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RESEARCH

Individual Risk Factors of Preeclampsia in M. Djamil General Hospital Padang

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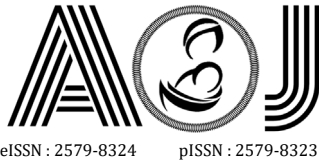
Abstract

Preeclampsia is an important issue in obstetrics because it is still a major cause of maternal mortality compared to bleeding and infection. Similarly, the national prevalence, preeclampsia prevalence in West Sumatra is also constantly increasing. Many factors have been identified as risk factors. This study purposed to identify and analyze risk factors of preeclampsia consist of individual factors. This study was an analytical observational study with case-control design, done in Obstetrics and Gynaecology Department of RSUP DR. M. Djamil Padang on January-December 2013 until samples were completed. Samples consist of 70 preeclampsia patients as the treatment group and 70 healthy maternity patients as the control group in RSUP DR. M. Djamil Padang. The results showed there were significant differences between individual risk factors in the preeclampsia group than the control group.

Keywords: Individual Risk Factors, Preeclampsia

INTRODUCTION

Preeclampsia is an important problem in the field of obstetrics because it is still the main cause of maternal death compared to bleeding and infection. Preeclampsia also causes perinatal death and preterm birth.¹ Preeclampsia is a pregnancy-specific syndrome in the form of reduced organ perfusion due to vasospasm and endothelial activation that occurs after 20 weeks of gestation. Proteinuria is an important sign of preeclampsia in addition to hypertension with or without edema. Preeclampsia consists of mild preeclampsia and severe preeclampsia. While eclampsia is the occurrence of seizures in a woman with preeclampsia that is not caused by anything else^{2,3}. Until now, preeclampsia is "the disease of theory" because the causes are so complex³. The prevalence of preeclampsia in West Sumatra also continues to increase. Based on data at the M.Djamil Padang Central General Hospital (RSUP) in 2012, there were 141 cases of preeclampsia eclampsia. It was found that the average age of preeclamptic eclampsia was 29.79 ± 6.832 years with the youngest age being 15 years and the oldest 43 years. The exact cause of preeclampsia is not known for sure at this time. However, many theories have been developed regarding changes in immunological intolerance, abnormal placental implantation, genetic, environmental factors, cardiovascular changes, and inflammatory factors³. The various pathophysiologies described suggesting a failure of trophoblast invasion of the spiral arteries leading to vasoconstriction and reduced



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perfusion to the fetus. In several studies, markers expressed on trophoblasts and decidua have also been identified that are thought to play an important role in the failure of trophoblast invasion so that they play a role in the pathophysiology of preeclampsia. 4 Many factors have been identified as risk factors, including parity, multiple pregnancies, age less than 20 years or more than 35 years, family history, obesity and a history of previous systemic diseases. However, among these factors, it is still difficult to determine which one is the dominant factor. Preeclampsia is more common in the early and late reproductive years, namely under 20 years and over 35 years. The increased risk of hypertension occurs in women experiencing severe preeclampsia/eclampsia in the first pregnancy. The incidence of severe preeclampsia is more common in nulliparous women than in multiparous women. Genetic and immunological mechanisms are thought to play a role and are being widely studied. Many genes that are thought to play a role include the activin A gene and the androgen receptor and its various polymorphisms 3.5. Besides, past medical history also has the potential to be a risk factor for preeclampsia and eclampsia, including a history of hypertension, diabetes, kidney disease, and a history of induced abortion. The risk of preeclampsia is 2 to 5 times higher in pregnant women with a history of preeclampsia. Rozikhan's research (August 2004-December 2006) in Kendal found that there was no significant difference between the level of education and the incidence of preeclampsia. Rozikhan also found that pregnant women who do not work have 2.01 times higher risk of developing severe preeclampsia compared to working pregnant women⁶. Of all these risk factors, not all of them can be explained in detail. Nutrition of pregnant women is also a factor that also plays a role in the occurrence of preeclampsia. Macro and micronutrients synergize in cardiovascular diseases including preeclampsia.

Apart from risk factors, several factors that are thought to be protective were also identified. For example, a history of previous abortion and a history of smoking. Several studies have shown that smoking can reduce the risk of developing preeclampsia. Likewise, the previous history of provocative abortion.⁷ Seeing the increasing number of risk factors for preeclampsia that has been identified and there is no data on the description of the risk factors for preeclampsia at the M.Djamil General Hospital, the authors are interested in researching the analysis of risk factors for preeclampsia at the General Hospital. M. Djamil Padang.

METHOD

This research is an analytical study with a case-control design that will analyze the risk factors for preeclampsia at RSUP M. Djamil Padang in the period January - December 2013 until the sample is met. The sample of this study consisted of a treatment group, namely the preeclamptic patient group who were treated in the obstetric ward and the control group, namely uncomplicated pregnant patients who were treated in the midwifery ward or went to



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the midwifery polyclinic of M.Djamil Hospital according to the inclusion and exclusion criteria. An in-depth history of the past medical history questions and the FFQ was performed after the patient had given birth and was calm. Meanwhile, a brief history can be carried out at the time of admission.

RESULTS & DISCUSSION

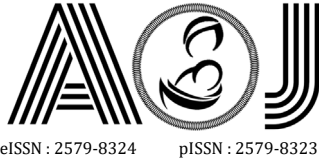
In the study of risk factor analysis for preeclampsia with a sample size of 140 people consisting of 70 patients with preeclampsia (PE) who were treated in the obstetrics department of Dr. M Djamil Padang Hospital and 70 patients without preeclampsia disorder (not PE) who were treated in the obstetrics department or those who control at the polyclinic of RSUP M Djamil Padang. With the division based on individual characteristics, each of them were divided into 3 groups, namely a total sample of 140 samples, 44 samples of the group who had never given birth (nulliparous), and those who had given birth (multiparous) were 96 samples. Data tabulation is performed based on the distribution of each risk factor, while the Chi-Square test is used for significance, if there is uneven or abnormal distribution, then test it with the Fishers Exact Test. The magnitude of the strength of the relationship is known through the RO value parameter.

Table 1. The risk factors for preeclampsia are based on individual characteristics

FACTOR RISK	All mothers pregnant	NULIPARA MULTIPARA	
Age	p> 0.05	p> 0.05	p> 0.05
Activity	p 0,000 OR16.9 (6.93- 4.57 (1,2-41.3)	p 0.033 OR 16.3	p 0.001 OR 4.4 (1.9-10.4)
Level Education	p> 0.05	p> 0.05	p> 0.05
History Marriage	p> 0.05		p> 0.05
History Interval Wedding and Pregnancy	P 0,000 OR 7.2 (2,6-20,3)	P 0,000 OR 33.6 (5,8-196.1)	p> 0.05
BMI	p> 0.05	p> 0.05	p> 0.05
Addition	p 0.027 OR 2.3 (1.15-4.5)	Body weight	p 0.005 OR 3.4 (1.5-7,8)
History Smoke	p> 0.05	p> 0.05	p> 0.05

Preeclampsia by Age

Obtained p value> 0.05, this proves that there is no significant relationship between the age group and the incidence of preeclampsia. This is different from previous research studies



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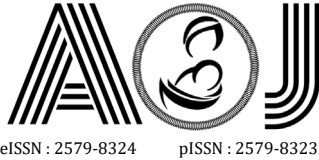
because the description of preeclampsia sufferers in RSUP Dr. M Djamil Padang at the time of the study was that the average age was 31 years.

Preeclampsia Based on Education

Obtained p value > 0.05, this proves that there is no significant relationship between education and the incidence of preeclampsia, both the data as a whole and divided into nulliparous and multiparous. This is consistent with research by Rozikhan (August 2004-December 2006) in Kendal, it was found that pregnant women whose education level is an elementary school (SD) or junior high school (SMP) have the same chance of developing severe preeclampsia compared to pregnant women whose education is secondary school above (SMA) / college.

Activity-Based Preeclampsia

There were no patients with strenuous activity, only limited to light and moderate activity. Most of the activities were light activities at 50.7%. As many as 34.3% had moderate activity in the preeclampsia group. By using the Fisher's exact test, the p-value was obtained <0.05, this proves that there was a significant relationship between activity and the incidence of preeclampsia, with a probability of 94.4% (p 0.000: OR 16.9: CI 95% 6.93 - 41,28) or has a risk of developing preeclampsia 16.9 times greater than those with moderate activity. In nulliparous, the probability was 97.86% (p 0.033: OR 45.72: 95% CI 1.28 - 16.27) or had 4.57 times the risk of developing preeclampsia in those who did not work compared to those with moderate activity. Whereas in multiparous, the probability was 81.48% (p 0.001: OR 4.4 95% CI 1.87 - 10.35) or had 4.4 times the risk of developing preeclampsia in those who did not work compared to those with moderate activity. This is consistent with research by Rozikhan (August 2004-December 2006) in Kendal which found that pregnant women who do not work have 2.01 times higher risk of developing severe preeclampsia compared to working pregnant women. Research by Amirah (2010) in Medan shows the results of 50 cases, the most frequent cause of severe preeclampsia are housewives, 88% and 11 cases of eclampsia sufferers, the highest frequency of eclampsia sufferers is housewives, namely 81.8%. Work activities have an impact on blood circulation and muscle work. Changes in blood circulation in pregnant women occur with increasing gestational age, this occurs due to enlargement of the uterus. Increasing gestational age results in increased work of the heart to meet its needs during pregnancy. Work activities can be done as long as it's not too heavy, so that blood circulation is maintained and pregnant women can avoid preeclampsia. Work that is a risk of preeclampsia is not defined as the mother's profession, but rather the characteristics of the activities carried out with her work. Activity daily life (ADL) characteristics can predict sympathetic activity associated with preeclampsia. 8



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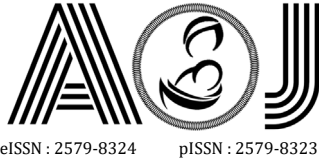
Preeclampsia Based on Number of Married

The highest number of married people was once, namely 94.3% or 132 people. The highest number of married 2 times was in multipara with preeclampsia, namely 5 people. From table 2, it is found that p value > 0.05 , this proves that there is no significant relationship between the number of married groups and the incidence of preeclampsia. This happened because there was no sufficient sample of patients who married more than once, where the sample obtained was only 8 people who married more than once.

Preeclampsia Based on Interval between Marriage and Pregnancy

There was a significant relationship between the length of marriage and pregnancy to the incidence of preeclampsia, with a probability of 87.85% (p 0.000: OR 7.23 95% CI 2.58 - 20.29) or having a 7.23 times greater risk of developing preeclampsia. In nullipara, the probability was 97.11% (p 0.000: OR 33.6 95% CI 5.76 - 196.10) or had a 33.6 times greater risk of developing preeclampsia. In nulliparous, the mean interval between marriage and pregnancy was 6.64 ± 7.89 months, with the fastest value being 1 month and the longest being 40 months. In the preeclampsia sample group, the average time needed was 4.17 ± 7.93 months. The fastest time is 1 month and the longest is 40 months. In the sample group without preeclampsia, it took 9.33 ± 7.07 months, with the fastest time being 3 months and the longest being 30 months. However, after the exclusion of 3 patients with infertility, namely 1 person from the preeclampsia group and 2 people from the non-preeclamptic group, the meantime for sperm exposure in the preeclampsia group was 2.55 ± 1.40 months, while in the non-preeclamptic group the mean sperm exposure was 7.263 ± 2.85 months.

If patients with primary infertility in both groups were excluded, Fisher's exact test was p 0.000 with OR 58.8 95% CI 6.2 - 558.45. In other words, there is a 58.8 times greater risk at an exposure of fewer than 4 months with a probability of 98.4%. This is different from the research conducted by Kho et al. In 2009 in New Zealand, where it was found that those exposed to < 6 months had an OR 2,3 95% CI 1,09-4,98 with a frequency of 12 times/month whereas at 3 months, OR 3, 22 CI 1.18 - 8.79 with a frequency of 12 times/month. And in people who have had their first relationship with an average of 2 times already pregnant OR 3.22 95% CI 0.66 - 15.7. Another theory states that if the trophoblast is after ischemic, the trophoblast experiences apoptosis. This has something to do with immunology too. Because in that situation IL-2, IFN γ and TNF are produced which are responsible for cell apoptosis. These cytokines result from the activity of macrophages and neutrophils (in non-specific immune responses). Ultimately activated T lymphocytes. So what happens in the endothelium? there is an imbalance of prostacyclin and thromboxane so that vasoconstriction.^{9,10} This trophoblast exposure cannot be protected optimally by blocking antibodies because of the inadequate amount. Besides, there was a decreased expression of Human Leucocyte Antigen-G (HLA-G) on cytotrophoblasts. This results in decreased



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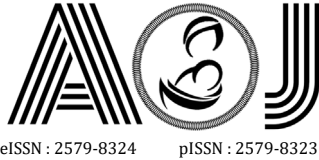
trophoblast protection by the destruction of NK and the cytotoxic cytokine IL2. This results in inhibition of trophoblast invasion of the spiral arteries. 11 In nulliparous, especially conception that occurs too quickly after sperm exposure does not provide sufficient time for the mother to form blocking antibodies.

Preeclampsia Based on BMI

The largest distribution of respondents was norm weight BMI, both preeclampsia and non-preeclampsia. In the analysis, there was no relationship between BMI and the incidence of preeclampsia. However, other variables related to BMI, namely lipid profile, showed a significant relationship between lipid profile and the incidence of preeclampsia where dyslipidemia was prevalent in the preeclampsia group. This shows that even though it is a normal weight, many preeclamptic patients experience dyslipidemia. Besides obesity as a risk factor for preeclampsia, especially in conditions of central obesity. In this study, only tests were performed to determine peripheral obesity. Being overweight in pregnancy increases the risk of developing preeclampsia. This is associated with increased serum triglycerides and lower lipoprotein levels in obese women. Such a lipid profile can induce oxidative stress caused by ischemia of reperfusion mechanisms and neutrophil activation which results in endothelial cell dysfunction. 12 Also, it causes atherothrombosis and induces platelet aggregation which ultimately leads to coagulopathy which is a characteristic of preeclampsia. Central obesity characterized by visceral fat has a higher risk of preeclampsia compared to peripheral fat. Visceral fat produces C Reactive Protein (CRP) and proinflammatory cells, PAI-1, and leptin which all contribute to oxidative stress. Visceral fat will also increase fat production by the liver. Apart from being overweight, a body weight that is less than normal is also at risk of preeclampsia. This is caused by a lack of protein which results in immunological deficiency and reduced expression of proteins responsible for trophoblast invasion. Also, people with nutritional status are more or less prone to experiencing oxidative stress which leads to preeclampsia, one of them.

Preeclampsia Based on a History of Weight Gain

There was a significant relationship between weight gain and the incidence of preeclampsia, with a probability of 69.29% (p 0.027: OR 2.26 95% CI 1.15 - 4.44) and in multiparous probability 77.11% (p 0.005: OR 3.37 95% CI 1.45 - 7.80). Whereas in nullipara there was no significant increase in body weight towards the onset of preeclampsia. The highest amount of weight gain is the criteria for normal weight gain. The mean weight gain during pregnancy in the preeclampsia group was significantly higher than in the non-preeclamptic group. This suggests that high weight gain increases the risk of preeclampsia. In addition to being overweight (overweight and obese) and underweight, the risk of preeclampsia also occurs in excess weight gain in pregnancy even though the weight before pregnancy is normal. This is



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related to the occurrence of acute oxidative stress due to the release of free fatty acids and the occurrence of fluid resistance.

Preeclampsia Based on a History of Smoking

There was a significant relationship between smoking history and the incidence of preeclampsia, with a probability of 72.83% (p 0.049: OR 2.68 95% CI 1.08 - 6.67) or with a 2.68 times higher risk of developing preeclampsia. In several studies, it was reported that smoking can reduce risk factors for preeclampsia. The mechanism that can explain this is through the biological effects of carbon monoxide (CO) which is formed during smoking. Carbon monoxide plays a role in inhibiting the production of placental antiangiogenic proteins such as SFlt1 and inhibiting placental apoptosis and necrosis. However, molecular biological research is necessary to see the effect of CO. Carbon monoxide acts like a neurotransmitter that inhibits platelet aggregation and acts as a muscle relaxant for blood vessel walls. Lack of carbon monoxide causes vasoconstriction of blood vessels. The effect of CO is amplified by NO activity. Smoking provides external CO input because in preeclampsia there is a decrease in CO due to a decrease in HO-2 expression. 13

CONCLUSION

There was a significant relationship between activity, the interval between marriage and pregnancy, and weight gain.

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