Characteristic Comparison between Pregnant Women With and Without Preeclampsia

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Abstract

Preeclampsia is still the leading cause of maternal mortality in developing countries, including Indonesia. However, there is a discrepancy between national and regional data regarding the cause of maternal death in Indonesia. National data shows that peripartum hemorrhage is the main cause of maternal death, while data from East Java region shows that the leading cause is preeclampsia. Thus, we believe that there is still lack of understanding about preeclampsia in East Java region. This study aims to scrutinize the characteristic of pregnant women with preeclampsia in East Java, Indonesia.

This study was a matched case-control study conducted from June to October 2018 at secondary referral government hospitals. Variables analyzed in this study were demographic characteristic, pregnancy history, preeclampsia risk factors, and infant outcomes. Logistic regression was used to analyze preeclampsia risk factor.

There were 67 preeclamptic women as case group and 67 women with normal pregnancy as control group participated in this study. Cesarean delivery was more common in case group compared to control group (59.7% vs 40.3%, p = 0.025). There were also more women in case group with familial history of preeclampsia than in control group (14.9% vs 4.5%, p = 0.041). Multivariate analysis showed that pregnant women with familial history of preeclampsia were more likely to develop preeclampsia (OR = 4.923, p = 0.036).

Close monitoring to the pregnant women with familial history of preeclampsia in East Java region should be done, because they were more likely to develop preeclampsia throughout their pregnancy.

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Introduction

International coordinated efforts on development such as Multiple Development Goals (MDGs) and Sustainable Development Goals (SDGs) have reduced the number of maternal mortalities worldwide. However, this reduction does not seem to exclude maternal mortality as a global health problem since 94% of maternal morality worldwide occurs in low and middle-income countries.[1] Furthermore, according to CDC, 60% of pregnancy-related deaths are preventable.[2] This underlines that understanding the nature of maternal mortality causes especially in low and middle-income settings is still relevant and important. Among the causes of maternal mortality, hypertensive disorder is one which has significant proportion. According to a WHO systematic analysis

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published in 2014, hypertensive disorder is identified as the most common cause of maternal deaths after haemorrhage.[3]

One of types of hypertensive disorder called pre-eclampsia becomes one of the main causes of neonatal, foetal, and maternal deaths. It is a condition of high blood pressure during pregnancy with elevated protein level in the urine.[4] WHO estimated that in developing countries, the incidence of preeclampsia is seven times higher compared to developed countries.[5] Therefore, the gap between what developed countries have achieved in preeclampsia management and what is really happening in the developing world needs to be addressed. Research on risk factors of pre-eclampsia in low- and middle-income settings still much needed to give more understanding about this phenomenon.

In Indonesia, latest data showed that the incidence of pre-eclampsia is 27.1%, while globally the estimated incidence of pre-eclampsia is between 2% - 8% of all pregnancies.[6,7] In East Java region, data from tertiary referral hospital in 2013-2014 showed that the incidence of pre-eclampsia is 21% (1106 cases in 5266 deliveries), where 10.2% (113 cases) developed into eclampsia and 5.6% (62 cases) developed into pulmonary oedema. Over that period, preeclampsia contributes to 31% of all maternal death (42 out of 135 deaths), where postpartum haemorrhage contributes to 17% of all maternal death.[8] In contrast, national data in 2013 showed that haemorrhage is the main contributor for maternal death and the prevalence is higher than preeclampsia.[9] Based on those data, we believe that there is still lack of understanding about preeclampsia in East Java region. This study aims to scrutinize the characteristic of pregnant women with preeclampsia in East Java, Indonesia.

Materials and methods

This study was a matched case-control study conducted from June to October 2018 at 2 secondary referral government hospitals in East Java. Study protocol was submitted to the Faculty of Medicine Universitas Airlangga Ethical Review Board and accepted before the study began (Ethical Clearance Number 68/EC/KEPK/FKUA/2018). This study follows the principles of the Declaration of Helsinki. All subjects gave their informed consent prior to their inclusion in the study. Information for informed consent was given before subjects signed the informed consent. Details that might disclose the identity of the subjects under study were omitted. EpiInfo™ was used to calculate the sample size.[10]

Subjects of this study were pregnant women who gave birth at the hospital where the study conducted during the study period. All patients diagnosed with preeclampsia and gave birth at one of the hospitals where the study conducted during study period were offered to participate in the study as the case group, with exclusion criteria of unavailable or incomplete documented data regarding the current pregnancy. History taking from each subject was done by the investigator in the hospital wards after giving birth, while evaluation regarding the current pregnancy was done using medical records. Acquired data was filled in the case report form. Diagnosis of preeclampsia was performed by the attending obstetrician in the hospital using International Society for the Study of Hypertension in Pregnancy criteria.[11]

Cases and controls were matched for study site. Every time the investigator acquired samples from the case group, one random woman with normal pregnancy that had been giving birth and still in the hospital ward was offered to participate in the study as control group, with same exclusion criteria as case group.

Pre pregnancy BMI and additional weight gain during pregnancy was categorized according to latest ACOG guideline.[12] The minimum antenatal (ANC) visit during pregnancy was according to Ministry of Health of the Republic of Indonesia (Total visit at least 4 times throughout pregnancy, with at least 1 visit on 1st trimester, 1 visit on 2nd trimester, and 2 visits on 3rd trimester).[13] Gestational age and intrauterine growth were categorized based on Lubchenco chart.[14] It categorizes the gestational age to: preterm (<37 weeks), term (37 – 42 weeks), or postterm (>42 weeks) and the intrauterine growth to: Small for Gestational Age (SGA) (<10th percentile), Appropriate for Gestational Age (AGA) (10th – 90th percentile), or Large for Gestational Age (LGA) (>90th percentile).

SPSS for Windows, version 25.0 (IBM Corp., Armonk, N.Y., USA) was used for all statistical analysis. Data normality distribution was evaluated using Kolmogorov Smirnov test. Data with normal distribution was presented in

Mean ± SD, and data with abnormal distribution was presented in Median [IQR]. Statistical analysis for normally distributed interval / ratio data was evaluated with independent t-test, for abnormally distributed interval / ratio data or ordinal data was evaluated with Mann-Whitney U test, and nominal data was evaluated with Chi Square test. Preeclampsia risk factor analysis was conducted in two phases. First, univariate logistic regression with entry method was used to identify independent variables that were associated with preeclampsia. Variables with $p < 0.2$ were included in the next phase. In second phase, multivariate logistic regression using backward selection was used. Variables with $p < 0.05$ in the multivariate analysis were considered as risk factor for preeclampsia.

Results

Characteristic of study population

There were 67 women with preeclamptic pregnancy included in this study as case group and the equal number of women with normal pregnancy as control group. In case groups, 12 (17.9%) women had early-onset preeclampsia and 55 (82.1%) women had late onset preeclampsia. The mean age of women in case group was 27.81 ± 6.27 years old, and in control group was 26.1 ± 5.82 years old. There was no significant difference of age between two groups ($p = 0.106$). Women in both groups mainly graduates from senior high school, and most of them were housewives. Ten (14.9%) women in case group had a familial history of preeclampsia, while only 3 (4.5%) women in control had the familial history of preeclampsia ($p = 0.041$) (table 1). All women in both groups had no history of chronic hypertension, chronic kidney disease, type 2 diabetes mellitus, or autoimmune disease.

Pregnancy history

There were 10 (14.9%) women in case group and 8 (11.9%) women in control group that did not expect the current pregnancy. More than half of the women in both groups had normal pre-pregnancy BMI and had appropriate weight gain during pregnancy. Pre-pregnancy BMI of women from case group was higher than control group (22.64 [20.52 – 26.68] vs 21.93 [19.39 – 23.77] kg/m^2), but the difference was not statistically significant ($p = 0.055$). Based on pre-pregnancy BMI categorization by ACOG guideline, the prevalence of underweight was lower in case group than in control group (4.5% vs 10.4%) and the prevalence of overweight and obese in case group was higher than in control group (31.3% vs 19.4%). However, the difference but not statistically significant ($p = 0.068$).

Characteristic	Control group N = 67	Case group N = 67	*p*-value
Maternal age, n (%)			
< 20 years old	2 (3)	1 (1.5)	0.238*
20 – 35 years old	59 (88.1)	56 (83.6)	
> 35 years old	6 (9)	10 (14.9)	
Maternal education, n (%)			
Elementary school graduates	13 (19.4)	14 (20.9)	0.546*
Junior high school graduates	14 (20.9)	16 (23.9)	
Senior high school graduates	34 (50.7)	33 (49.2)	
University graduates	6 (9)	4 (6)	
Occupation, n (%)			
Housewife	59 (88.1)	56 (83.6)	0.307#
Worker	7 (10.4)	11 (16.4)	
Student	1 (1.5)	0 (0)	
Number of marriages, n (%)			
1	61 (91)	64 (95.5)	0.302*
2	6 (9)	3 (4.5)	
Contraception used, n (%)			
No	43 (64.2)	29 (43.3)	0.152#
Pill	4 (6)	9 (13.4)	
Oestrogen injection	4 (6)	4 (6)	
Progesterone injection	10 (14.9)	16 (23.9)	
IUD	6 (9)	9 (13.4)	
Familial history of preeclampsia, n (%)			
Yes	3 (4.5)	10 (14.9)	0.041#
No	64 (95.5)	57 (85.1)	

Table 1. Characteristic of study population. IUD = Intrauterine device.

IUD = Intrauterine device.
*Mann Whitney U test was used; #Chi Square test was used
$p < 0.05$ was considered statistically significant.

There were 54 (79.6%) women in both case and control group that did ANC at least once in the 1st trimester (median ANC 2 [1 – 3] vs 2 [1 – 2] times, $p = 0.538$). For the 2nd trimester, 64 (95.5%) women in both case and control group did ANC at least once (median ANC 2 [2 – 4] vs 3 [2 – 3] times, $p = 0.57$). In the 3rd trimester, 54 (79.6%) women in case group and 49 (73.14%) women in control group attend ANC at least twice (median ANC 3 [2 – 5] vs 3 [3 – 4] times, $p = 0.723$). In total, there were 3 (4.5%) women in case group and 4 (6%) women in control group that attend the ANC less than 4 times throughout their pregnancy (median ANC 8 [7 – 10] vs 8 [7 – 10] times, $p = 0.825$). Gestational age of both groups was mainly term, and the delivery method was mainly caesarean section in case group and vaginal delivery in control group ($p = 0.025$) (table 2). All women in both groups had singleton pregnancy. History of preeclampsia in previous pregnancy in case group was higher than the control group (10.4% vs 3%), but not significantly different ($p = 0.084$) (table 3).

Variables	Control group N = 67	Case group N = 67	*p*-value
Number of pregnancies, n (%)			0.095*
1	35 (52.2)	26 (38.8)	
2	21 (31.3)	24 (35.8)	
3	6 (9)	10 (14.9)	
> 3	5 (7.5)	7 (10.5)	
Expected pregnancy, n (%)			0.612#
Yes	59 (88.1)	57 (85.1)	
No	8 (11.9)	10 (14.9)	
Pre-pregnancy BMI, n (%)			0.068*
Underweight	7 (10.4)	3 (4.5)	
Normal	47 (70.1)	43 (64.2)	
Overweight	8 (11.9)	14 (20.9)	
Obese	5 (7.5)	7 (10.4)	
Weight gain during pregnancy, n (%)	21 (31.3)	16 (23.9)	0.169*
Decrease	36 (53.7)	35 (52.2)	
Normal	10 (14.9)	16 (23.9)	
Over			
ANC 1st trimester, n (%)			1.0#
Yes	54 (79.6)	54 (79.6)	
No	13 (19.4)	13 (19.4)	
ANC 2nd trimester, n (%)			1.0#
Yes	64 (95.5)	64 (95.5)	
No	3 (4.5)	3 (4.5)	
ANC 3rd trimester, n (%)			0.306#
Yes	49 (73.14)	54 (79.6)	
No	18 (26.86)	13 (19.4)	
Total ANC, n (%)			1.0#
≥ 4	63 (94)	64 (95.5)	
< 4	4 (6)	3 (4.5)	
Smoking exposure, n (%)			0.284#
Yes	39 (58.2)	45 (67.2)	
No	28 (41.8)	22 (32.8)	
Gestational age, n (%)			0.056*
Preterm	15 (22.4)	24 (35.8)	
Term	47 (70.1)	41 (61.2)	
Post term	5 (7.5)	2 (3)	
Delivery method, n (%)			0.025#
Vaginal	40 (59.7)	27 (40.3)	
Caesarean section	27 (40.3)	40 (59.7)	

Table 2. Present pregnancy history.
ANC = Antenatal care; BMI = Body mass index.
*Mann Whitney U test was used; #Chi Square test was used.
p < 0.05 was considered statistically significant.

Risk factors for preeclampsia

In univariate logistic regression analysis, there were no factors that associated with the preeclampsia (all p > 0.05). In the multivariate logistic regression analysis, variables with p-value of < 0.20 from the univariate logistic regression (number of pregnancies, pre-pregnancy BMI, history of preeclampsia, and familial history of preeclampsia) were included in the analysis. Multivariate analysis indicated that pregnant women with familial history of preeclampsia were more likely to develop preeclampsia (OR = 4.923, 95% CI [1.108 – 21.87]; p = 0.036) (table 4).

Infant outcomes

The mean birthweight between case and control groups showed no significant differences (2917.61 ± 515.31 vs 2931.19 ± 552.65 grams, p = 0.883). There were 14 (21.9%) infants from case group and 9 (13.4%) infants from control group that had 1-minute APGAR score below 7 (8 [7 – 8] vs 8 [7 – 8], p = 0.344), and 3 (4.5%) infants from case group and 5 (7.5%) infants from control group that had 5-minutes APGAR score below 7 (9 [8 – 9] vs 9 [8 – 9], p = 0.383). Twenty (29.9%) infants from case group and 16 (23.9%) infants in control group treated at the Neonatal Intensive Care Unit (table 5).

Variables	Control group N = 67	Case group N = 67	*p*-value
History of abortus, n (%)			
Yes	8 (11.9)	5 (7.5)	0.381#
No	59 (88.1)	62 (92.5)	
History of preterm, n (%)			
Yes	1 (1.5)	4 (6)	0.362#
No	66 (98.5)	63 (94)	
History of IUGR, n (%)			
Yes	2 (3)	5 (7.5)	0.437#
No	65 (97)	62 (92.5)	
History of preeclampsia, n (%)	2 (3)	7 (10.4)	0.084#
Yes	65 (97)	60 (89.6)	
No			

Table 3. Previous pregnancy history.
IUGR = Intrauterine growth restriction.
#Chi Square test was used.
p < 0.05 was considered statistically significant.

Variables	Univariate			Multivariate		
	COR	95% CI	*p*-value	AOR	95% CI	*p*-value
Maternal age						
< 20 years old	0.527	[0.046 – 5.973]	0.605			
20 – 35 years old (ref)	-	-	-			
> 35 years old	1.756	[0.599 – 5.151]	0.305			
Maternal education, n (%)						
Elementary school graduates	1.110	[0.454 – 2.713]	0.82			
Junior high school graduates	1.177	[0.497 – 2.790]	0.71			
Senior high school graduates (ref)	-	-	-			
University graduates	0.687	[0.178 – 2.657]	0.586			
Number of marriages						
1	2.098	[0.502 – 8.765]	0.31			
2 (ref)	-	-				
Number of pregnancies						
1	0.58	[0.292 – 1.152]	0.12			
> 1 (ref)	-	-				
ANC 1st trimester						
Yes (ref)	-	-	-			
No	1.0	[0.425 – 2.354]	1.0			
ANC 2nd trimester						
Yes (ref)	-	-	-			
No	1.0	[0.194 – 5.142]	1.0			
ANC 3rd trimester						
Yes (ref)	-	-	-			
No	1.526	[0.678 – 3.435]	0.307			
Total ANC						
< 4	1.354	[0.291 – 6.298]	0.699			
≥ 4 (ref)	-	-	-			
Expected pregnancy						
Yes (ref)	-	-	-			
No	1.294	[0.477 – 3.512]	0.613			
Pre-pregnancy BMI						
Underweight	0.468	[0.114 – 1.927]	0.293			
Normal (ref)	-	-	-			
Overweight	1.913	[0.731 – 5.006]	0.186			
Obese	1.530	[0.452 – 5.183]	0.494			
Weight gain during pregnancy						
Decrease	0.784	[0.352 – 1.744]	0.550			
Normal (ref)	-	-	-			
Over	1.646	[0.658 – 4.117]	0.287			
Smoking exposure						
Yes	1.469	[0.726 – 2.969]	0.285			
No (ref)	-	-	-			
History of abortus						
Yes	0.595	[0.184 – 1.922]	0.385			
No (ref)	-	-				
History of preterm						
Yes	4.190	[0.456 – 38.52]	0.206			
No (ref)	-	-	-			
History of IUGR						
Yes	2.621	[0.490 – 14.01]	0.260			
No (ref)	-	-				
History of preeclampsia						
Yes	3.792	[0.758 – 18.97]	0.105			
No (ref)	-	-	-			
Familial history of preeclampsia						
Yes	3.743	[0.981 – 14.27]	0.053	4.923	[1.108 – 21.87]	0.036
No (ref)	-	-		-	-	

Table 4. Risk factors for preeclampsia.
ANC = antenatal care; AOR = adjusted odds ratio; COR = crude odds ratio;
IUGR = intrauterine growth restriction.

Outcomes	Control group N = 67	Case group N = 67	*p*-value
Sex, n (%)			
Male	40 (59.7)	34 (50.7)	0.297#
Female	27 (40.3)	33 (49.3)	
Birthweight, n (%)			
Low birthweight	10 (14.9)	8 (11.9)	0.783*
Normal birthweight	56 (83.6)	59 (88.1)	
Over birthweight	1 (1.5)	0 (0)	
Intra uterine growth, n (%)			
SGA	8 (11.9)	8 (11.9)	1.0*
AGA	54 (80.6)	54 (80.6)	
LGA	5 (7.5)	5 (7.5)	
APGAR minute-1, n (%)			
≥ 7	58 (86.6)	53 (79.1)	0.252#
< 7	9 (13.4)	14 (21.9)	
APGAR minute-5, n (%)			
≥ 7	62 (92.5)	64 (95.5)	0.466#
< 7	5 (7.5)	3 (4.5)	
NICU, n (%)			
Yes	16 (23.9)	20 (29.9)	0.436#
No	51 (76.1)	47 (70.1)	

Table 5. Infant outcomes.
SGA = Small for Gestational Age; AGA = Appropriate for Gestational Age; LGA = Large for Gestational Age; NICU = Neonatal Intensive Care Unit.
*Mann Whitney U test was used; #Chi Square test was used
$p < 0.05$ was considered statistically significant.

Discussion

Our study showed that the age of both preeclamptic and control groups does not differ significantly. However, another study noted that extreme age (women <20 and >35 years old) increase the preeclampsia rate in pregnant women more than 2 folds.[15] The difference between our study and other study is might be because more than 80% of our study samples are aged between 20 – 35 years old. Moreover, there is also no difference in the maternal socioeconomic status, as the education and the occupation of mothers in both groups are similar, dominated by senior high school graduate and housewives respectively. The socioeconomic status can be referred to the influence of educational level and occupational class.[16,17] Our findings contradict the finding from Silva et al. which correlates low socioeconomic status as one of the risk factors for preeclampsia.[18] We found that there are more pregnant women in case group with overweight or obese pre-pregnancy BMI than in control group, although the difference was not statistically significant. Multivariate logistic regression model analysis of another study showed that higher BMI is associated with gestational hypertension and preeclampsia in overweight and obese women.[19]
In our study, we found that there was no significant difference in the number of ANC in total or in each trimester between case and control groups. This finding is in line with previous WHO ANC trial study which showed that women with less antenatal visit are only slightly more frequent to have preeclampsia than those with more visits (1.7% vs 1.4%).[20] Latest WHO recommendation for prevention of preeclampsia also did not mention the minimum number of ANC visit that should be done throughout pregnancy.[21] However, it should not be forgotten that quality of ANC should also be taken into consideration. Latest WHO guideline for ANC stated that preeclampsia screening during ANC is an essential part of good ANC.[22] Unfortunately, we did not evaluate the quality of ANC received by women from both groups in this study.

We found that 11.9% of women in control group do not expect the current pregnancy, whilst the prevalence in case group was 14.9%. It has been discovered that psychological stress of the mothers during pregnancy will increase the risk of preeclampsia by 3.1-fold.[23] However, even if unexpected pregnancy can affect the psychological condition of the mothers and cause stress, poorer health outcome experienced is also affected by other factors such as social circumstances and support.[24,25]

Number of participants in this study with history of preeclampsia in case group was thrice higher than in control group. Previous study found that women with history of early onset preeclampsia have 25-fold risk of developing another early-onset preeclampsia in the present pregnancy, while women with history of intermediate-onset preeclampsia have 20-fold risk of developing another intermediate onset preeclampsia.[26] Another study found that the risk of developing preeclampsia during second pregnancy in women with previous history of preeclampsia is 14.7%, and the risk becomes 31.9% if the women have a history of preeclampsia in her previous two pregnancy.[27] A systematic review study also revealed that pregnant women with history of preeclampsia have a relative risk of 7.19 times to develop preeclampsia in the current pregnancy.[28]
Other than personal history of preeclampsia in previous pregnancy, family history of hypertensive disease and preeclampsia also holds a crucial spot in preeclamptic cases.[29] In this study, we found that the prevalence of familial history of preeclampsia in case group was significantly higher than the control group. Previous study also find that a maternal family

history increases the risk of developing preeclampsia.[26] Other studies also support the findings that familial history was associated with the incidence of preeclampsia.[30,31]

The delivery method of choice for preeclampsia has been a tough decision to make, since it needs a good clinical judgement from the physician by acknowledging the real-time conditions of the mothers. Vaginal delivery and induction of labor for preeclampsia has a success rate of 66% at 23-36 weeks and 72% at term gestational age, respectively.[32] Whereas women with severe preeclampsia who undergo caesarean delivery have greater tendency to suffer pulmonary complications for both them and their babies.[33] We find that the caesarean delivery rate of preeclamptic women is significantly higher than that of the control group ($p = 0.025$). The indication of caesarean section among preeclamptic women is dominated by severe preeclampsia and followed by foetal distress.[34] Furthermore, as our study notes that 59.7% of preeclamptic women deliver through caesarean, which exceeds the national rate (6.8%).[35] However, to choose between planned caesarean section versus vaginal birth is still a difficult thing because the evidence for the difference of such interventions in preeclamptic women is still lacking and need further observation for future studies.[36]

Regardless of the mode of delivery, neonatal morbidity and/or mortality did not differ significantly among early preterm preeclamptic women.[37] However, in the long term, caesarean delivery is associated with increased odds of childhood overweight, and obesity at up to 5 years for the baby and subsequent pregnancies.[38] We found that there was no significant difference in the outcome of the neonate from both groups, including birthweight, intrauterine growth, APGAR score in 1 and 5 minutes respectively, and same NICU admission rate.

Conclusions

Our study showed that characteristic difference between pregnant women with and without preeclampsia in East Java region, Indonesia were the familial history of preeclampsia and the delivery method. Close monitoring to the pregnant women with familial history of preeclampsia should be done, because they were 4.9 times more likely to develop preeclampsia throughout their pregnancy. Future study with larger participants and broader area needs to be done to scrutinize other risk factors of developing preeclampsia in East Java, Indonesia.

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Declaration of Interest

The authors report no conflict of interest.

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