

# Pre-Referral Management, Maternal and Perinatal Outcome of Preeclampsia Patients with Severe Feature In Coastal Region

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## Abstract

**Background:** Preeclampsia (PE) with severe features, as one of the hypertensive disorders in pregnancy, often becomes a problem in health services for pregnant women. Nusa Tenggara Barat (NTB) Province is in the Eastern part of Indonesia with archipelagic characteristics. Sea transportation is the main transportation used to refer patients live in coastal area and small islands. Travel distance, limited facilities on ships and weather conditions are challenges for the referral system in this province. **Methods:** This study employed a retrospective cross-sectional design to describe the pre-referral management of severe preeclampsia cases referred to the Regional Hospital of NTB Province between January 2023 and July 2024. **Results:** This study found a total of 60 subjects. Of the four pre-referral treatments for preeclamptic pregnant women, administration of MgSO<sub>4</sub> is the most common therapy. There were 80% (n=48) of subjects receiving antihypertensives. 21 subjects (35%) were given steroids. As many as 30% of patients experienced eclampsia, 6.7% with HELLP syndrome, 20% with severe hypertension and one with CVA. The majority of babies born with APGAR scores <7 at one and five minutes, 10% with RDS and 21.7% in the NICU for >3 days. **Conclusion:** Our findings show pre-referral care needs to be better, especially for patients living on the coast as it takes more challenges due to extreme weather and distance. The provision of low-dose aspirin in groups at high risk of preeclampsia needs to be improved.

**Keywords:** preeclampsia, coastal, pre-referral, maternal, perinatal.

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## Introduction

With the development of technology and health facilities, Maternal Mortality Rate (MMR) is decreasing in low and middle-income countries, however, the incidence of maternal mortality in Southeast Asia is still quite high when compared with other parts of Asia and Europe. Even though the United Nations (UN) Sustainable Development Goal 3.1 targets reducing the MMR to less than 70 per 100 000 live births in 2030(United Nations, 2023). In 2023, Indonesia's maternal mortality ratio was 140.5 deaths per 100,000 live births, showing an improvement compared to 2019(WHO, 2024). Within Southeast Asia, this figure

places Indonesia fourth in maternal mortality, after Timor-Leste (192), Papua New Guinea (189), and Myanmar (185) (WHO et al., 2024).

Preeclampsia with severe features, as one of the hypertensive disorders in pregnancy, often becomes a problem in health services for pregnant women. In Indonesia, hypertensive disorders in pregnancy are the second highest cause of maternal death after obstetric hemorrhage (23% vs. 25%). This figure continues to increase compared to 1990 to 2022 (8 to 19%). Preeclampsia/eclampsia and HELLP syndrome (n=1884, 14.6%) are the highest cases of hypertensive disorder reported as causes of maternal death(Syairaji et

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al., 2024). Preeclampsia caused nearly 25% of maternal deaths in a study in Bangladesh. The highest maternal mortality occurs during intrapartum and postpartum is still high. The incidence of preeclampsia/eclampsia in the first trimester, during labor and within 48 hours of birth indicates the need for regular examinations before and during pregnancy (Syairaji et al., 2024).

Nusa Tenggara Barat (NTB) province is in the Eastern part of Indonesia. Eastern region of Indonesia has the highest MMR. There are many factors why the maternal mortality rate is still high. Sparse population, low socioeconomic status, poorer infrastructure and difficult access to health facilities are some of the contributing factors (Badan Perencanaan Pembangunan Daerah Provinsi NTB, 2013). This makes it difficult to carry out management according to standard procedures to reduce poorer outcomes and risk of maternal and neonatal death. Poorer referral conditions also influence this (National Research Council, 2013). NTB Province has an area of 20,153.20 km<sup>2</sup> consisting of 2 large islands, namely Lombok Island and Sumbawa Island as well as hundreds of small islands. Of the 280 existing islands, there are 32 inhabited islands. Sea transportation is the main transportation used to refer patients. Travel distance, limited facilities on ships and weather conditions are challenges for the referral system in this province.

Health services for pregnant women in this province are centered at the NTB Provincial Hospital which serves referral patients from peripheral health facilities with varying pre-referral conditions. It is important to study the characteristics of pre-referral management and its appropriateness in order to determine the patient's maternal and perinatal outcomes.

## Materials and Methods

### *Study design*

This research is a cross-sectional study that describes the pre-referral management of preeclampsia cases with severe symptoms referred in the period January 2023 – July 2024. The research was conducted at the Regional Hospital of NTB Province, Indonesia. Data was collected retrospectively on preeclamptic pregnant women with severe feature who were referred and received treatment at the NTB Provincial Regional Hospital.

### *Participants*

Participants in this study were preeclamptic pregnant women accompanied by severe features who were referred to the NTB Provincial Hospital in the period January 2023 - July 2024. The sample was selected using a purposive sampling technique. The inclusion criteria for this study were pregnant women with a diagnosis of

preeclampsia accompanied by severe features; referred to the NTB Provincial Regional Hospital; complete data regarding pre-referral management, maternal and perinatal outcomes. Incomplete medical record data and pregnant women with complications other than preeclampsia were excluded.

Preeclampsia is defined as hypertension that occurs in pregnancy or above 20 weeks of gestation with organ disorders. The criteria for preeclampsia with severe symptoms in this study refer to the fulfillment of one of the criteria issued by the Indonesian Society of Obstetricians and Gynecologists: (1) blood pressure of at least 160 mmHg systolic or 110 mmHg diastolic on two examinations 15 minutes apart using the same arm ; (2) thrombocytopenia: platelets < 100,000/microliter; (3) kidney disorders: serum creatinine >1.1 mg/dL or there is an increase in serum creatinine levels in conditions where there are no other kidney disorders; (4) liver disorders: increased transaminase concentration 2 times normal and/or pain in the epigastric area/upper right region of the abdomen; (5) pulmonary edema; (6) neurological symptoms: stroke, headache, visual disturbances; (7) impaired fetal growth is a sign of impaired uteroplacental circulation: oligohydramnios, fetal growth restriction (FGR) or absent or reversed end diastolic velocity (ARDV).

### *Data collection*

Data was taken from the medical records of participants who met the inclusion criteria. Data collected included (1) pre-referral management: history of previous aspirin consumption, receiving antihypertensive drugs, receiving MgSO<sub>4</sub>, receiving steroids for lung maturation; (2) maternal outcomes: eclampsia, pulmonary edema, HELLP Syndrome, acute renal failure, severe hypertension, cerebrovascular accident (CVA), maternal death, preterm labor < 37 weeks, preterm labor < 34 weeks, intrauterine growth restriction (IUGR), pressure systolic blood pressure 1 day after labor, diastolic blood pressure 1 days after labor, admission to ICU and (3) perinatal outcome: intrauterine fetal death (IUFD), newborn weight, APGAR score at one minute, APGAR score at five minutes, length of stay in the NICU, respiratory distress syndrome (RDS), intracranial hemorrhage (ICH), necrotizing enterocolitis (NEC), neonatal sepsis and neonatal death.

### *Outcomes*

The outcomes of this study are pre-referral management, maternal and perinatal outcome characteristics of preeclamptic pregnant women with severe features.

### *Statistical analysis*

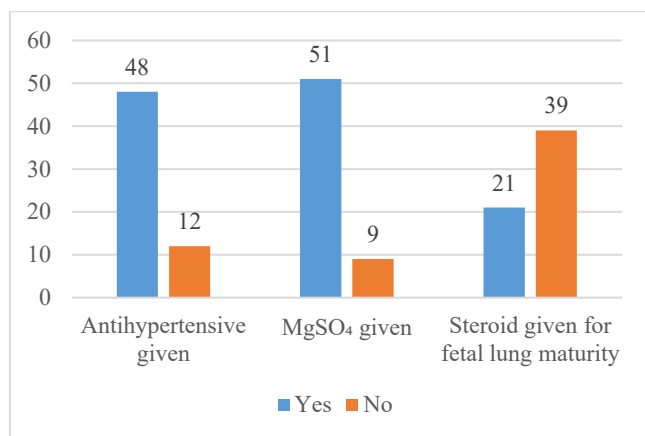
Data were analyzed using SPSS (version 25; IBM, Armonk, NY). The data obtained was then analyzed univariately to describe characteristics of pre-referral management, maternal and perinatal outcome. Data is presented in tabular form.

## Result and Discussion

This study had a total of 60 preeclamptic pregnant women with severe features after excluding patients with incomplete data.

### *Pre-referral management characteristics*

Out of the three pre-referral management for preeclamptic pregnant women with severe features (Figure 1), administration of MgSO<sub>4</sub> was the most common therapy given (n=51; 85.0%); of these, 8 (15.7%) were referred from primary health centers (Puskesmas), 40 (78.4%) from hospitals, and 3 (5.9%) from private obstetric clinics. There were 80% (n=48) of preeclamptic pregnant women with severe features who also received antihypertensive; of these, 8 (16.7%) were referred from Puskesmas, 37 (77.1%) from hospitals, and 3 (6.2%) from private obstetric clinics. There were only 21 pregnant women (35%) who were given steroid to mature the fetus' lungs; of these, 3 (14.3%) were referred from Puskesmas and 18 (85.7%) from hospitals. One patient (referred from a hospital) had received aspirin prophylaxis; however, she still developed severe-feature preeclampsia and was referred without standard pre-referral management (antihypertensive, MgSO<sub>4</sub>, or steroid).

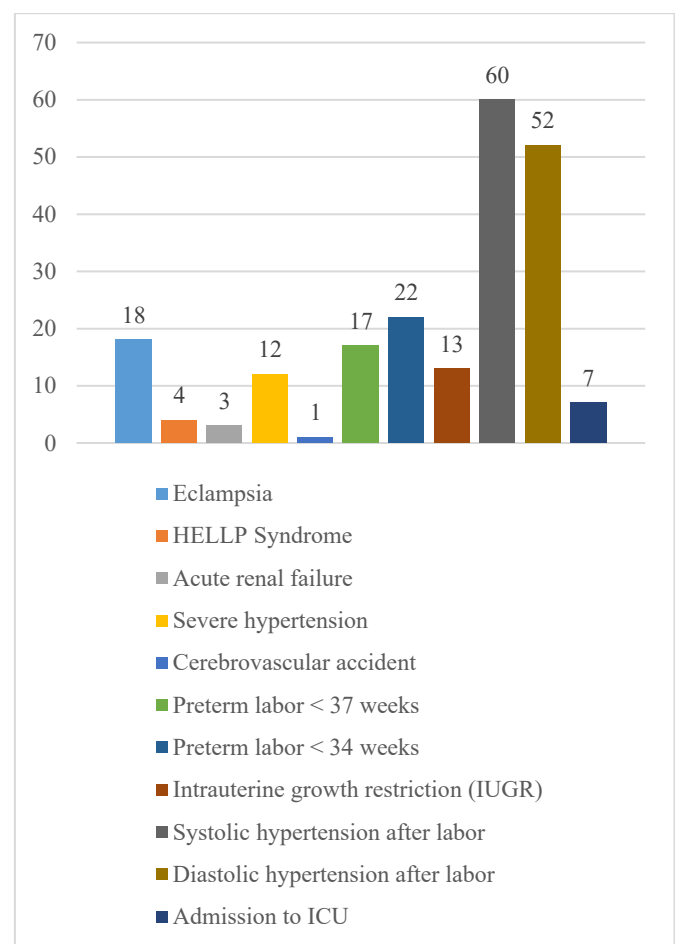


**Figure 1.** Characteristics based on pre-referral management (n)

### *Maternal outcome characteristics*

In this study, it was found that all patients still had systolic hypertension (n=60; 100%) while 52 of them also experienced diastolic hypertension after labor (86.7%)

(Figure 2). There were 12 patients (20.0%) who had severe hypertension and three patients (5.0%) experienced acute renal failure. Cerebrovascular accident was experienced by one patient (1.7%) and 7 patients (11.7%) required treatment in the ICU. Out of 60 patients, one third (n=18; 30%) of them experienced a worsening of their condition to eclampsia and 4 of them with HELLP syndrome. Preterm labor was also observed in this study where more patients underwent preterm labor at gestational age < 34 weeks compared to gestational age < 37 weeks (36.7% vs. 29.3%). More than one fifth of patients had intrauterine growth restriction (IUGR) during pregnancy (n=13; 21.7%). In this study, there were no maternal deaths or pulmonary edema.

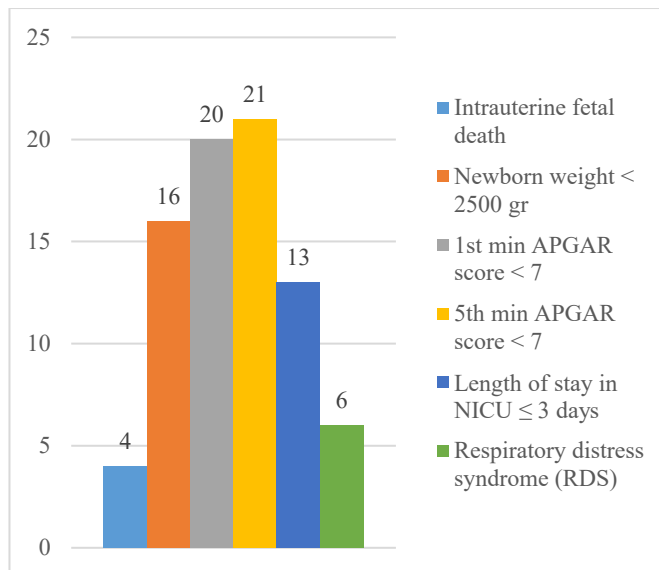


**Figure 2.** Characteristics based on maternal outcome (n)

### *Perinatal outcome characteristics*

Patient characteristics based on perinatal outcomes are summarized in figure 3. In this study, there were 4 incidents of intrauterine fetal death in preeclamptic pregnant women with severe features (6.7%). Most newborns had a birth weight < 2500 gr (n=44; 73.3%), had APGAR score at 1 minute < 7 (n=40; 66.7%) and had

APGAR score at 5 minutes < 7 ( $n=39$ ; 65.0%). There were 13 newborns (21.7%) who required NICU care for more than 3 days. Respiratory distress syndrome was found in 6 newborns meanwhile, no other complications were found such as ICH, NEC, neonatal sepsis and neonatal death.



**Figure 3.** Characteristics based on perinatal outcome (n)

Nusa Tenggara Barat Province is one of the provinces in Indonesia which has many islands and its population lives on the coast. NTB Province has an area of 20,153.20 km<sup>2</sup> and consists of 2 (two) large islands, namely Lombok Island and Sumbawa Island and hundreds of small islands. Of the 280 existing islands, there are 32 islands that are inhabited. Most coastal residents in NTB make their living as fishermen. They occupy the main island and also several small islands around it. Sea transportation using ships is the main vehicle used by coastal residents, especially to move between islands. To date, efforts have been made to equalize facilities, especially health facilities, on small inhabited islands. Although to get treatment for complex cases, patient is still referred to a referral center hospital in the city of Mataram. Sea transportation is the main transportation used to refer patients (Badan Perencanaan Pembangunan Daerah Provinsi NTB, 2013). Travel distance, limited facilities on ships and weather conditions are challenges for the referral system in this province. Difficult cases such as preeclampsia require immediate treatment for the safety of mother and baby.

Preeclampsia is a dangerous condition which, if not treated immediately, can harm the mother and fetus. Therefore, initial treatment at peripheral service facilities

needs to be carried out appropriately to ensure a smooth patient referral process to the central referral hospital. Inadequate facilities and medicines as well as a lack of health workers in health facilities, especially in remote areas, can increase the risk of worsening conditions during the transport process and upon arrival at the referral center (Syairaji et al., 2024). Another factor that should be considered such as appropriate exchange of information and feedback between the health workers involved is important to ensure smooth referrals. Gap in communication feedback leading to delayed and inappropriate referrals and poor maternal health outcomes (Sari et al., 2023). The expertise of health workers is very important to recognize risk factors that can occur in pregnant women to reduce the risk of complications due to referring patients who are already in an intrapartum condition (Kurniawan et al., 2023).

Treatment of preeclamptic pregnant women with severe features includes administration of MgSO<sub>4</sub>, and antihypertensives, steroids for fetal lung maturation. Meanwhile, low-dose aspirin is given as a preventive measure for pregnant women at high risk of developing preeclampsia. In this study, most patients received MgSO<sub>4</sub> (85%) and antihypertensives (80.0%) before referral, more than a third received steroids to mature the fetal lung (35.0%) and only one patient was given aspirin during pregnancy (1.7%). This is different from a study in Ethiopia where only 15.7% of patients were given MgSO<sub>4</sub> and 86.6% of patients did not receive antihypertensives before being referred. In the study in Ethiopia, only 3.1% of patients received dexamethasone injection (Sium et al., 2024). A study in a district hospital, Southeast Sulawesi, Indonesia also observed pre-referral treatment in preeclamptic pregnant women with severe features. It was found that 89% of patients had received antihypertensives but 100% of patients were not given MgSO<sub>4</sub> due to fear of health workers in providing such therapy (Pardomuan et al., 2020). Inadequate knowledge of pre-referral management from health providers and unavailability of drugs and supplies are the reasons why the first dose of MgSO<sub>4</sub> was not given before the patient was referred (Sari et al., 2023). MgSO<sub>4</sub> is the main treatment of choice for pregnant women with preeclampsia with severe symptoms to prevent seizures. One of its mechanism is vasodilation obtained from smooth muscle relaxation in the peripheral vasculature and uterus (Sharma et al., 2024). Administration of MgSO<sub>4</sub> has been proven to improve the outcome of pregnant women with preeclampsia by reducing the incidence of recurrent seizures and maternal death (Birungi et al., 2024). Perinatal outcomes were also reported to be better in patients given MgSO<sub>4</sub> compared to other groups. Administration of MgSO<sub>4</sub> reduces the risk of APGAR score at 5 minutes < 7 and NICU admission in newborns (Birungi et al., 2024).

The interesting finding in this study is one patient, referred from a hospital, had received aspirin prophylaxis; however, she developed severe-feature preeclampsia and was transferred without standard pre-referral management (antihypertensives,  $\text{MgSO}_4$ , or steroids). Low-dose aspirin (75 mg/day) is recommended by the Indonesian Society of Obstetricians and Gynecologists (2016) for pregnant women at high risk of developing preeclampsia, ideally initiated before 20 weeks of gestation (Indonesian Society of Obstetricians and Gynecologists, 2016). Low-dose aspirin has anti-angiogenesis, anti-inflammatory and antiplatelet effects which are useful for reducing the impact of an overreactive inflammatory response in preeclampsia. Administration of low-dose aspirin has been proven to reduce the risk of preeclampsia, recurrent preeclampsia, premature labor, neonatal death, IUFD and newborn babies weighing <2500 grams (Davidson et al., 2021; Han et al., 2024). Factors that increase the risk of severe preeclampsia include chronic hypertension, diabetes mellitus, obesity, previous history of preeclampsia, kidney disease, multiple pregnancies, nullipara, and autoimmune diseases (Barda et al., 2023). Screening at routine antenatal visits in primary health facilities should be able to identify such risk factors in pregnant women so that low-dose aspirin can be considered for prevention. However, aspirin is a preventive measure and cannot replace the standard pre-referral management required once severe preeclampsia has developed. In such cases, antihypertensive drugs,  $\text{MgSO}_4$ , and corticosteroids (for fetal lung maturation) remain the recommended standard of care. The case of this patient highlights an important gap in pre-referral management, as aspirin alone cannot provide adequate protection once preeclampsia is established.

This study observed the presence of serious complications in preeclamptic pregnant women with severe features who were referred to the NTB provincial hospital. As many as 30% of patients experienced eclampsia, 6.7% of patients with HELLP syndrome, 20% of patients with severe hypertension and one patient with cerebrovascular accident. Meanwhile, the perinatal outcomes observed in this study were that the majority of newborns with APGAR scores <7 in one and five minutes, 10% of neonates experienced RDS and 21.7% needed to be treated in the NICU for >3 days. Complications of intrauterine fetal death and low birth weight also need to be considered in this study. Babies born to preeclamptic mothers with severe features are at high risk of having poorer outcomes. This study found significant maternal and perinatal complications in preeclamptic pregnant women with severe features even though most had been given pre-referral  $\text{MgSO}_4$ . This may be influenced by a delay in administering the initial

dose of  $\text{MgSO}_4$  when given at the initial health facility or an inappropriate dose of  $\text{MgSO}_4$ . The recommended dose of  $\text{MgSO}_4$  is intravenous loading of magnesium sulfate 4 g for 5-10 minutes, followed by a maintenance dose of 1-2 g/hour for 24 hours post labor after the last seizure. The first dose of  $\text{MgSO}_4$  given as initial therapy within the first hour has a protective effect against low APGAR scores at five minutes. Giving an incomplete dose or maintenance dose with an inappropriate frequency either earlier or later than the recommended hour carries the risk of giving birth to a baby with low birth weight, prematurity, respiratory distress and admission to the NICU (Birungi et al., 2024).

Preeclampsia also causes long-term health problems. Women with a history of preeclampsia have an increased risk of cardiovascular disease-related death, end-stage renal disease, long-term cognitive dysfunction and neurological complications including stroke. Apart from that, preeclampsia also has a negative effect on the patient's psychosocial condition. This is related to the severity of preeclampsia, timing of diagnosis and pregnancy outcome. Patients are at risk of experiencing post-partum depression or post-traumatic stress disorder, especially if they have poor pregnancy outcomes. Long-term effects on the child of a preeclamptic pregnancy were also reported at higher risk of impaired cognitive abilities and neurodevelopmental outcomes (Dimitriadis et al., 2023). Considering the serious complications that arise from preeclampsia with severe features, it is necessary to continue to improve and increase the quality of services, especially pre-referral management and the transfer process to specialized care facilities. Not only that, screening for high-risk women and carrying out prevention in at-risk groups are also important. Adequate supply of resources, appropriate training for healthcare providers, and easy access to appropriate healthcare are crucial factors in preeclampsia management (Barda et al., 2023; De Oliveira et al., 2024).

The strength of our study is that it examines more maternal and perinatal outcomes compared to other studies. This research is also the first research conducted at the NTB provincial hospital so that it can provide an overview for future follow-up studies. The weakness of this study is that it is only descriptive research so it cannot provide information about the relationship between variables.

## Conclusion

Our findings show that pre-referral care needs to be better, especially for patients living on the coast as it takes more challenges due to extreme weather and distance. The provision of low-dose aspirin in groups at high risk of preeclampsia needs to be improved.



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