The Impact of Antenatal Care and Pre-Referral Emergency Management on Eclampsia-Related Maternal Mortality in a Low-Resource Setting

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KEYWORDS

Eclampsia, Ante Natal Care (ANC), Maternal Mortality, Maternal Health Services.

ABSTRACT

Backgrounds: Maternal mortality due to eclampsia had a high case fatality rate. This is frequently due to a failure in detection and monitoring during the ANC, as well as inadequate emergency management of eclampsia.
Objective: To determine the impact of ANC and pre-referral emergency management of eclampsia-related maternal death at Dr. Soetomo and Airlangga University Hospital, Surabaya, Indonesia
Methods: Analytical study with a retrospective cohort design from 2022-2023, using medical records of eclampsia patients referred to Dr. Soetomo Hospital and Airlangga University Hospital to investigate the relationship between ANC, pre-referral emergency management of eclampsia-related maternal death. Bivariate analysis used the Chi-square test, while multivariate analysis used logistic regression.
Results: A total of 59 out of 65 patients met the inclusion criteria. Statistical analysis showed that study subjects aged ≥ 35 years had an association with maternal mortality in eclampsia cases ($p = 0.007$). A significant relationship also occurred in subjects who were not screened for preeclampsia ($p = 0.013$) and subjects who did not receive inadequate management of eclampsia ($p = 0.000$).
Conclusion: Pre-referral emergency management of eclampsia is associated with eclampsia-related maternal death, hence health facilities must increase their ability to address eclampsia emergencies before referral.

1. Introduction

The Maternal Mortality Rate (MMR) is an essential indicator of a country's health standards, as evidenced by the ratio of maternal mortality during pregnancy, childbirth, and postpartum, as well as the quality of health services. WHO reported that in 2017, more than 800 women in the world died every day due to complications during pregnancy and childbirth (Vincent et al., 2018). To reduce MMR, the SDGs target that by 2030, the maternal mortality rate must be less than 70 per 100,000 live births. However, in 2021, Indonesia recorded 7,389 maternal deaths, an increase from 4,627 in 2020, showing that Indonesia is still far from the Sustainable Development Goal (SDG) target (Kementrian Kesehatan RI, 2022).

In 2020, one of Indonesia's provinces, East Java, recorded an MMR of 98.39 per 100,000 live births, with the main causes being hypertension in pregnancy at 26.90%, bleeding at 21.59%, and others at 37.17% (Timur, 2020). Eclampsia is one of the pregnancy hypertension spectrums that can appear during pregnancy, childbirth, and the postpartum period. At Dr. Soetomo Hospital, the fatality rate of eclampsia reached 31.74% in 2015–2016 due to the quality of ANC, timely antenatal visits, and appropriate and adequate management in patients with preeclampsia and eclampsia. Most of the causes of maternal complications and deaths are due to a lack of ANC, poor health facilities, difficult access to health facilities, misdiagnosis, and improper management (Sulistyono & Joewono, 2020).

The implementation of integrated antenatal care (ANC) is a preventive effort to detect early health complications, abnormalities, and high risks during pregnancy and childbirth to reduce maternal mortality. ANC services must meet the 10 T standard, following the Regulation of the Minister of Health No. 4 of 2019, which stipulates a minimum of four antenatal visits and the fulfillment of the 10 T criteria (Kementrian Kesehatan RI, 2022).

According to the 10 T standard, ANC services and antenatal visits can be monitored from the maternal child health (MCH) book as part of the government's efforts to reduce the maternal mortality rate (Decree of the Minister of Health of the Republic of Indonesia No. 284/MENKES/SK/III/2004). The MCH book is a simple but effective tool for early detection of pregnancy complications, as well as a means of information, education, and communication to pregnant women and their families about the pregnancy, childbirth, and postpartum process. Preeclampsia screening, which is part of early detection of at-risk pregnancies, is also included in the

mandatory MCH book component.

According to Khan (2019), maternal mortality due to eclampsia is often caused by failure of detection and monitoring at the initial ANC visit, as well as inadequate emergency management. Related to this background, this study examines the relationship between ANC history and eclampsia pre-referral emergency management and eclampsia-related maternal mortality. The results of this study are expected to be recommended for improving antenatal care service standards and eclampsia emergency management.

2. Methods

This is an observational analysis of a retrospective cohort design conducted at Dr. Soetomo and Airlangga University Hospital in Surabaya, Indonesia. The population is all eclampsia cases referred to these two hospitals from 2022 to 2023. This research uses a total sampling technique. The independent variables are the number of antenatal care (ANC) visits (K1, K4, K6) with all of its screening. Pre-referral emergency management is assessed by evaluating A-B-C (airway, breathing, and circulation), administering MgSO4 anti-convulsants, and administering appropriate anti-hypertension. Dependent data were eclampsia patients who either died or survived. The research used secondary data from the Maternal Perinatal Audit (AMP), Maternal Perinatal Death Notification (MPDN), medical record reviews, and patient MCH books. Bivariate analysis used the Chi-square test, while multivariate analysis used logistic regression.

3. Results

Participants in this study were 59 eclampsia patients who were referred to Dr. Soetomo Hospital (RSDS) and Airlangga University Hospital (RSUA) from 2022 to 2023. Before the analysis, we analyzed the demographics of the research subjects, ANC history, pre-referral eclampsia emergency management, maternal death, the causes of eclampsia cases in mothers, and the comorbidities that occurred in eclampsia cases

Table. 1 Descriptive Research Subject

Aspects	Category	N (%), Range (Median), Mean ± SD
Demographic		
Hospital	RSDS	47 (79.7%)
	RSUA	12 (20.3%)
Origin/City	Surabaya	33 (55.9%)
	Outside Surabaya	26 (44.1%)
Non Booked Case/Booked Case	NBC	55 (93.2%)
	BC	4 (6.8%)
Age		15 - 40 (26.00)
		24.49 ± 6.91
	< 35 Year	47 (79.7%)
	≥ 35 Year	12 (20.3%)
Parity	Primigravida	32 (54.2%)
	Multigravida	27 (45.8%)
Gestational Age	< 34 weeks	23 (39.0%)
	≥ 34 weeks	36 (61.0%)
ANC history		
Number of ANC visits	No ANC	0 (0%)
	< 4	14 (23.7%)
	≥ 4	45 (76.3%)
ANC K1	Not Compliant	22 (37.3%)
	Compliant	37 (62.7%)
ANC K4	Not Compliant	36 (61.0%)
	Compliant	23 (39.0%)
ANC K6	Not Compliant	43 (72.9%)
	Compliant	16 (27.1%)
10 T Inspection	Incomplete	19 (32.2%)
	Complete	40 (67.8%)
PE Screening & Management		
	No	45 (76.3%)
	Yes	14 (23.7%)
USG Frequency	Never	14 (23.7%)

	Only trimester 1	24 (44.1%)
	Only 2nd trimester	14 (23.7%)
	Every trimester	5 (8.5%)
Pre-Referral Eclampsia Management	Inadequate	17 (28.8%)
	Adequate	42 (71.2%)
Maternal mortality	Death	15 (25.4%)
	Life	44 (74.6%)
Maternal Causes of Eclampsia Cases (N = 15)	Septic shock	9 (60%)
	ICH	3 (20%)
	Cardiogenic shock	2 (13.3%)
	ARDS	1 (6.7%)
Comorbidities in Cases of Eclampsia	Pulmonary Edema	4 (27%)
	Acute Kidney Failure	7 (47%)
	Hypoalbuminemia	11 (73%)
	Metabolic Acidosis	6 (40%)
	HELLP syndrome	5 (33%)
	ADHF	1 (7%)

Hypothesis testing is carried out in two stages: bivariate test analysis and multivariate analysis. Significant results at the bivariate stage will be tested at the multivariate stage. The following are the results of demographic bivariate testing, ANC history, and pre-referral eclampsia emergency management for maternal mortality:

Table 2 Demographic Test, ANC History and Emergency Management of Pre-Referral Eclampsia with Maternal Mortality

Demographics, ANC History, Pre-Referral Eclampsia Emergency Management	Category	n	Maternal Mortality		p-value*
			Death	Life	
Hospital	RSDS	47	13 (27.7%)	34 (72.3%)	0.712
	RSUA	12	2 (16.7%)	10 (83.3%)	
Origin/City	Surabaya	33	7 (21.2%)	26 (78.8%)	0.592
	Outside Surabaya	26	8 (30.8%)	18 (69.2%)	
Non Booked Case/Booked Case	NBC/BC	55	15 (27.3%)	40 (72.7%)	0.564
	BC	4	0 (0%)	4 (100%)	
Age	< 35 Year	47	8 (17.0%)	39 (83.0%)	0.007*
	≥ 35 Year	12	7 (58.3%)	5 (41.7%)	
Parity	Primigravida	32	5 (15.6%)	27 (84.4%)	0.114
	Multigravida	27	10 (37.0%)	17 (63.0%)	
Gestational Age	< 34 week	23	7 (30.4%)	16 (69.6%)	0.689
	≥ 34 week	36	8 (22.2%)	28 (77.8%)	
ANC K1	Not Compliant	22	4 (18.2%)	18 (81.8%)	0.499
	Compliant	37	11 (29.7%)	26 (70.3%)	
ANC K4	Not Compliant	36	8 (22.2%)	28 (77.8%)	0.689
	Compliant	23	7 (30.4%)	16 (69.6%)	
ANC K6	Not Compliant	43	12 (27.9%)	31 (72.1%)	0.738
	Compliant	16	3 (18.8%)	13 (81.3%)	
10 T Inspection	Incomplete	19	7 (36.8%)	12 (63.2%)	0.207
	Complete	40	8 (20.0%)	32 (80.0%)	
PE Screening & Management	No	45	15 (33.3%)	30 (66.7%)	0.013*
	Yes	14	0 (0%)	14 (100%)	
USG Frequency	Never	14	5 (35.7%)	9 (64.3%)	0.451
	Only trimester 1	24	7 (26.9%)	19 (73.1%)	
	Only 2nd trimester	14	3 (21.4%)	11 (78.6%)	
	Every trimester	5	0 (0%)	5 (100%)	
Pre-referral eclampsia management	Inadequate	17	10 (58.8%)	7 (41.2%)	0.000*
	Adequate	42	5 (11.9%)	37 (88.1%)	

*The test using Chi-Square is declared significant if the p-value < 0.05

Based on the bivariate relationship test results, results that are significantly related to bivariate so it can continue to multivariate test are age demographics, PE screening and management, and pre-referral eclampsia emergency management with maternal mortality with a p-value of < 0.05.

The multivariate test on maternal mortality uses logistic regression tests to ensure that those influencing maternal mortality are the most significant of the three variables that pass the bivariate test. The following is a table containing the results of the logistic regression multivariate test on maternal mortality:

Table 3 Multivariate Test of Logistic Regression on Maternal Mortality

Factor	p-value	Exp(B)	CI95%
Age	0.006	13.290	2.111 - 83.652
Pre-referral eclampsia management	0.001	17.810	3.235 - 98.045

According to Table 3, the multivariate test using logistic regression results yielded outcomes related to age and pre-referral emergency management of eclampsia, with a p-value of less than 0.05. The management of pre-referral eclampsia emergencies has a significant impact on maternal outcome. The test results for the age factor obtained an Exp(B) value of 13.290, and the factor for eclampsia pre-referral management got an Exp (B) value of 17.810. This means that mothers under age of 35 have a 13 times higher survival rate than those 35 or older (95% CI 2,111-83,652) and adequate pre-referral management of eclampsia increases survival odds 17-fold (95% CI 3.235-98.045).

4. Discussion

According to research data, of the eclampsia patients referred in 2022–2023, 79.7% (47 subjects) were referred to Dr. Soetomo, while 20.3% (12 subjects) were referred to Airlangga University Hospital, with the majority (55.9%) coming from Surabaya. The average age of patients was 24.49 ± 6.91 years, with a range of 15–40 years, and 79.7% were in the age group under 35 years. Previous research stated that eclampsia is more common in young adults, especially 15–24-year-olds, with a 4.7% higher risk than in older adults (Sheen et al., 2020). Research in Indonesia by Tyas et al., also supports the idea that most mothers with preeclampsia are 20–35 years old (Tyas et al., 2019). Primigravida has a higher risk than secundigravida and multigravida, which can be explained by the theory of immunological intolerance (Vincent et al., 2018). However, pregnant women over 35 years old are also at risk of severe preeclampsia and eclampsia, likely caused by stiffness of the spiral artery, which reduces blood flow to the uteroplacental, causing hypoxia and placental ischemia (Arwan & Sriyanti, 2020; Vincent et al., 2018).

In this study, 54.2% were primigravida, while 45.8% were multigravida. Similar research in Padang (2020), East Nusa Tenggara (2017), and Pakistan (2023) also showed that most pregnant women with severe preeclampsia and eclampsia are primigravida (Arwan & Sriyanti, 2020; Sardeva, 2017). The high risk of preeclampsia in primigravida can be explained by the angiogenic factor sF1T-1, which has a higher level compared to multigravida, sF1T-1 is an endothelial dysfunction-related substance that blocks vascular endothelial growth factor. When there are high levels of sF1T-1, it affects the placenta and causes high blood pressure, which leads to preeclampsia (Vincent et al., 2018).

Most pregnancies are over the age of 34 weeks (61%). A similar study in Bali showed that most pregnancies with eclampsia are older than 37 weeks (Vincent et al., 2018). The current consensus is to use a 34-week cut-off in determining early and advanced preeclampsia (Robillard et al., 2020). In addition, preeclampsia and eclampsia increase the risk of morbidity and high mortality in neonates with a gestational age of less than 34 weeks (Sharami et al., 2023).

This study showed that most patients had an ultrasound only in the first trimester (44.1%), 23.7% never had an ultrasound, 23.7% only had an ultrasound in the second trimester, and only 8.5% of patients had an ultrasound in each trimester. Ultrasound is one of the noninvasive methods for preeclampsia screening, especially in assessing blood flow to the placenta. Poor placental perfusion, characterized by an increase in the pulsatility index of the uterine artery, is linked to the development of preeclampsia. This examination can be performed with Doppler in the first and second trimesters (Franco et al., 2015). According to the 2019 recommendation from ISUOG (The International Society of Ultrasound in Obstetrics and Gynecology), Doppler ultrasound examination is recommended from the first trimester and can detect 48% of patients who will develop early preeclampsia and 26% of patients who will develop preeclampsia. Ultrasound examinations in the second trimester can predict 85% of cases of early preeclampsia, with a false-positive rate of 10% (Sotiriadis et al., 2019).

As many as 71.2% of pregnant women with eclampsia have been given adequate pre-referral emergency management of eclampsia, and 74.6% mother are alive. However, research in Indonesia shows that maternal mortality due to severe preeclampsia and eclampsia is related to complications, inappropriate referrals,

inadequate management, long referral times, and a long duration of response to the operating room (Sriwandoko et al., 2023). The maternal mortality rate due to preeclampsia/eclampsia is 109.6 per 100,000 live births and covers 21% of maternal mortality with a case fatality rate of 2.6% (Dasari et al., 2022). Research in Surabaya in 2020 showed that the proportion of maternal mortality due to eclampsia was relatively high and was related to delays in accessing health facilities and adequate management (Sulistyono & Joewono, 2020).

The status of non-booked and booked cases (BC) referral patients in this study also did not provide a significant relationship with maternal mortality in eclampsia cases, with a p-value of 0.564. In a similar study by Butt S. et al., insignificant results were obtained in preeclampsia patients with both BC and NBC status (Butt et al., 2018). All patients with eclampsia cases in the study who died were NBC patients, this proves that the referral system and the ability to detect patients with high-risk pregnancies are still not running well. Additionally, it's possible that the patient himself may not be fully aware of the complications associated with preeclampsia and eclampsia during pregnancy.

In this study, there was no significant relationship between parity and maternal mortality in eclampsia cases, with a p-value of 0.114. Similar research by Aziz et al., showed that there was no bivariate relationship between gravida and parity in the incidence and mortality of preeclampsia (Aziz et al., 2022), but the research of Dasari et al., showed that there was an increase in the frequency of primigravida mothers in patients with eclampsia with a higher proportion of primigravida in patients with eclampsia than preeclampsia. The risk of developing eclampsia in primigravida patients is 2.68 times higher compared to multigravida (Dasari et al., 2022). This condition is related to the immunological theory, namely the formation of blocking antibodies in the first pregnancy against incomplete antigens, such as corialis, thus triggering disruption of the trophoblast implantation process in the maternal decision. The mother's body will trigger the production of cortisol, which increases the sympathetic response (Aziz et al., 2022), so from this difference, it can be concluded that parity is not directly related to maternal mortality in cases of eclampsia, but in primigravida, there is a risk of progression of preeclampsia.

A significant relationship was obtained between age and maternal mortality in eclampsia cases, namely that the age group of less than 35 years has a higher percentage of survival probability compared to the age group over 35 years old. Age is one of the factors that can determine the health of pregnant women (Hamzah et al., 2021). Pregnant women over 35 years old are more likely to experience preeclampsia and die, which is estimated to be due to physical weakness at that age. Women at that age are related to various health comorbidities, such as high blood pressure, diabetes, and other diseases, as well as physiological changes in reproductive tissues and organs (Aziz et al., 2022). The mortality of eclampsia was found to be highest at extreme maternal age (Sheen et al., 2020; Sulistyono & Joewono, 2020). The study showed that the risk of placental abruption, acute kidney failure, acute heart failure, pulmonary edema, and stroke was lower in the group of pregnant women aged 15-24 years and increased as the gestational age increased (Sheen et al., 2020).

This study shows that as many as 45 (76.3%) patients have had ANC visits for a total of ≥ 4. However, the majority of these patients fail to meet the Ministry of Health's guidelines for visit distribution, which state that ANC K1 requires a visit or the first visit to occur at least once in the first trimester if the gestational age is less than 8 weeks. ANC K4 requires a minimum of four visits, with one in the first trimester, one in the second trimester, and two in the third trimester, while ANC K6 requires a minimum of six visits, with one in the first trimester, two in the second trimester, and three in the third trimester. This causes the percentage of ANC in K1, K4, and K6 in this study to be low with values of 62.7%, 39%, and 27.1%, respectively, so it is necessary to carry out more integrated socialization to increase the insight of pregnant women in making visits or ANC visits, both in terms of the total number of visits and the proper distribution of visits in each trimester.

The results of this study also showed that there was no association between ANC K1, K4, and K6 and maternal mortality in cases of eclampsia, with p-values of 0.499, 0.689, and 0.738, respectively. The ANC assessment needs to be seen not only in terms of quantity, but also in terms of the quality of care received by pregnant women. Therefore, it is crucial to understand the quality of reasonable care in order to maximize the effectiveness of ANC services (Mardiyah et al., 2022). Tesfa et al., conducted research from the pillar of safe motherhood to reduce maternal mortality through early detection of various complications that can occur in pregnant women. Their findings revealed that the risk of a pregnant woman who does not complete an ANC visit is 5.43 times higher than that of a woman who completes an ANC visit (95% CI) (Tesfa et al., 2023).

This study found a significant relationship between preeclampsia screening, low-dose aspirin and calcium supplements, and maternal mortality in eclampsia cases. The administration of low-dose aspirin to pregnant

women with positive PE screening has been proven to reduce the incidence of preeclampsia by up to 62% compared to those given a placebo (Gajbhiye et al., 2023).

This study reveals that adequate eclampsia management provides a higher percentage of maternal life outcomes than inadequate management, with a p-value of 0.000. Inadequate management in this study included the administration of anti-convulsant drugs other than MgSO4, the administration of inappropriate doses of MgSO4, not giving MgSO4 at the time of repeated seizures, and not being given antihypertensive drugs until patients were directly referred without the administration of anti-convulsants or anti-hypertension. In contrast, most of the referred patients had stabilized A-B-C (airway, breathing, and circulation) and monitored fluid balance with catheter installation. Studies often show that most pregnant women die due to a lack of preparedness in managing and responding to emergencies, delays in recognizing the exacerbation of preeclampsia, and inadequate treatment so as not to receive adequate therapy. One of the problems with eclampsia management in developing countries is the cost of therapy and the lack of adequate facilities and infrastructure. The administration of MgSO4 is an effective first-line therapy in preventing and managing eclampsia, which is given for at least the first 24 hours after a seizure and requires close monitoring related to toxicity (Padda et al., 2021). Research in Nigeria shows that immediate therapy in the form of stabilization, appropriate use of MgSO4, and termination of labor lowers the risk of maternal mortality with eclampsia (Rabiu et al., 2018).

Adequate management of eclampsia is highly dependent on the readiness of health facilities to deal with eclampsia emergency cases. In a study conducted in Bangladesh, as many as two-thirds of health facilities do not have anti-convulsants, which illustrates the low preparedness of health facilities in dealing with eclampsia, in addition to the fact that only 14% of eclampsia cases are given MgSO4 injections. The lack of readiness of a health facility can have a collateral impact; when a health facility is not ready to handle an emergency case, it can result in patients experiencing a change of several referral places, which will prolong patients who experience an eclampsia emergency to an adequate referral place and increase the patient's morbidity (Khan et al., 2023).

The provision of adequate hypertension management also dramatically affects the morbidity and mortality of eclampsia referral patients. In a study in Nigeria, CVA (Cerebrovascular Accident) is a common cause of death for patients with eclampsia; in the study, it was said that 4.2% of patients experienced CVA, of which up to 50% of them died. The high CVA rate here illustrates the inadequate management of eclampsia in previous health facilities for eclampsia patients who came after experiencing several seizures without initial management of seizures and hypertension. (Jido, 2012)

Comorbidities are also a determinant of maternal mortality in eclampsia cases; in this study, there are several comorbidities in maternal mortality in eclampsia cases with a case fatality rate (CFR) of 25.4%, where the highest number of comorbidities include acute kidney failure, sepsis, HELLP syndrome, intracranial hemorrhage, and pulmonary edema. In line with this research, Sulistyono et al. (2020), show that eclampsia has a case fatality rate (CFR) of 31.74%, where the three highest comorbidities can cause maternal mortality in eclampsia cases, namely HELLP syndrome, acute kidney failure, and intracranial hemorrhage.

The multivariate analysis using logistic regression revealed that age and effective management of eclampsia emergencies were the primary factors influencing the outcome, with a significant p-value of less than 0.05. Age less than 35 years had a 13,290-fold chance of survival outcomes compared to age more than or equal to 35 years (95% CI 2,111–83,652). Previous studies have shown mixed results. Some studies have indicated that young mothers, defined as those under or equal to 24 years of age, often experience mortality due to eclampsia. This is often linked to high rates of early marriage and pregnancy, with pulmonary edema being the most common cause of death (Ratan Das & Saumya Biswas, 2015). Meanwhile, a similar study by Sheen et al., showed that older women, namely 45–54 years old, had a 2.28 times higher risk of experiencing acute heart failure or pulmonary edema and a 2.76 times higher risk of experiencing acute kidney failure (Sheen et al., 2020)

Those who received adequate eclampsia emergency management had a 17.810 times higher chance of survival outcomes compared to those who received inadequate care (95% CI 3.235 – 98.045). Research shows that delays in management are related to an increased risk of death. There was a twofold increased risk of maternal mortality in patients with eclampsia due to delays in obtaining treatment, delays in transport and referrals, inadequate management, and inadequate intensive care for patients. Proper management with the administration of magnesium sulfate immediately after referral is related to good outcomes (Sk, 2023).

5. Conclusion

The age of pregnant women, preeclampsia screening, and pre-referral emergency management are related to maternal mortality in eclampsia cases. In cases of eclampsia, pregnancy above the age of 35 has a higher mortality risk and adequate pre-referral management of eclampsia provides a greater chance of survival in eclampsia-related maternal mortality.

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