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Pre-eclampsia Risk factors of Pregnant women in Semarang, Indonesia

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Abstract

Maternal mortality cases in Semarang increased during the last years. The largest portion of maternal death was caused by pre-eclampsia/eclampsia. The causes of pre-eclampsia/eclampsia are not clear yet, thus this study aimed to find the risk factors of pre-eclampsia, which can be prevented. These factors are environmental condition (passive smokers and hormonal contraception used) and nutritional status (BMI, Mid upper arm circumference (MUAC) and nutrient intake). This study was done in a case control design, in Semarang. The population was pregnant mothers in 3 primary health care center' working areas which have the highest cases of pre-eclampsia in Semarang: Bandarharjo, Rowosari and Gayamsari. The subjects were 50 pregnant/post partum women with pre-eclampsia in the case and 150 pregnant/post partum women in the control groups. Cases and control subjects were matched by age and address. Data were collected by interviews using structured questionnaires and semi quantitative food frequency questionnaires. Data were analyzed by calculating odd ratios by multiple logistic regression. The results showed that there was no difference in socioeconomic status between the case and control groups. The independent risk factors found were passive smokers (OR=16.4; 95% CI: 2.1-130.3), hormonal contraception used (OR= 2.5; 95%CI: 1.2-5.3), overweight (OR= 6.2; 95% CI:2.9-13.4), and low protein intake (OR= 2.3; 95%CI: 1.1-4.9). It is recommended to prevent pre-eclampsia by health education for the pregnant mothers to encourage adequate protein intake and avoid cigarette smoke.

Keywords: pre-eclampsia; risk factor; protein intake; passive smoking; hormonal contraception.

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1. Introduction

Data on maternal mortality in 2012 to 2013 in Semarang city showed that pre-eclampsia was one of the important causes of maternal death. Therefore pre-eclampsia has to be prevented in order to reduce maternal mortality rates. Pre-eclampsia prevention and treatment may also results in a decline of infant mortality rate, thus prevention is one of the strategic keys action to decrease maternal and infant mortality rates.

Pre-eclampsia is one of the pregnancy problem which occur after 20 weeks of gestation, at deliveries and post natal period. It is signed by hypertension (systolic ≥ 140mmHg or diastolic ≥ 90 mmHg) and proteinuria [1]. Pre-eclampsia is the results of placenta disturbance. Pre-eclampsia influence all organ system in the body and caused by three factors: genetic, auto immune and paternal factors [2] Epidemiologic studies showed that health condition of the mothers before pregnancy such as hypertension, diabetes, obesity, renal diseases and auto immune disease are related to pre-eclampsia incidence. Women with chronic hypertension has 10-25% risk to develop pre-eclampsia, while on diabetes has 21% risk to develop pre-eclampsia. Pre-eclampsia history in the family increase the risk by 3 times [3].

Obesity increase pre-eclampsia incidence by 2 or 3 times higher [4]. This problem is related to insulin resistance, inflammation, oxidative stress and adipokine, an angiogenic factor which present in obesity [5]. The other factors which are related to preeclampsia incidence were cigarette smoking. Smoking mothers is protective to pre-eclampsia incidence [6,7], but the impact of passive smoking was not clear yet. [7] In Indonesia, 67% of the adult males are smokers [8], thus passive smoking is an important factor to be investigated. It is suggested that intake of energy, carbohydrate, protein, fat [9] and micronutrients such as vitamin D [9,10], calcium and antioxidants such as vitamin A, vitamin C, vitamin E, zinc and selenium may influence pre-eclampsia incidence [9]. Double burden of nutrition problem in Indonesia including Semarang, makes pre-eclampsia prevention more difficult. This study was conducted as a preliminary study to have an input for pre-eclampsia prevention.

2. Material and Method

This case control study was conducted in the working areas of 3 primary healthcare centers in Semarang (Bandarharjo, Gayamsari and Rowosari), which have the highest cases of pre-eclampsia. The list of pregnant women who were diagnosed as pre-eclampsia at antenatal services were gathered from the chosen primary healthcare centers. The diagnosis of pre-eclampsia used are: hypertension (systolic blood pressure of≥140 mmHg and/ or diastolic blood pressure of ≥ 90 mmHg and proteinuria). Cases were 50 pregnant and post partum women and the control group were 150 pregnant and post partum women who were matched to the cases in age and living area. Data on risk factors were collected by interviews using structured questionnaires. Data on mid upper arm circumference, weight before pregnancy, were gathered from maternal and child health book of each subject. Heights were measured by *microtoise*.

The dependent variable was pre-eclampsia incidence and the independent variables were the nutritional status of pregnant women, which were measured by BMI and MUAC, nutrient intake: energy, protein, vitamin A, B1, B6, B12, C, D, E, calcium, zinc and magnesium adequacy level, cigarette smoke exposure and hormonal

contraception used. Nutrient intake was measured by semi quantitative food frequency questionnaires. The adequacy levels on each nutrient were calculated based on Indonesian Recommended Dietary Allowance 2013, adjusted for bodyweight and additional need for pregnancy. BMI and MUAC data used were from the first ante natal visit. Data on cigarette smoke exposure/ passive smokers were collected from interviews to the subjects regarding the number of family members who were smoking inside the house multiplied by the number of cigarette smoked by each family member.

Minimal sample size was calculated based on alpha, power and odd ratio of 0.05, 80% and 2, respectively. Based on case and control ratio of 1:3, the minimal sample size was 44 cases. Analysis was conducted by calculating Odd ratio of each risk factor and followed by multiple logistic regression.

3. Results

The population of the study lives in urban areas: Bandarharjo (40%), Gayamsari (36%) and sub urban area Rowosari (24%). Most of the subjects were post partum women (88%), only 12 % were pregnant women. Table 1 shows the characteristics of the subjects (age, education and income level). There was no difference in age, schooling years and income per person per month between the cases and control group.

Table 1: Characteristics of the subjects

Variables	Case		Control	
	Mean	SD	Mean	SD
Age (years)	29.3	6.58	28.6	6.06
Schooling years	9.8	2.67	10.0	2.67
Income per person per month (in thousand rupiahs)	620	301	640	477

The contraception used by the subjects before their pregnancy are described in Table 2. Most of the subjects used contraception before their pregnancy and most of the subjects who used contraception chose hormonal contraception. Pills and implants were used by cases group more than the injection. Most of the user of injection contraception chose progesterone ones.

The mean BMI of the cases was in overweight category (25.9±5.74kg/m^2), while of the controls was in normal category (22.2±4.41kg/m^2). The mean protein intake in the case group was lower than the required (90.9±31.17%), while in the control group was higher than the required (105.5±32.79). Intake of calcium, vitamin D, vitamin E, vitamin B1, folic acid and zinc intake in both groups were very low, thus the cut off used for ORs calculation was 50% of adequacy level. The mean intake of vitamin C in the case group was 100.1±117.29%, while in the control group was 133.8±116.82%. Mean zinc intake in the case group was only 42.1±13.21%, while in the control group was higher (48.1±14.32%). Intake of magnesium (78.5±28.89%) in the case group was lower compared to the control group (91.9±33.75%). No was a smoker, but most of the passive smokers and cigarette smoke exposure in both group was high. However, cigarette smoke exposure in the case

group (10.1±5.82) was higher than the control group (6.4±5.67). Table 3 shows the unadjusted Odd Ratios of the risk factors studied (environmental and nutritional).

Table 2: Contraception used by the subjects before their pregnancy

Contraception	Cases		Control		Total	
	n	Percentage	n	Percentage	N	Percentage
Contraception used						
Yes	23	46	117	78	140	70
No	27	56	33	22	60	30
Contraception methods						
Injection	11	47,9	66	70,2	77	65,8
Pills	9	39,1	20	21,3	29	24,8
Implant	2	8,7	2	2,1	4	3,4
IUD	1	4,3	6	6,4	7	6,0

Analysis by multiple logistic regression method by including all the important risk factors in one model and chose the independent variables which were significant are shown in Table 4. This final model have an R^2 of 0.32. The Odd ratios of the independent variables were passive smoking, hormonal contraception use, overweight before pregnancy and low protein intake.

Table 3: Odd Ratios and 95% *confidence interval* of the risk factors before controlled

Variable	OR	95% CI	P
Environmental factors			
Passive smokers	**12.765**	**1.695-96.121**	**0.013**
Hormonal contraception use	1.806	0.947-3.447	0.073
Nutritional factors			
Overweight at before pregnancy (BMI>23kg/m^2)	**4.620**	**2.308- 9.247**	**0.0001**
MUAC < 23.5 cm	0.304	0.088-1.053	0.060
Energy adequacy level <100%	1.882	0.869-4.079	0.109
Protein adequacy level <100%	**2.441**	**1.251-4.763**	**0.009**
Calcium adequacy level <50%	1.435	0.741-2.78	0.683
Vitamin D adequacy level <50%	0.85	0.389-1.858	0.683
Vitamin A adequacy level <100%	1.251	0.625-2.505	0.527
Vitamin C adequacy level <100%	**2.771**	**1.365-5.627**	**0.005**
Vitamin E adequacy level <50%	1.600	0.656-3.902	0.301

Vitamin B1 adequacy level <50%	1.446	0.734-2.851	0.286
Vitamin B6 adequacy level <100%	1.80	0.297-4.271	0.153
Vitamin B12 adequacy level <100%	1.455	0.764-2.770	0.254
Folic acid adequacy level <50%	2.345	0.858-6.405	0.097
Zinc adequacy level <50%	**2.176**	**1.070-4.425**	**0.032**
Magnesium adequacy level <100%	**2.471**	**1.077-5.667**	**0.033**

Table 4: Odd Ratios and 95% *confidence intervals* of the risk factors after controlled

Variable	**OR**	**95% CI**	**p**
Environmental factors			
Passive smokers	16.4	2.1-130.3	0.008
Hormonal contraception use	2.5	1.2-5.31	0.017
Nutritional factors			
Overweight at before pregnancy (BMI>23kg/m^2)	6.2	2.9- 13.4	0.0001
Protein adequacy level <100%	2.3	1.1-4.9	0.029

4. Discussion

Pregnant women who had high exposure to cigarette smoke had the highest odd ratio for pre-eclampsia compared to the low exposure to cigarette smoke. Several studies have shown that that smoking is a protective factor for pre-eclampsia [6,7]. However, a study in Canada showed that passive smokers which is measured by plasma cotinine level of 0.20-3.00 ng/mL have an odd ratio of 6.06 for pre-eclampsia, while the current smokers have the same risk as non-smokers for pre-eclampsia [11]. It is hypothesize that carbon monoxide is the protective factor to prevent pre-eclampsia in the current smokers [12,13]. However, in the passive smokers, there is no carbon monoxide exposure while chronic exposure to the certain tobacco chemicals is present.

In Indonesia, the prevalence of smokers among adult women (3%) were much smaller compared to the adult men (67%) [8], thus pregnant women in Indonesia were at high risk of being passive smokers, which in turn lead to the higher risk for pre-eclampsia. Public health actions should be done in Indonesia and other countries which have the same problem, to prevent pregnant women from developing pre-eclampsia through reducing cigarette exposure to pregnant women.

In this study, hormonal contraception used was a risk factor for pre-eclampsia. Hormonal contraception use was increased in Indonesia among the last years. The use of progesteron injection was among the the popular contraception among women as the practical use of it. However, in this study the hormone used for contraception were mixed. A previous study showed that the use of oral contraceptive increased the pre-

eclampsia risk [14]. It is not clear yet, what mechanism may cause preeclampsia. Larger studies are needed to investigate the effect of each type of hormone on pre-eclampsia. Among the nutritional risk factors, overweight (BMI>23kg/m^2) is one of the strong risk factors for pre-eclampsia. Overweight women in this study have an odd ratio of 4.6 times to have pre-eclampsia compared to the lean women. Study by Bodnar et al. [5] showed that obese women have an OR of 2-3 times more than the non obese women. The cut off used for overweight in this study was smaller 23 kg/m^2 instead of 25 kg/m^2. Thus it means that the women in this study was more vulnerable to preeclampsia at the lower level of fatness. Other studies by [15, 16] also shows that preeclampsia women had higher bodyweight compared to the non preeclampsia women.

Among the nutritional factors, low protein adequacy level was one of the risk factors of pre-eclampsia. This condition could occur as low protein intake influence glutathione concentration. Low glutathione concentration, which is an antoxidant, increase oxidation stress. This oxidation stress lead to pre-eclampsia condition [9].

5. Conclusion

It is concluded that the risk factors of pre-eclampsia on pregnant women were passive smokers, overweight, low protein intake and hormonal contraception used before pregnancy. Public health actions can be done to prevent pre-eclampsia.

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