

## RISK FACTORS OF PREECLAMPSIA

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### ABSTRACT

*Preeclampsia affects about 4% of all pregnancies and is the major cause of maternal morbidity and mortality, fetal, and neonatal worldwide. There are risk factors that lead to preeclampsia in the pregnant woman. The purpose of this study was to determine the risk factors which most influence the incidence of preeclampsia. This was an observational analytic study with case-control study design. The populations were all pregnant and postpartum mothers who were treated in RSUD dr. Soeselo Slawi from January to June 2018. Total of samples were 222 which consist of 111 cases and 111 control sample. The sampling method of the case used simple random sampling technique. Data were obtained from medical records. The analyses which used in this study were chi-square test and multiple logistic regressions. The results showed there were a significant difference between the previous preeclampsia ( $p$ -value = 0,047), hypertension ( $p$ -value = 0,000), and diabetes mellitus ( $p$ -value = 0,057) in the case group and the control group. Multiple logistic regression analysis showed that hypertension is the most dominant risk factor that causes preeclampsia. Previous preeclampsia, hypertension, and diabetes mellitus are the risk factors that most influence the incidence of preeclampsia.*

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## INTRODUCTION

Preeclampsia affects about 4% of all pregnancies and is a major cause of maternal, fetal and neonatal morbidity and mortality worldwide. Preeclampsia is defined as a collection of hypertensive disorders that appear at more than 20 weeks gestation characterized by high blood pressure ( $\geq 140/90$  mmHg) and proteinuria. An increase in systolic blood pressure of 30 mmHg or diastolic blood pressure of 15 mmHg is no longer part of the definition because these criteria do not always predict the incidence of preeclampsia. Edema has also been removed from the definition because it is a common clinical finding during pregnancy.<sup>1,2</sup>

Preeclampsia is divided into two, mild preeclampsia and severe preeclampsia. Mild preeclampsia is characterized by blood pressure  $\geq 140/90$  mmHg after 20 weeks gestation and urinary protein excretion  $\geq 300$  mg/24 hours or  $\geq +1$  dipstick or protein creatinine ratio  $\geq 30$  mg/mmol. Severe preeclampsia is diagnosed if there are symptoms such as blood pressure  $\geq 160/110$  mmHg and proteinuria  $\geq 5$  g/24 hours or  $\geq +2$  dipsticks. In addition to these symptoms there are other symptoms that commonly occur in severe preeclampsia i.e. thrombocytopenia ( $< 100,000/\mu\text{l}$ ), increased of SGOT (serum glutamic oxaloacetic transaminase) and SGPT (serum glutamic pyruvic transaminase), epigastric

pain or right upper quadrant, persistent headache, scotoma of vision, oliguria ( $\leq 500$  ml/24 hours), creatinine  $\geq 1.2$  mg/dL, pulmonary edema and congestive heart failure.<sup>3,4</sup>

The cause of preeclampsia is not yet fully understood, but it is most likely due to abnormal placental implantation and the release of placental factors that trigger an inflammatory response and systemic endothelial activation and give rise to preeclampsia syndrome.<sup>1,5</sup> Factors that contribute to inflammatory reactions are triggered immunologically by placental microparticles and adipocytes. In addition, genetic factors also have a role in the incidence of preeclampsia, including inherited predisposing genes, and epigenetic influences. This hereditary tendency is the interaction of genes inherited from parents who control a large number of metabolic and enzymatic functions in each organ system.<sup>5</sup>

There are several risk factors that influence the incidence of preeclampsia including high-risk age, primipara, grande multipara, previous preeclampsia, diabetes mellitus, anemia, gemelli, and leukocytosis.<sup>1,6,7,8</sup> In this study the risk factors will be analyzed simultaneously so that the relationship is known to the incidence of preeclampsia.

## METHOD

This was a case-control study design. Case-control study design can be used to assess how much the role of risk factors in a cause-effect relationship. In this study, the author examined the role of risk factors for preeclampsia on the incidence of preeclampsia. The study did in the Nusa Indah room for pregnant and postpartum women at the dr. Soeselo Regional General Hospital (*RSUD dr. Soeselo*) Slawi, Tegal Regency. The study was conducted in July 2018. The sampling method of the case used simple random sampling technique. The sample in this study consisted of pregnant women and postpartum mothers who had preeclampsia. Control samples were pregnant women and postpartum mothers who had no history of preeclampsia. The total number of samples was 222 consisting of 111 case samples and 111 control samples. The risk factors studied were age, parity, gemelli, previous preeclampsia, hypertension, diabetes mellitus, anemia, and leukocytosis. Data were analyzed using chi-square and multiple logistic regressions.

## RESULTS

The univariate and bivariate analysis used to find out the relationship of risk factors to the incidence of preeclampsia. Univariate analysis in this study aims to obtain an overview of the distribution of the proportion of variables studied. Univariate analysis was carried out by distributing the frequency of research subjects into observed variables to assess the comparability of the characteristics studied between cases and controls. Bivariate analysis was conducted to determine the significant relationship between the dependent variable and the dependent variable. The analysis used the chi-square test for the one-sided hypothesis at the 95% confidence level of the 2x2 case-control crosstable.

Table 1. The relationship between Risk Factors and Preeclampsia

Risk Factors	Preeclampsia				P- value	Crude OR (95% CI)
	Yes		No			
	n	%	n	%		
<b>Age</b>						
- Yes	50	45%	39	35,1%	0,171	1,513 (0,882-2,597)
- No	61	55%	72	64,9%		
<b>Parity</b>						
- Yes	33	29,7%	49	44,1%	0,037	0,535 (0,308-0,931)
- No	78	70,3%	62	55,9%		

<b>Gemelli</b>						
- Yes	6	5,4%	7	6,3%	1,000	0,849
- No	105	94,6%	104	93,7%		(0,276-2,611)
<b>Previous preeclampsia</b>						
- Yes	20	18%	8	7,2%	0,026	2,830
- No	91	82%	103	92,8%		(1,189-6,374)
<b>Hypertension</b>						
- Yes	87	78,4%	8	7,2%	0,000	46,672
- No	24	21,6%	103	92,8%		(19,958-109,144)
<b>Diabetes mellitus</b>						
- Yes	11	9,9%	2	1,8%	0,010	5,995
- No	100	90,1%	109	98,2%		(1,297-27,710)
<b>Anemia</b>						
- Yes	70	63,1%	81	73%	0,150	0,632
- No	41	36,9%	30	27,0%		(0,358-1,117)
<b>Leukocytosis</b>						
- Yes	93	83,8%	89	80,2%	1,277	1,277
- No	18	16,2%	22	19,8%		(0,642-2,540)

Based on the results of the study in table 1 it can be seen that the risk factors which most experienced preeclampsia was leukocytosis (83,8% or 93 people), whereas gemelli was the least risk factor for preeclampsia (5,4% or 6 people). The results of the chi-square statistical test of this study showed that there were significant differences between parity (p-value = 0,037), previous preeclampsia (p-value = 0,026), hypertension (p-value = 0,000), and diabetes mellitus (p-value = 0,010) between the case and control group. Significant p-value was included in the further analysis with multiple logistic regression analysis above:

Table 2. Multiple Logistic Regression Analysis of Risk Factors for Preeclampsia

Variable	B	Sig.	Adjusted OR	95% CI	
				Lower	Upper
Previous preeclampsia	1,183	0,047	3,263	1,017	10,642
Hypertension	3,848	0,000	46,882	19,664	111,773
Diabetes mellitus	1,837	0,057	6,279	0,949	41,530
Constant	-12,048	0,000	0,000		

Table 2 shows the significance of log likelihood (0,000) <math>\alpha</math> (0,05) indicating that the model is significant (previous preeclampsia, hypertension, and DM). Parity is excluded from the regression model because it has a significance value > 0,05.

The equation of the logistic regression final model based on the table is:

$$\text{Log} \left( \frac{p}{1 - p} \right) = \alpha + \beta_1 X_1 + \beta_2 X_2 + \dots + \beta_i X_i$$

$$\text{Log } p \text{ (PPP)} = -12,048 + \{1,183 \text{ (previous preeclampsia)}\} + \{(3,848) \text{ (hypertension)}\} + \{(1,837) \text{ (diabetes mellitus)}\}.$$

## DISCUSSION

The results of multiple logistic regression analysis showed that the risk factors for preeclampsia were most influential on the incidence of preeclampsia were previous preeclampsia, hypertension, and diabetes mellitus. Based on the results of the study, it can be seen that previous preeclampsia significantly influences the incidence of preeclampsia. The results of the multiple logistic regression statistical test obtained a significance p-value = 0,047 (p < 0,05) and OR = 3,263. Previous preeclampsia has an effect on the incidence of preeclampsia. The previous study also showed that previous preeclampsia influences the incidence of preeclampsia (p = < 0,0001).<sup>9</sup> Mothers with previous preeclampsia have the potential to experience preeclampsia again up to 3 times greater than pregnant women without previous preeclampsia. Mothers who have

preeclampsia in the first pregnancy are known to be more at risk of developing preeclampsia in the next pregnancy. Multipara patients with a history of severe preeclampsia are a high-risk population that must be identified early in pregnancy. In preeclampsia damage to the vascular endothelium causes a decrease in prostacyclin and platelet activation occurs. Platelet activation can result in vasospasm and endothelial damage which occurs again in women who have a history of preeclampsia.<sup>10,11,12</sup> The risk of preeclampsia in women with previous preeclampsia was 38,6% at gestational age less than 28 weeks, 29,1% at 29-32 weeks gestation, 21,9% at 33-36 weeks gestation, and 12,9% at gestational age 37 weeks or more. Pregnant women with previous preeclampsia have more potential to experience severe preeclampsia and eclampsia because they reflect a condition that is more severe than the first preeclampsia.<sup>13,14</sup>

Hypertension significantly influences the incidence of preeclampsia. Multivariate statistical test results obtained p-value = 0,000 ( $p < 0.05$ ) and OR = 46,882. Hypertension increases the risk of preeclampsia 47 times in pregnant women. The previous study in the primary health care of Mexico also told that hypertension significantly affects the incidence of preeclampsia ( $p = < 0,0001$ ).<sup>9</sup> The development of normal blood pressure into mild hypertension to severe hypertension results in a decrease in endothelial function resulting in a narrowing of the spiral arteries and thickening of muscle media, vasoconstriction, decreased vasodilation capacity and decreased peripheral resistance followed by increased blood volume and cardiac output compensation. These symptoms can develop into mild preeclampsia to severe preeclampsia and even eclampsia. Hypertension in pregnant women increase tissue damage or organ disruption which affects in more severe bodywork so edema and proteinuria can occur as a tissue damage response.<sup>15,16</sup> Continuous tissue damage and the inflammatory response causes systemic vasospasm which results in a decrease in organ system function in cases of preeclampsia.<sup>13,17,18</sup>

Diabetes mellitus significantly affects the incidence of preeclampsia. The results of the multiple logistic regression statistical test obtained p-value = 0,057 ( $p < 0,05$ ) and OR = 6,279. Mothers with diabetes mellitus are at risk of experiencing preeclampsia as much as 6 fold greater than pregnant women without risk factors for diabetes mellitus. The result of the study seems with a systematic review in middle-income countries which showed that diabetes increased the incidence of preeclampsia up to 2 fold.<sup>19</sup> Diabetes mellitus is a disorder of carbohydrate metabolism, where blood glucose cannot be used properly, causing a condition of hyperglycemia. Diabetes mellitus is a systemic disorder in the metabolism of carbohydrates, proteins, and fats. Diabetes mellitus is characterized by hyperglycemia or an increase in blood glucose caused by inadequate insulin production or ineffective use of insulin at the cellular level. The placenta blocks the work of insulin so that insulin resistance can occur in the body.<sup>20,21</sup> Insulin resistance results in an excessive inflammatory response and increases oxidative stress in pregnancy. Increased interleukin-6 (IL-6) in pregnant women with diabetes mellitus is associated with the incidence of preeclampsia. The increase in IL-6 levels in pregnant women with diabetes mellitus is higher than that of normal pregnant women, which is one marker of the risk of preeclampsia in pregnant women with diabetes mellitus. Metabolic imbalances in diabetes mellitus increase the risk of the occurrence of preeclampsia.<sup>14,21,22</sup>

Other risk factors that do not have an association with the incidence of preeclampsia possibility caused by the other factors such as healthy lifestyles, nutritional diets, and routine ANC examinations which can affect the incidence of preeclampsia.

## CONCLUSION

Preeclampsia is defined as many of hypertensive disorders that appear at more than 20 weeks gestation characterized by high blood pressure ( $\geq 140/90$  mmHg) and proteinuria. Previous preeclampsia, hypertension, and diabetes mellitus are the risk factors that most influence the incidence of preeclampsia.

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