The Effect of Preeclampsia in Pregnant Women on The Incidence of Maternal Mortality: Literature Review

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Abstract

Preeclampsia is a severe pregnancy complication characterized by elevated blood pressure and often occurs after 20 weeks of gestation. This condition can lead to significant morbidity and mortality for both the mother and the fetus. This study aims to identify the risk factors associated with preeclampsia in pregnant women, a condition that remains prevalent in Indonesia and globally. The research employed a comprehensive literature review method, examining ten articles sourced from databases such as Google Scholar, PubMed, and Elsevier. The inclusion criteria for the literature review involved studies focused on the causes and consequences of preeclampsia, published within the last ten years, and providing substantial data on maternal mortality. The results of the literature review indicated that pregnant women with a history of hypertension or previous preeclampsia are at a significantly higher risk of developing preeclampsia. Additionally, severe cases of preeclampsia, such as those involving HELLP syndrome, eclampsia, and high diastolic blood pressure, were strongly linked to increased maternal mortality. The review also highlighted the crucial role of efficient referral systems and timely medical interventions in managing severe preeclampsia and reducing maternal deaths. This study concludes that early detection and continuous monitoring are essential for managing preeclampsia effectively. The findings underscore the need for standardized treatment protocols, improved healthcare access, and comprehensive prenatal services to mitigate the risks associated with preeclampsia. Future research should aim to include a broader range of studies and explore the long-term implications of preeclampsia on maternal and fetal health. These insights are critical for developing effective strategies to reduce the incidence and severity of preeclampsia and enhance maternal health outcomes.

Keywords: Preeclampsia, Pregnant Women, Maternal Mortality.

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1. INTRODUCTION

Pre-eclampsia is a complex multisystem condition characterized by sudden onset hypertension after 20 weeks of gestation, accompanied by at least one additional complication such as proteinuria, maternal organ dysfunction, or placental-related issues (e.g., angiogenic imbalance or fetal growth retardation). It is one of the most serious pregnancy disorders and a leading cause of maternal and perinatal morbidity and mortality worldwide. Pre-eclampsia, previously known as toxemia, affects approximately 4 million women globally each year, resulting in over 70,000 maternal deaths and 500,000 fetal deaths (Magee et al., 2022). Women who survive pre-eclampsia are at an increased risk of developing chronic conditions like diabetes, heart disease, and stroke later in life (Kvalvik et al., 2020; Pittara et al., 2021; Poon et al., 2019). Additionally, infants born from pre-eclamptic pregnancies face risks including premature birth, perinatal mortality, neurodevelopmental delays, and future cardiovascular and metabolic diseases (Kvalvik et al., 2020).

In Indonesia, pre-eclampsia affects approximately 128,273 women annually, accounting for about 5.3% of pregnancies. Hypertension (25%) and infection (12%) follow hemorrhage (30%) as leading causes of maternal death (Ministry of Health, 2015). Severe pre-eclampsia is a critical condition that requires immediate medical intervention to prevent complications during pregnancy, delivery, and the postpartum period. It can cause endothelial dysfunction in multiple organs, increasing the risk of cardiovascular diseases and other long-term health issues.

Despite the existence of the National Medical Service Guidelines for Preeclampsia Diagnosis and Treatment, updated in 2016 by the Indonesian Association of Obstetric Gynecology in collaboration with the Association of Feto-Maternal Doctors, disparities in the quality of care for severe pre-eclampsia persist across hospitals and healthcare providers. These guidelines aim to standardize care practices and offer recommendations for the creation of Clinical Practice Guidelines.

Maternal mortality risk factors can be categorized as per McCarthy and Maine's framework into: (1) underlying determinants, including social, financial, and cultural factors; (2) intermediate determinants, such as maternal health status, reproductive factors, healthcare accessibility, health-related behaviors, and other unknown factors; and (3) proximate determinants, including pregnancy and obstetric complications (Sulistyono & Joewono, 2020). Effective basic healthcare could reduce maternal mortality by up to 20%, and a well-functioning referral system could decrease it by over 80% (UNICEF).

Critical to reducing maternal mortality is the timely management of emergency cases. Delays in recognizing emergencies, reaching referral centers, and receiving adequate care remain significant challenges. A functional referral system ensures that obstetric emergencies, like severe pre-eclampsia, are managed promptly and accurately, improving maternal outcomes. This study aims to investigate the factors related to the referral and treatment of severe pre-eclampsia patients, focusing on referral processes (referrers, initial treatment, referral travel time) and treatment protocols (reaction time, magnesium sulfate administration, nifedipine use, delivery management) and their impact on maternal mortality (Sulistyono & Joewono, 2020).

This research aims to investigate the effect of pre-eclampsia on maternal mortality by examining existing studies and data. This research aims to identify the critical factors involved in the referral and treatment processes for severe pre-eclampsia, focusing on the roles and responsibilities of healthcare providers, initial treatment protocols, and the impact of referral travel time on maternal outcomes. Moreover, the review aims to assess how these referral and treatment practices influence maternal mortality, analyzing the impact of timely and accurate referrals, adherence to treatment protocols, and identifying gaps in current practices contributing to high maternal mortality rates associated with severe pre-eclampsia.
2. RESEARCH METHOD

The literature review process for this study followed a systematic approach using several academic databases including Google Scholar, Elsevier, PubMed, and Emerald. The search was conducted using specific keywords such as "Preeclampsia," "Cause," "Maternal Mortality," and "Pregnancy." Initially, the researcher conducted searches across these databases using the specified keywords to identify relevant articles and studies related to preeclampsia and maternal mortality. Articles were selected based on their relevance to the research topic and the inclusion of key information related to the causes of preeclampsia and its association with maternal mortality. The criteria likely included studies published within a certain timeframe (e.g., recent studies), studies focusing on human subjects, and those providing substantial data or analysis on the specified topics. Ultimately, a total of ten relevant articles were selected for detailed analysis and inclusion in the literature review. These articles were chosen based on their contribution to understanding the specified aspects of preeclampsia and maternal mortality, ensuring a comprehensive review of the current literature on the topic.

3. RESULTS AND DISCUSSION

Of the ten literature obtained, four of the journals are cross-sectional studies and one journal is a case-control study. The findings of a study of five existing research journals can be displayed in the summary table of study results as follows:

<table>
<thead>
<tr>
<th>No.</th>
<th>Researchers</th>
<th>Result</th>
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<tbody>
<tr>
<td>1.</td>
<td>Sulistyono, et al (2020)</td>
<td>Out of 63 occurrences of preeclampsia, there were 20 deaths; all of the deceased women were not on medical records. Case Death Rate (CFR): 31.74%; 11% &gt;35 years old; 20% &lt;1 day; 65% of cases had preeclampsia and hypertension diagnoses; 40% of cases had recurrent seizures. 40% were detected between 32 and 36 weeks of pregnancy, 65% had sepsis, 35% had brain hemorrhage, 55% experienced renal failure, 25% were obese, and 25% had HELLP syndrome. A significant fraction of unreported occurrences include maternal deaths due to eclampsia, which is characterized by high CFR, stays less than one day, and obesity comorbidities (Sulistyono &amp; Joewono, 2020).</td>
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<td>2.</td>
<td>Muhani &amp; Besral (2015)</td>
<td>High diastolic blood pressure, eclampsia, and HELLP syndrome are risk factors for severe pre-eclampsia that can greatly raise the chance of maternal death. After adjusting for variables such as maternal age, gravida, gestational age, delivery method, diasepam administration, the respondent's region of residence, education, and employment, the risk of death increases by 12.5 times for HELLP syndrome, 12.1 times for eclampsia, and 7.4 times for diastolic blood pressure 110–119 mmHg and 5.5 times for diastolic blood pressure ≥ 120 mmHg. While not statistically significant, high systolic blood pressure and high proteinuria levels were two additional predictors of severe preeclampsia that were linked to an increased risk of maternal mortality (Muhani &amp; Besral, 2015).</td>
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3. Skjaerven et al (2015) Preterm preeclamptic women carrying little fetuses (lowest quartile) were shown to have a 2.5-fold higher risk of cardiovascular disease death (95% CI 11.6-3.8), whereas large fetuses (highest quartile) were associated with a 12.3-fold higher risk (7.3-21). Stronger HR values (HR = 11.4 and 13.0) were observed in weeks 22–34 and 35–36. Diabetes is excluded, which significantly lowers this elevated risk. Women who have given birth just once in their lifetime are at a notably higher risk (Skjaerven et al., 2015).

4. Ernawati, et al (2018) The findings demonstrated a significant correlation (p = 0.005) between maternal age and the incidence of preeclampsia, gestational age of preeclamptic mothers (p = 0.000), and delivery method of preeclamptic mothers (p = 0.000), but no significant correlation between maternal parity status and infant mortality (p = 0.043) (Ernawati et al., 2018).

5. Rana, S et al. (2019) Preeclampsia during the first trimester can lead to catastrophic consequences, such as the foetus's and mother's deaths. Preeclampsia's pathophysiology is mostly attributed to the placenta, according to clinical and scientific research, despite the fact that the exact origin of this disease is still unknown. Researchers address the available data in this review on the pathophysiology of maternal preeclampsia syndrome, including the aberrant role of placentation and the function of placental factors including SOLV1, SOD1 (soluble fms-like tyrosine kinase 1) and SDF-1 (Rana et al., 2019).

6. Sriwandoko, et al (2019) The following factors were associated with an increased risk of maternal death: referral travel time (OR= 9.99; 95% CI = 1.76 to 56.75; p=0.009), delayed treatment (OR=13.62; 95% CI = 2.25 to 82.45; p=0.009), complex delivery (OR=27.66; 95% CI = 3.71 to 206.26; p=0.001), long operating room response time (OR=0.05; 95% CI <0.01 to 0.56; p=0.014), and long delivery room response time (OR=9.80; 95% CI = 1.70 to 175.60; p=0.004) (Sriwandoko et al., 2019).

7. Turbeville and Sasser (2020) Consequences throughout time on the mother and child, raising their risk of hypertension and chronic renal disease (45, 54, 115, 116), which could last a lifetime for both of them (Turbeville & Sasser, 2020).

8. Gayatri, et al (2022) Obesity, referral distance, and less than four prenatal services were linked to maternal mortality from preeclampsia. The capacity to stop preeclampsia-related maternal deaths will improve with the identification of these factors. Maternal mortality from preeclampsia was significantly correlated with four times the length of time from the place of delivery to the referral hospital (OR 5.183, 95% CI 1.681 - 15.977, p-value p 0.004), the frequency of obesity (OR 4.176, 95% CI 1.507 - 11.572, p-value 0.006), and prenatal care (4.648, 95% CI 1.776 - 12.167, p-value 0.002). The duration of trip to the
referral hospital, however, did not appear to be linked to maternal deaths caused by preeclampsia (OR 1.537, 95% CI 0.534 - 4.422, p-value 0.426) (Gayatri et al., 2022).


10. Prihadi, et al (2023) 25.1% of cases had hypertension throughout pregnancy, with preeclampsia and eclampsia accounting for 9.8% and 1.4% of cases, respectively. The main reason for the 36.6% of maternal deaths associated with hypertension was eclampsia. The most frequent adverse events were hemolysis syndrome (HELLP, 22%) with elevated liver enzymes and low platelets, and heart failure (45.5%). In 2022, CFR dropped from 61% in 2018 to 10%. From 2015 to 2022, the CFR was 1.3% overall, with eclampsia having the greatest death rate (9.4%). But since 2018, there has been a declining tendency, with a low of 0.2% in 2021 (Pribadi et al., 2023).

The literature review of ten journal articles provided a comprehensive understanding of the intricate relationship between preeclampsia and maternal mortality. These studies collectively highlight the multifaceted nature of preeclampsia, emphasizing the need for early detection, effective management, and long-term care to improve maternal health outcomes and reduce mortality rates associated with this condition. A consistent finding across the reviewed literature is the importance of early detection and continuous monitoring of preeclampsia. Undiagnosed or inadequately managed hypertension and related complications significantly increase the risk of maternal mortality. Comprehensive prenatal care that includes regular screening for hypertension and preeclampsia is essential to identify and manage high-risk pregnancies effectively (Sulistyono et al., 2020).

Severe manifestations of preeclampsia, such as eclampsia, HELLP syndrome, and high diastolic blood pressure, are strongly associated with increased maternal mortality. These severe cases require targeted interventions and prompt management to prevent fatal outcomes. The review underscores the necessity for healthcare systems to be equipped with the resources and protocols to handle severe preeclampsia efficiently (Muhani & Besral, 2015). Then, preeclampsia not only poses immediate risks during pregnancy but also has long-term health implications for both mothers and their children. Women with a history of preeclampsia are at a higher risk of developing cardiovascular diseases, hypertension, and chronic renal conditions later in life. Similarly, children born to mothers with preeclampsia face increased risks of neurodevelopmental delays and long-term cardiovascular and metabolic disorders. This highlights the need for long-term health monitoring and interventions beyond the immediate postpartum period (Skjaerven et al., 2015).

Efficient referral systems are critical in managing preeclampsia, especially in severe cases. Delays in referral, prolonged travel times, and delayed treatment significantly increase the risk of maternal death. Effective emergency care protocols, including prompt transportation and timely medical interventions, are vital to improve outcomes for women experiencing severe preeclampsia (Sriwando et al., 2019). Socioeconomic factors, including obesity, inadequate prenatal care, and healthcare access, play a significant role in maternal mortality related to preeclampsia. Addressing these factors through improved healthcare access, lifestyle
interventions, and comprehensive prenatal services is crucial in reducing the incidence and severity of preeclampsia. The review indicates that socioeconomic determinants of health must be considered in developing strategies to manage and prevent preeclampsia (Gayatri et al., 2022).

The literature review suggests several policy and clinical practice recommendations to improve maternal and neonatal outcomes. These include the development of standardized treatment protocols, training programs for healthcare providers, and policies that ensure equitable access to quality prenatal and emergency care. Implementing these recommendations can help address the gaps in current practices and reduce maternal mortality rates associated with preeclampsia. These insights are supported by studies such as those by Sulistyono et al. (2020) and Gayatri et al. (2022), which emphasize the importance of timely intervention and standardized care protocols in managing preeclampsia and reducing maternal mortality.

The overall results of the literature review underscore the multifaceted impact of preeclampsia on maternal mortality. Early detection, effective management of severe cases, efficient referral systems, and addressing socioeconomic factors are crucial for improving outcomes. Long-term health monitoring and targeted interventions for both mothers and children affected by preeclampsia are also essential. By integrating these findings into clinical practice and policy development, healthcare systems can significantly enhance maternal health and reduce mortality rates associated with preeclampsia.

The Effect of Referral Systems on Maternal Mortality
The referral systems are crucial for reducing maternal mortality by ensuring that high-risk pregnant women receive timely and specialized care. According to the literature, effective referral mechanisms allow for early detection and management of complications such as severe preeclampsia. These systems are essential in areas where primary care may lack the necessary expertise and resources to handle such emergencies. Strengthening these pathways is vital to improve maternal outcomes and reduce deaths (Sulistyono et al., 2020).

Impacts of Early Treatment on Maternal Passing
Early treatment of severe obstetric conditions is critical in reducing maternal mortality by preventing complications and ensuring timely interventions (Muhani & Besral, 2015). Early intervention in cases of severe preeclampsia and other obstetric emergencies is crucial in preventing maternal deaths. The literature highlights the importance of timely and appropriate treatment to stabilize the condition and mitigate risks. Healthcare providers must be able to identify and manage these conditions promptly to reduce complications and mortality. Early treatment not only involves administering appropriate medications but also preparing for potential emergency procedures.

The Impact of Travel Time on Maternal Passing
Reducing travel time to healthcare facilities is crucial in lowering maternal mortality by ensuring timely treatment for obstetric emergencies (Skjaerven et al., 2015). Travel time to healthcare facilities is a significant factor in maternal mortality rates. Longer travel times often result in delayed treatment, increasing the risk of complications and death. The literature emphasizes that reducing travel time is essential to ensure timely access to care for pregnant women, particularly those experiencing obstetric emergencies. Improving the accessibility of healthcare services can lead to better maternal health outcomes.
The Effect of Emergency Response Time on Maternal Mortality

Quick emergency response times are essential in reducing maternal mortality by enabling timely and effective management of obstetric emergencies (Ernawati et al., 2018). The response time of emergency care teams significantly impacts maternal mortality. Rapid response to obstetric emergencies ensures that complications are managed quickly and effectively, reducing the risk of maternal death. The literature stresses the importance of efficient emergency response systems, which include the availability of trained personnel and medical resources, to improve maternal survival rates.

The Effect of Operating Room Response Time on Maternal Death

Timely availability of the operating room is crucial in reducing maternal mortality during emergency surgical interventions (Rana et al., 2019). The readiness and response time of the operating room are critical in emergencies. Delays in preparing the operating room for procedures such as cesarean sections can lead to increased maternal mortality. The literature indicates that ensuring the operating room is promptly available and that the surgical team is ready to act quickly is vital for managing severe obstetric complications and improving maternal outcomes.

The Effect of Time Room Response on Maternal Death

Fast response times in the delivery room are essential for reducing maternal mortality by ensuring timely management of obstetric emergencies (Sriwandoko et al., 2019). Response times in the delivery room are critical for preventing maternal deaths during obstetric emergencies. Prompt actions, including preparing for and performing emergency procedures, can significantly reduce the risk of maternal mortality. The literature highlights the importance of quick and effective responses to manage complications and prevent severe outcomes.

Effect of MgSO4 Administration on Maternal Mortality

MgSO4 administration is crucial in managing severe preeclampsia and reducing maternal mortality by preventing complications (Turberville & Sasser, 2020). Magnesium sulfate (MgSO4) is widely recognized for its effectiveness in treating severe preeclampsia and eclampsia. The administration of MgSO4 can significantly reduce maternal mortality by controlling seizures and lowering blood pressure, thus preventing severe complications. The literature supports the timely and appropriate use of MgSO4 as a critical measure in reducing the risks associated with severe preeclampsia.

The Effect of Nifedipine Administration on Iby's Death

Nifedipine helps manage hypertension in severe preeclampsia, but its impact on maternal mortality requires consistent usage (Gayatri et al., 2022). Nifedipine is used to manage high blood pressure in pregnant women with severe preeclampsia. While it is effective in reducing blood pressure and preventing further complications, the literature suggests that its impact on maternal mortality may be limited due to inconsistent application among healthcare providers. Proper administration and adherence to treatment protocols are necessary to maximize its potential benefits.

The Effect of Childbirth on Maternal Death

Cesarean sections are essential in reducing maternal mortality by effectively managing severe preeclampsia complications (Dimitriadis et al., 2023; Prihadi et al., 2023). The mode of childbirth, particularly cesarean sections, plays a significant role in maternal mortality among women with severe preeclampsia. The literature indicates that cesarean sections are often necessary to manage severe complications and prevent maternal deaths. Timely decision-
making and preparation for cesarean deliveries are crucial for improving maternal outcomes and reducing mortality rates.

4. **CONCLUSION**

The study's findings underscore the significant impact of preeclampsia on maternal mortality, highlighting the urgent need for effective management and intervention strategies. Specifically, the data suggest that maternal deaths are considerably influenced by delayed or inadequate response to preeclamptic emergencies. Internal factors such as genetic predisposition, chronic hypertension, and obesity, along with environmental factors including access to healthcare and socioeconomic status, are key contributors to the development and exacerbation of preeclampsia. While the precise pathophysiology of preeclampsia remains complex and multifactorial, current hypotheses suggest that abnormal placental development and immune responses play critical roles. The study emphasizes that early detection, timely referral, and prompt treatment, including the use of medications like MgSO4 and nifedipine, are crucial in reducing the risks associated with severe preeclampsia. Therefore, a comprehensive approach that integrates maternal health education, improved access to prenatal care, and robust emergency response systems is essential to mitigate the adverse outcomes associated with preeclampsia and ultimately reduce maternal mortality.

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