk of preeclampsia in subsequent pregnancies, depending on the presence of preeclampsia in previous pregnancies.(57) Paternal genetics plays an important role in the development of preeclampsia. Triploid (69 XXX), with paternal isodisomy in the placenta and fetus, increases preeclampsia-like symptoms at 19 weeks of gestation.(58) Based on this, it is

necessary to carry out intense monitoring of mothers with different partners, as well as preventive measures to reduce the risk of preeclampsia.

Based on the results of the study, it was found that pregnant women with a waist circumference of 80 cm tended to experience preeclampsia by 1,996 times more. Waist circumference can be a predictive indicator of preeclampsia with OR:2,7.(59) Waist circumference has been used as a reference to determine a person's nutritional status,(60) but rarely done during pregnancy. Waist circumference is associated with obesity, obesity increases insulin resistance and is associated with endothelial dysfunction and vasoconstriction, which contribute to cardiovascular disease.(61) Central fat accumulation causes hypertension, insulin resistance, and increased plasma fat.(62) Increasing waist circumference can be a way for health promotion to increase awareness of reducing waist circumference in mothers who are planning pregnancy.(63)

CONCLUSION

Based on the results of the analysis, it was found that there was a significant relationship between maternal factors and the incidence of preeclampsia, where primigravida had a risk of 3.6 times, age had a risk of 1.9 times, BMI > 35 kg/m2 had a risk of 1.8 times, women those who have a family history of preeclampsia have a risk of 20.2 times and if the mother is primigravida then the tendency is 3.6 times to experience preeclampsia, and mothers who are married more than once have a risk of 1.2 times to get preeclampsia. So that these factors can be used as the basis for promotive and preventive actions in the incidence of preeclampsia.

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