Verbal Autopsy of Preeclampsia-related Maternal Death in Jember District, Indonesia: A Case Control Study

Mergy Gayatri, B. App. Sc., MSc* Anin Indriani, MD**, Oluwadamilare Akingbade, RN., MSc*** Jesica Mulyadi, B. App. Sc**, Nurul fathiyah, B. App. Sc** Roland Arung Pirade, MD., MPH**** Dr I Wayan Agung Indrawan, MD***** Dr Diadjeng Setya Wardani, MPH*** Dr Sutrisno Sutrisno, MD*****

ABSTRACT

Objective: The aim of the study was to determine the effect of antenatal visits, body-mass index, referral travel distance, and referral travel time on preeclampsia maternal mortality in Jember district, Indonesia.

Methods: A case-control study was conducted to assess factors associated with preeclampsia maternal death in Jember district, from January 2017 to December 2019. 40 cases of mothers who died from preeclampsia and 80 controls of mothers who had preeclampsia but survived were included in this study. A Verbal Autopsy (VA) was administered. Hypotheses were tested using the chi-square, Spearman's correlation and multivariate logistic regression tests.

Results: Four times of antenatal care (4.648, 95% CI 1.776 - 12.167, p-value 0.002), obesity (OR 4.176, 95% CI 1.507 - 11.572, p-value 0.006), distance to referral hospitals from place of birth (OR 5.183, 95% CI 1.681 - 15.977, p-value p 0.004) were significantly associated with preeclampsia maternal death. However, travel time to referral hospitals *(*OR 1.537, 95% CI 0.534 - 4.422, p-value 0.426*)* was not associated with maternal mortality from preeclampsia.

Conclusions: Maternal death from preeclampsia was associated with less than four times of antenatal care, obesity, and referral distance. Identification of the mentioned predictors would enhance the ability to prevent maternal death from preeclampsia.

Keywords: preeclampsia, maternal mortality, verbal autopsy, low-middle income country, case-control

INTRODUCTION

Preeclampsia, a hypertensive disease during pregnancy, includes 2% to 8% of pregnancy-related complications, over 50,000 maternal deaths, and more than 500,000 neonatal mortality worldwide[1]. Occurring after 20 weeks of gestation with increased blood pressure as the main symptom (≥ 140 mmHg systolic and ≥ 90 mmHg diastolic pressure) and proteinuria (> 0.3 g/24 hours), preeclampsia has complex complications for both mother and fetus[2,3]. Although the cause of preeclampsia remains unknown, this disease can be detected by examining blood pressure and protein in urine during pregnancy[4].

Antenatal care is crucial as, during the visits, symptoms of preeclampsia might be detected[4]. A systematic review revealed that mothers who had antenatal care visits less than four times during pregnancy had a higher risk of developing preeclampsia compared to those who had four times of antenatal care[5]. Another predictor is obesity, which is recognised as one of the risk factors for preeclampsia. Obesity can be identified through body mass index; mothers with a body mass index of 30 kg/m^2 increase the risk of developing preeclampsia 1.8 times compared to mothers with a normal body mass index[6].

* Assistant Professor
Department of Midwifery, Faculty of Medicine
Universitas Brawijaya, Malang, Indonesia
Researcher
Center for Health Financing Policy and Insurance Management, Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada, Indonesia
** Master of Midwifery Program, Department of Midwifery, Faculty of Medicine
Universitas Brawijaya, Malang, Indonesia
E-mail: draninspog@ub.ac.id
*** The Nethersole School of Nursing, Faculty of Medicine,
Chinese University of Hong Kong, Hong Kong
Institute of Nursing Research, Nigeria
**** School of Global Public Health, New York University, New York, United States
Center for Health Financing Policy and Insurance Management, Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada, Indonesia
***** Department of Obstetrics and Gynaecology, Faculty of Medicine,
Universitas Brawijaya, Malang, Indonesia

Indonesia continues to have a high Maternal Mortality Ratio (MMR), which constituted 305 deaths per 100,000 live births[7]. This ratio is among the highest in Southeast Asia and below the target set by the Sustainable Development Goal 3[8,9]. Jember, a district in East Java Province, Indonesia, consistently has the highest MMR in the province (173 per 100,000 live births in 2020)[10]. In addition, preeclampsia (26.2%) was the second main cause of death among mothers[11].

A study assessing contributing factors to maternal death in East Java reported that mothers who died were more likely to spend approximately 24 hours at the primary health facilities before being transferred to referral hospitals[12]. Three delays associated with maternal deaths include a delay in deciding to seek care, a delay in accessing care; and a delay in receiving care [13].

This study has addressed the question 'what factors contribute to preeclampsia maternal deaths' by analysis of maternal verbal autopsy, which its usage was regulated in a joint regulation of the Minister of Home Affairs and the Minister of Health number 15 of 2010N 2009, number 162 / MENKES / PB / I / 2010 article number 6[14]. This verbal autopsy comprises measurements, for instance mothers' sociodemographic information, history of pregnancy, labour, and postpartum, as well as risk factors of deaths[15,16]. These questions must be completed by doctors or trained nurses and midwives, who do interviews with the mothers' family or other related parties to complete the questions[6].

MATERIALS AND METHODS

Objective: This study aimed to determine the association between antenatal visits, body-mass index, referral travel distance, referral travel time and preeclampsia-related maternal mortality.

Study Design: This study uses a case-control study design.

Study Setting: Jember is a district in East Java, Indonesia. Although the percentage of maternal mortality related to hypertensive disorder dropped in 2020 (26.9%), hypertensive disorder has consistently been the leading cause of maternal mortality in East Java since 2015[10]. Gestational hypertension (26.90%) and haemorrhage (21.59%) remain the main contributors to maternal death in this province[10].

In 2020, 2,536,729 people who are from the Java, Madu and Osing tribes resided in Jember [17,18]. In general, Madurese dominantly live in the north, while the Javanese reside in the south and the coast of the district[18]. Although four antenatal visits, institutional birth coverage, and three postnatal visits were high (82%, 94.3%, and 92.3% respectively) in 2020; nevertheless, the MMR was constantly the highest in the province for the last several years. In 2020, the MMR reached 173 per 100,000 live births, with the second highest deaths being women under 20 years old and the majority of deaths occurring in referral hospital[19].

Data and Sample: Data in the study were obtained from Verbal Autopsy (VA), complemented by maternal records in 26 community health centres in Jember. The data encompassed preeclampsia cases from January 2017 to December 2019. The data included frequency of antenatal visits, obesity status, referral travel distance, and referral travel time. The respondents were 120 mothers who had preeclampsia. A total sampling of 40 cases of mothers, who died from preeclampsia, and a random sampling of 80 controls (women who suffered preeclampsia but survived). The inclusion criteria of the study were women having full-term gestation, and not suffering from other complications, including intrauterine fetal death.

Methods of Data Analysis: Data were presented using frequencies and percentages. A bivariate test was done using the chi-square test while a multivariate logistic regression test was conducted to assess the risk factors for preeclampsia-related maternal mortality. Association between the variables and pre-eclampsia-related outcomes was assessed using Spearman's correlation test. If the absolute value of *r* is around ±.10, the relationship was regarded as 'weak', if the absolute value of *r* is around .30, it was regarded as 'moderate', and if *r* is ±.50, it was regarded as 'substantial'. A statistical significance level of 0.05 was applied for all statistical analyses. Statistical Package for the Social Sciences (SPSS) version 25.0 was utilised for data analysis.

RESULTS

Table 1: Socio-demographic and risk factors for preeclampsia maternal mortality in Jember district, Indonesia from January 2017 to December 2019

Risk factor	Women who died from preeclampsia (*N* = 40)	Controls (*N* = 80)	*p-value*
Antenatal visit			
<4 times	31 (77.5%)	35 (43.75%)	0.000
≥ 4 times	9 (22.5%)	45 (56.25%)	
Obesity (BMI 30 kg/m^2)			
Yes	33 (82,5%)	42 (52.5%)	0.001
No	7 (17.5%)	38 (47.5%)	
Distance to referral hospitals from place of birth			
Far (≥ 5 km)	34 (85%)	46 (57.5%)	0.003
Close (< 5 km)	6 (15%)	34 (42.5%)	
Travel time to referral hospitals			
≥ 10 Minutes	15 (37.5%)	13 (17.5%)	0.011
<10 Minutes	25 (62.5%)	66 (82.5%)	

The sociodemographic, characteristics of respondents are presented in table 1. Less than four antenatal visits was 77.5% among cases and 43.75% among controls and was significant. Obesity status was higher among cases compared to controls (82.5% among cases and 52.5% among controls). The association is statistically significant as p =0.000. Therefore, there is a significant relationship between number of antenatal visits and preeclampsia-related maternal mortality.

Obesity was higher among cases compared to controls (82.5% among cases and 52.5% among controls). The association is statistically significant as p = 0.001. Therefore, the null hypothesis is rejected and thus restated as there is a significant relationship between obesity and preeclampsia maternal mortality.

Giving birth ≥ 5 km to referral hospitals was 85% among cases and 57.5% among controls. The association is statistically significant as p = 0.003. Therefore, there is a significant relationship between distance to referral hospitals from the place of birth giving birth ≥ 5 km and preeclampsia-related maternal mortality.

Lastly, being transferred to referral hospitals for ≥ 10 minutes was higher among cases compared to controls (37.5% among cases and 82.5% among controls). The association is statistically significant p=0.011. Therefore, there is a significant relationship between travel time to referral hospitals and preeclampsia-related maternal mortality.

Table 2: Multivariate logistic regression analysis. Risk factors associated with preeclampsia maternal mortality in Jember district, Indonesia, from January 2017 to December 2019

Risk factor	Beta coefficient	OR	*p*-value	95% CI	
				Lower	Upper
Four-time antenatal visit status	1.536	4.648	0.002	1.776	12.167
Obesity	1.429	4.176	0.006	1.507	11.572
Distance to referral hospitals from place of birth	1.645	5.183	0.004	1.681	15.977
Travel time to referral hospitals	0.430	1.537	0.426	0.534	4.422
Pseudo R^2 = 34.5%					

Referring to table 2, mothers with less than 4 times of antenatal visits were at greater odds of being died from preeclampsia as compared to those who had four or more antenatal visits (OR = 4.648, CI; 1.776 – 12.167). This means that antenatal visit is associated with the outcome of preeclampsia and mothers with less than four-time antenatal visits have an increased risk of 4.648 times experiencing death from preeclampsia compared to those who had antenatal visit four times or more.

Similarly, mothers with obesity are at greater odds of dying from preeclampsia than those who were not obese (OR = 4.176, CI; 4.176 – 11.572). This means that obesity is associated with the outcome of preeclampsia and obese women have an increased risk of 4.176 times experiencing death from preeclampsia compared to those who are not obese.

Regarding referral, mothers who gave birth far from referral hospitals (≥ 5 km) were associated with an increased risk of preeclampsia maternal mortality (OR = 5.183, CI; 1.681– 15.977). This means that women who gave birth far from referral hospitals (≥ 5 km) were 5.183 times more likely to experience death from preeclampsia compared to those who gave birth near referral hospitals (< 5 km).

Lastly, mothers who were delayed transferring to a referral hospital (≥ 10 minutes) were at greater odds of dying from preeclampsia as compared to those who reached the referral hospitals faster (OR = 1.537, CI; 0.534 – 4.422). This means that women who were delayed in being transferred to the hospital (≥ 10 minutes) were 1.537 times more likely to experience death from preeclampsia compared to those who were transferred less than 10 minutes to referral hospitals.

Figure 1 illustrates obesity has an r-value of 0.292 and p-value of 0.015 which suggests a moderate positive relationship between obesity and the incidence of pre-eclampsia and was significant. Distance to the referral hospital has an r value of 0.275 with a p-value of 0.012. This suggests the distance to the referral hospital has a moderate positive relationship with the incidence of pre-eclampsia and was significant. The r-value for four-time antenatal visits was 0.320 and the p-value was 0.002. This suggests a moderate positive relationship between the variable and incidence of pre-eclampsia and was significant. Duration to referral hospitals has an r-value of 0.234 and a p-value of 0.266 which suggests a moderate positive relationship and was significant.

DISCUSSION

Our study has provided evidence that several factors influence maternal mortality from preeclampsia. Four antenatal visits or more, obesity (BMI 30 kg/m^2), being far from referral hospitals (≥ 5 km) and being delayed reaching referral hospitals (≥ 10 minutes) were associated with preeclampsia maternal mortality.

Antenatal visits less than four times may cause risk factors and culminate in failure to detect symptoms of preeclampsia. This is consistent with research conducted in Ethiopia, stating that women who had antenatal care less than four times during pregnancy had increased morbidity and mortality due to pregnancy complications, including preeclampsia[20]. A systematic review reported that women with less than four antenatal visits during pregnancy had 2.71 times increased risk of developing preeclampsia as a result of symptoms and risk factors not being detected earlier. This subsequently has an impact on delaying medical care that will be obtained[5].

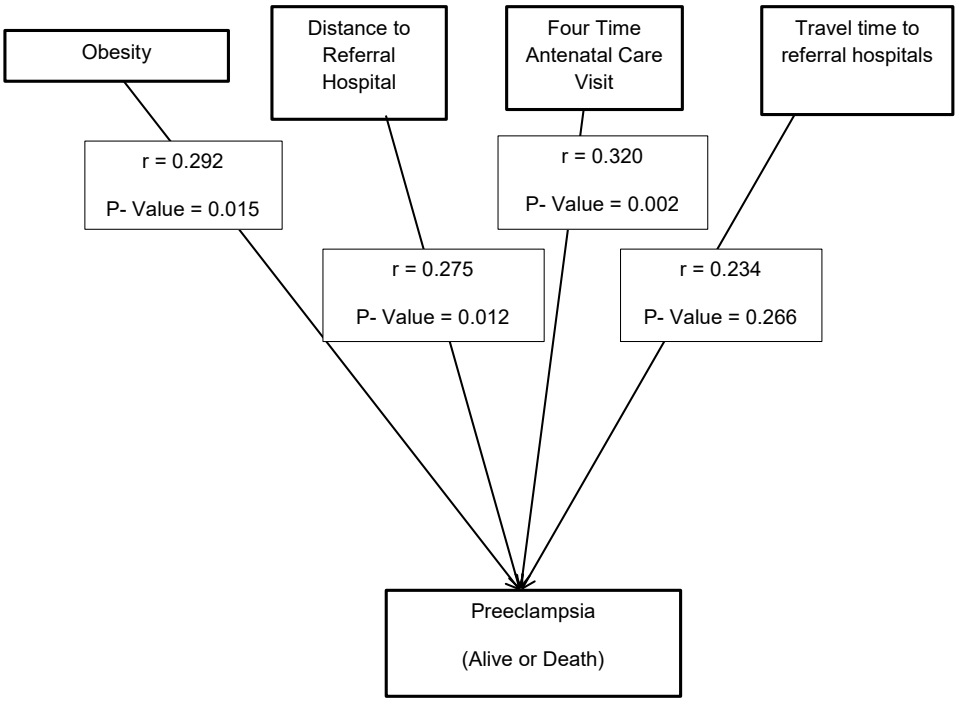

Figure 1: The correlation model of risk factors for preeclampsia maternal death

In our study, obese women (BMI 30 kg/m^2) either during pregnancy or before pregnancy increased the risk of death from preeclampsia by 4.176 times compared to women with normal BMI. A study conducted in Tanzania revealed that women with a body mass index 30 kg/m^2 had a higher risk of developing preeclampsia compared to women with a normal body mass index[6]. Obesity causes insulin resistance, dyslipidaemia, chronic inflammation, and oxidative stress[21]. Another study reported that maternal obesity caused a lipotoxic environment in the placenta, an increase in lipids that can affect mitochondria[22]. Genetic factors, lifestyle, dietary patterns, physical activity, stress, culture, race, and low frequency of antenatal visits affect obesity[23].

We found that the referral distance increased the risk of death from preeclampsia by 5.183 times. The distance of referrals to health facilities can affect maternal mortality from preeclampsia associated with the time of providing adequate treatment to mothers. Mothers who experience complications or risk of childbirth will take longer to be treated by professional health workers with more adequate infrastructure due to delays[24]. Another study revealed that a long referral distance significantly affected maternal mortality. 78% of preeclampsia maternal deaths during childbirth were experienced by mothers who live far from referral places or live remotely.[12] A previous study reported that the distance between one facility and the other can influence the utilization of the referral system[22]. Strategies must be implemented to assist mothers in reaching the receiving facility within a shorter time.

There was no relationship between travel time to referral hospital with maternal death from preeclampsia. Most of the mothers who died in the referral process were those who were referred with a process of approximately 24 hours being at the primary health facility before being transferred to referral hospitals[12]. A good referral process for pregnant women who experience complications, including preeclampsia, can affect the incidence of maternal death during childbirth; the sooner the referral time, the higher the chances of the mother getting treated adequately during childbirth[12,23,24].

The strength of this study is that we included all mothers who suffered from preeclampsia, which were obtained from actual data by the Jember District Health Office and the 26 public health centres. However, our findings might not be generalisable beyond the study region.

CONLUSIONS AND FUTURE DIRECTIONS

Overall, the results of our study have important implications for optimising maternal health services. We found strong evidence that antenatal visits, obesity, referral distance of 10 km, and travel time to referral hospital affected preeclampsia maternal mortality. These mentioned factors can be the detection tools to prevent maternal death from preeclampsia. In addition, these findings should be taken into account by the local government to develop programs in decreasing maternal mortality.

DECLARATIONS

Ethics Approval:

Ethical approval was sought from the Ethical Committee Board of Faculty of Medicine, Universitas Brawijaya, Indonesia (55/EC/KEPK-S2/02/2022)

Author Contribution:

MG Study design, Data collection, Statistical analysis, Data interpretation, Manuscript preparation, Literature search, Funds collection. **AI** Study design, , Statistical analysis, Data interpretation, Manuscript preparation, Literature search**. OA** Study design, , Statistical analysis, Data interpretation, Manuscript preparation, Literature search**. JM** Data collection, Statistical analysis, Manuscript preparation. **NF** Data collection, Statistical analysis, Manuscript preparation. **RA** Manuscript preparation, Critical revision. **IW** Manuscript preparation, Critical revision. **DS** Manuscript preparation, Critical revision. **SS** Manuscript preparation, Critical revision. SS Manuscript preparation, Critical revision.

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Potential Conflict of Interest: None.

Competing Interest: None.

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