

ORIGINAL ARTICLE

Preeclampsia correlates with maternal and perinatal outcomes in Regional Public Hospital, Madiun, Indonesia

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ABSTRACT

Objectives: This research aimed to find correlation between preeclampsia and maternal as well as perinatal outcomes in Regional Public Hospital, Madiun, Indonesia, from 1 January 2017 to 30 September 2020.

Materials and Methods: An observational analysis was applied in this study with a cross-sectional design. This study used secondary data from medical records of Regional Public Hospital, Madiun, Indonesia, with retrospective sampling and total sampling methods. Samples were 250 preeclamptic mothers with or without severe symptoms.

Results: Of 250 preeclamptic mothers, only 216 samples could participate in this study. Maternal outcomes included spontaneous PV delivery (12.22%), SC (87.78%), antepartum hemorrhage (0.45%), postpartum hemorrhage (6.33%), eclampsia (0.45%), HELLP syndrome (0.90%), and maternal mortality (0.45%), while perinatal outcomes covered IUGR (7.69%), LBW (33.94%), preterm birth (12.67%), perinatal mortality (2.71%), and asphyxia neonatorum (13.12%).

Conclusion: There was a significant correlation between preeclampsia with or without severe symptoms and maternal outcomes, which was the delivery process, and perinatal outcomes, which were the IUGR, LBW, and preterm birth. However, there was no significant correlation for antepartum hemorrhage, postpartum hemorrhage, eclampsia, HELLP syndrome, maternal mortality (maternal outcomes), perinatal mortality and neonatal asphyxia (perinatal outcomes).

Keywords: preeclampsia; maternal outcomes; perinatal outcomes; maternal mortality

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ABSTRAK

Tujuan: Mengetahui adanya hubungan kehamilan dengan preeklampsia terhadap maternal outcomes dan perinatal outcomes di RSUD Kota Madiun, Indonesia, periode 1 Januari 2017 sampai 30 September 2020.

Bahan dan Metode: Penelitian ini menggunakan metode analitik observasional dengan rancangan penelitian cross-sectional. Penelitian ini menggunakan data rekam medik di RSUD Kota Madiun, Indonesia, dengan pengambilan sampel retrospektif serta metode total sampling sejumlah 250 ibu dengan preeklampsia tanpa ataupun dengan gejala berat.

Hasil: Terdapat 250 ibu preeklampsia dari 4636 ibu bersalin (5,39%). Namun hanya 216 sampel yang termasuk dalam penelitian ini. Maternal outcomes meliputi proses persalinan dengan pervaginam (12,22%), SC (87,78%), terjadi perdarahan antepartum (0,45%), perdarahan postpartum (6,33%), eklampsia (0,45%), sindrom HELLP (0,90%), kematian maternal (0,45%), IUGR (7,69%), BBLR (33,94%), kelahiran preterm (12,67%), kematian perinatal (2,71%), asfiksia neonatorum (13,12%).

Simpulan: Didapatkan hubungan yang bermakna antara preeklampsia dengan atau tanpa gejala berat terhadap maternal outcome yaitu proses persalinan, dan perinatal outcomes yaitu IUGR, BBLR, kelahiran preterm. Hubungan yang tidak bermakna pada perdarahan antepartum, perdarahan postpartum, eklampsia, sindrom HELLP, kematian maternal (maternal outcomes), kematian perinatal dan asfiksia neonatorum (perinatal outcomes).

Kata kunci: preeklampsia; luaran maternal; luaran perinatal; kematian ibu

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INTRODUCTION

Preeclampsia is a hypertension or high blood pressure in pregnancy with systolic per diastolic pressure at or above 140/90 mmHg which occurs after 20 weeks of gestational age followed by proteinuria of quantitatively 300 mg protein in the urine for 24 hours or semi-quantitatively equal to ≥ 1 + dipstick or by other organ system symptoms.¹ The cause of preeclampsia is still unknown that Zweifel in 1916 called it “the disease of theories.” The prevalence of preeclampsia occurrences in Indonesia has reached 3-10% of pregnancies, specifically 23.6 preeclampsia occurrences per 1,000 births.² Preeclampsia and its complications hold a significant role for maternal outcomes, such as maternal mortality which remains one of the world’s health problems. According to WHO, every day in 2017, approximately 810 women died from pregnancy and labor complications which could have been prevented.³

The prevalence of maternal mortality with eclampsia resulting from preeclampsia in developed countries is from 0.4% to 7.2%. Meanwhile, inadequate tertiary medical services in developing countries result in deaths from eclampsia up to more than 25%.³ On the other hand, the percentage of maternal mortality from preeclampsia in East Java reached 31.32%, based on the the data from Public Health Office of East Java Province, Indonesia, in 2018.⁴ According to Sarwono Prawirohardjo, there are four main causes of maternal, fetal, and newborn mortalities from the perspectives of obstetrics: bleeding, infection and sepsis, hypertension in pregnancy (preeclampsia/eclampsia), and dystocia.⁵

Infant mortality rate in East Java is still rather high. As proven by the data from the Health Department of Republic of Indonesia in 2009 in East Java, the infant mortality resulted from asphyxia neonatorum (23.14%), premature birth (21.3%), low birth weight (16.4%), infection (9.2%), and congenital abnormalities (4.6%).⁴ Preeclampsia causes one of the above outcomes. Even though preeclampsia is a disease in pregnancy with great impacts to perinatal outcomes, it can actually be diagnosed and prevented from possible mortality and morbidity.

MATERIALS AND METHODS

This research used analytical observational method with retrospective sampling. The design used in this research was cross-sectional. The research was conducted in the Medical Record and Maternity Room at the Regional Public Hospital, Madiun, Indonesia from October to December 2020 with secondary data taken from the medical records at the hospital.

Total sampling method was used in this study with inclusion criteria: all age groups of mothers who gave birth with all types of preeclampsia (preeclampsia without severe symptoms or preeclampsia with severe symptoms) recorded in the medical records within the period from January 1, 2017 to September 30, 2020 at Regional Public Hospital, Madiun, Indonesia. The exclusion criteria in this study were mothers with gemellary pregnancy who were not completely recorded in the medical records of the hospital. Finally, there were 216 mothers included in this study.

The analysis of this study used Chi-square and Fisher Exact Test on outcomes that did not fulfil the Chi-Square test requirements. The analysis used had a significance level of 95% and p value of 0.05.

RESULTS AND DISCUSSION

In this study, 250 preeclampsia mothers were found from 4636 mothers who gave birth at the Regional Public Hospital, Madiun, Indonesia, from January 1, 2017 to September 30, 2020 (5.39%). This was also found in a previous study where the incidence of preeclampsia in Indonesia was around 3-10% of all pregnancies, with 23.6 cases per 1,000 births.² The frequency of pregnant women with preeclampsia in this study was 216 mothers of 4636 women who gave birth at the Regional Public Hospital, Madiun, in the period from January 1, 2017, to September 30, 2020 (4.65%) with the frequency of preeclampsia without and with severe symptoms were 104 mothers (48.15%) and 112 mothers (51.85%) respectively. The frequency of preeclampsia with severe symptoms was higher than the preeclampsia without severe symptoms, while the distribution of the types of preeclampsia with severe symptoms was predominantly found in a study by Ika (2017) in Dr. H Abdul Moeloek Regional General Hospital in Lampung Province, Indonesia, where 58.4% of 154 preeclampsia mothers had severe symptoms.⁶

Some of the risk factors for preeclampsia include gravida, age of pregnant women, history of previous chronic diseases, obesity, pregnancy with more than one baby (gemellary) and previous history of preeclampsia.⁷ The age of pregnant women can be a risk factor for causing complications in pregnancy, including preeclampsia. According to previous studies, pregnant women of less than 20 years easily have increased blood pressure and tends to cause seizures quickly, while age of more than 35 years is also a predisposing factor for the occurrence of pre-eclampsia.^{7,8} Age distribution the preeclampsia women were 20-35 years in as many as 140 mothers (64.81%) (Table 1). The highest frequency

at that age proves the possibility of increasing public awareness of getting pregnant at a physiological age of 20 to 35 years. This is because the age of 20-35 years is the period of regulating pregnancy, which is also a fertile age for pregnancy and childbirth. However, in this productive age, they are also in the active period of activity, causing mothers to pay less attention to her pregnancy, resulting in less regular antenatal care.⁸

Table 1. Distribution of preeclamptic mothers characteristics

Characteristics of pregnant mothers		
Mothers' age	Frequency (n)	Percentage (%)
<20 years	2	0.93
20-35 years	140	64.81
>35 years	74	34.26
Gravide		
1	69	31.94
2-5	145	67.13
>6	2	0.93
Parity		
0	71	32.87
1-4	143	66.20
>5	2	0.93
History of disease		
Hypertension	17	7.87
Diabetes melitus	8	3.70
No history of disease	191	88.43
Pregnancy interval		
Gravide 1	69	31.94
<2 years	4	1.85
2-10 years	106	49.07
>10 years	37	17.13
Body mass index		
Underweight (<18.5)	1	0.46
Normal (18.5-22.9)	6	2.78
Overweight (23-24.9)	23	10.65
Obesity 1 (25-29.9)	84	38.89
Obesity 2 (>30)	102	47.22
Total	216	100.00

Based on previous research, gravida had an influence on pregnancy and childbirth in pregnant women due to a higher risk for disturbances during pregnancy, especially in the first pregnancy or primigravida. This was due to the imperfect formation of antibody blocking against placental antigens. In the first pregnancy, the antigenic location of the placenta was wider than the number of antibodies, so it causes an immune response that is detrimental to the histoincompatibility of the placenta.⁸ In this study, the frequency of primigravida was 31.94%, comprising 69 mothers. According to a previous study by Windaryani, such primigravida frequency can be regarded as high. Primigravida often experience stress in dealing with pregnancy and childbirth. This stress can trigger the release of CRH and causes increasing cortisol. The effect of cortisol is to prepare the body to respond to various stressors by increasing sympathetic responses, including responses to increased cardiac output and blood pressure.⁹

Parity also affects the incidence of preeclampsia, for example, in nulliparity and pregnant women who give birth more than three times. In multiparous mothers, there is excessive uterine stretching and can effect in excessive ischemia which can lead to preeclampsia.⁹ Multiparity is a woman who has given birth between 2 and 4 times, while grande-multipara is a woman who has given birth 5 times or more. The multiparous mothers have a 1% risk of developing preeclampsia. It based on the results of this research where there were 68 nulliparous mothers (31.48%), 68 multiparous mothers (31.48%), and grandemultipara 2 mothers (0.93%).

In addition, preeclampsia is more common in women with risk factors for autoimmune disease, hydatidiform mole, parity, diabetes and gestational diabetes, twin pregnancies/gemelli, chronic hypertension, history of preeclampsia, age, kidney disease. A study found that a mothers with a history of hypertension comprised 17 cases (7.87%) and diabetes mellitus was cases (3.70%) and those without history of previous disease as many as 191 cases (88.43%).⁹

In our findings, 37 mothers (17.13%) gave birth with an interval more than 10 years. When the interval is more than equal to ten years, then the risk for these mothers to experience preeclampsia is the same as nulliparous mothers or those who have never given birth before.¹⁰ While those with an interval of less than 2 years, the number was 4 mothers (1.85%). Pregnant women with a birth interval of less than 2 years have a twice greater risk of experiencing complications during pregnancy or during childbirth compared to longer birth intervals. Therefore, the recommended interval of pregnancy is at least 2 years or more for women to recover after pregnancy, childbirth and lactation. Roberts et al. (2011) stated that the risk of preeclampsia became three times higher in obese women. Cardiovascular disorders that arise due to obesity are the cause of preeclampsia in pregnant women.¹¹

There was a significant result relationship ($p=0.00$) between preeclampsia with severe symptoms or without severe symptoms on the childbirth process in this study, which was in line with Basri's study (2020) that there is a significant relationship between preeclampsia and the childbirth process (spontaneous vaginal and caesarean section).¹² The results of this study obtained 189 mothers from 216 preeclampsia mothers (87.5%) who were terminated by caesarean section (Table 2). The high incidence of pregnancy termination by caesarean section is indicated if the mother and the fetus were in emergency, such as fetal position abnormalities, fetal distress, eclampsia and preeclampsia, narrow pelvis, old parturition, premature rupture of membranes, macrosomia, cephalopelvic disproportion, oligohydramnios.

Table 2. Childbirth process

Variables	Spontaneous Vaginal N=27 (%)	Caesarean Section N = 189 (%)	<i>p</i> *
Degree of preeclampsia			
Without severe symptoms	20 (9.26)	84 (38.89)	0.00
With severe symptoms	7 (3.24)	105 (48.61)	

In this study, there was no significant relationship between preeclampsia with or without severe symptoms and antepartum bleeding cases ($p=0.48$) (Table 3). The results of this study were in line with Hartanto's study (2021) which concluded that there was no significant relationship between preeclampsia with or without severe symptoms and placental abruption.¹³ Based on the development theory, placental abruption occurs as a result of less strong vascular relationship between maternal and fetal vasculature in preeclampsia due to abnormal trophoblastic invasion which causes easy separation of the placenta from the mother's basal decidua cell layer, so that it causes placental abruption easily.¹⁴

Table 3. Antepartum bleeding

Variables	No Antepartum Bleeding N=215 (%)	Antepartum Bleeding N = 1 (%)	<i>p</i> *
Degree of preeclampsia			
Without severe symptoms	103 (47.69)	1 (0.46)	0.48
With severe symptoms	112 (51.85)	0 (0.00)	

In this study, there were 14 cases of postpartum hemorrhage with 9 mothers experiencing preeclampsia without severe symptoms, and 5 of them had preeclampsia with severe symptoms. There was an insignificant relationship between preeclampsia without or with severe symptoms when it was associated with postpartum hemorrhage ($p=0.21$) (Table 4). In this research, uterine atony was found as the most common cause of postpartum hemorrhage, as it was explained in Julizar's research (2019) that the use of MgSO₄ (magnesium sulfate) was indicated in pre-eclampsia or severe eclampsia and it was known that magnesium sulfate had a tocolytic effect that contributed to uterine atony.¹⁵

Table 4. Postpartum bleeding

Variables	No Postpartum Bleeding N=202 (%)	Postpartum Bleeding N = 14 (%)	<i>p</i> *
Degree of preeclampsia			
Without severe symptoms	95 (43.98)	9 (4.17)	0.21
With severe symptoms	107 (49.54)	5 (2.31)	

According to Sarwono Prawirohardjo, eclampsia is a complication of pregnancy with preeclampsia with manifestations of generalized seizures or coma.¹ In this study, there was an insignificant relationship between preeclampsia without severe symptoms or with severe symptoms if it was associated with the incidence of eclampsia ($p=1.00$) (Table 5).

Table 5. Eclampsia

Variables	Not Eclampsia N=202 (%)	Eclampsia N = 14 (%)	<i>p</i>
Degree of preeclampsia			
Without severe symptoms	104 (48.15)	0 (0.00)	1.00
With severe symptoms	111 (51.39)	1 (0.46)	

Although it was not statistically significant, there was a tendency for severe preeclampsia to become eclampsia clinically. Before a patient with severe preeclampsia becomes eclampsia, symptoms such as severe headache, vomiting, epigastric pain, visual disturbances, and a progressive increase in blood pressure are known as impending eclampsia. This is due to vascular disorders that occur in the cerebral cortex, so that it causes hypersynchronization and hyperactivity of electrical activity that can cause seizures.¹

Table 6. HELLP syndrome

Variables	No HELLP Syndrome N=214 (%)	HELLP Syndrome N = 2 (%)	<i>p</i>
Degree of preeclampsia			
Without severe symptoms	104 (48.15)	0 (0.00)	0.50
With severe symptoms	111 (50.39)	2 (0.93)	

HELLP syndrome is a complication of pregnancy with pre-eclampsia accompanied by the onset of hemolysis, liver dysfunction characterized by an increase in liver enzymes, and thrombocytopenia.¹ In this study, there was a non-significant relationship between preeclampsia without severe symptoms or with severe symptoms in relations to the incidence of HELLP syndrome ($p=0.50$), indicating that the incidence of HELLP syndrome is not affected by the degree of preeclampsia with or without severe symptoms (Table 6). Although it was not significant statistically, there is a tendency for severe preeclampsia to develop into the HELLP syndrome clinically. There is an uncertain mechanism related to the occurrence of HELLP syndrome in preeclampsia, but most believe that this is caused by systemic arterial vasoconstriction causing blood accumulation in the veins, one of which is in the hepatic veins, which causes enlargement of the liver, and stretching of the liver capsule which causes damage and dysfunction in the liver, leading to hemolysis, increased liver enzymes and thrombocytopenia and activation of nociceptors so that it induces pain in the right upper quadrant of the

abdomen. The results of this study were in line with Kinay's research (2015) that there is the same level of morbidity between mothers with HELLP syndrome and severe preeclampsia at the same gestational age. Therefore, the management of severe preeclampsia and HELLP syndrome must be carried out properly in order to simultaneously reduce maternal morbidity and perinatal outcomes.¹⁶

Table 7. Maternal death

Variables	No Maternal Death N=215 (%)	Maternal Death N = 1 (%)	<i>p</i>
Degree of preeclampsia			
Without severe symptoms	103 (47.69)	1 (0.46)	0.48
With severe symptoms	112 (51.85)	0 (0.00)	

In this study, there was an insignificant relationship between preeclampsia without severe symptoms or with severe symptoms in relations to the incidence of maternal death ($p=0.48$) (Table 7). Mothers with preeclampsia are more likely to experience hemodynamic disturbances when compared to women without preeclampsia with the same amount of bleeding. Based on the previous studies, more than 90% of maternal deaths were due to obstetric complications which have been predicted during pregnancy. Most of these complications occur at or around childbirth. However, there are also mother who are not categorized as at risk, but they are actually experience complications.^{7,17} This was also found in our study that maternal deaths occurred precisely in women with preeclampsia without severe symptoms. Therefore, the recommended approach is to assume all pregnancies are at risk and that every pregnancy is considered risky and pregnant women have an access to safe childbirth assistance and obstetric services.

Low frequency maternal outcomes, such as antepartum bleeding, eclampsia, HELLP syndrome and maternal deaths, that occurred in pregnant women with preeclampsia at Regional Public Hospital Madiun from January 1, 2017 to September 30, 2020 might be affected by referral system implemented at this hospital. As a type C hospital, it refers patients to referral hospitals with higher type. Another factor that might have caused low incidence of preeclampsia complications in this hospital was the control and management of preeclampsia that had been carried out properly that resulted in the low incidence found in this study.

In a previous study, pre-eclampsia mothers with severe symptoms have a 4.5 times greater chance of giving birth to babies with complications than pre-eclamptic mothers without severe symptoms.¹⁸ Based on the PNPk diagnosis and management of preeclampsia in 2016, IUGR or Intra Uterine Growth Restriction is an

indicator of impaired organ function, especially disruption of uteroplacental circulation that occurs in preeclampsia.¹⁹ In this study, the relationship between preeclampsia with or without severe symptoms when associated with IUGR ($p=0.01$) was found to be significant (Table 8).

Table 8. IUGR (Intra Uterine Growth Restriction)

Variables	No IUGR N=199 (%)	IUGR N = 17 (%)	<i>p</i>
Degree of preeclampsia			
Without severe symptoms	101 (46.76)	3 (1.39)	0.01
With severe symptoms	98 (45.37)	14 (6.48)	

In this study, there was a significant relationship between preeclampsia without severe symptoms or with severe symptoms in relations to the incidence of Low Birth Weight (LBW) ($p=0.00$) (Table 9). The results of this study were in line with Dewi's research (2018) which indicated that there was a significant relationship with an odd ratio of 2.042, indicating an increased risk of mothers with preeclampsia to give birth to babies with low birth weight, especially in those with severe preeclampsia with an increased risk of 2.042 times higher than preeclampsia without severe symptoms. This is because in women with preeclampsia there are physiological and pathological alterations, such as alterations in the placenta and uterus, which result in decreased blood flow to the placenta and cause inadequate nutrition for the fetus, leading to Low Birth Weight.²⁰

Table 9. LBW (Low Birth Weight)

Variables	No LBW N=145 (%)	LBW N = 71 (%)	<i>p</i> *
Degree of preeclampsia			
Without severe symptoms	81 (37.50)	23 (10.65)	0.00
With severe symptoms	64 (29.63)	48 (22.22)	

Table 10. Preterm birth

Variables	No Preterm Birth N=189 (%)	Preterm Birth N = 27 (%)	<i>p</i> *
Degree of preeclampsia			
Without severe symptoms	98 (45.37)	6 (2.78)	0.00
With severe symptoms	91 (42.13)	21 (9.72)	

In this study, there were 216 women with preeclampsia and 27 women who gave preterm birth with 6 of them being women with preeclampsia without severe symptoms and 21 women with preeclampsia with severe symptoms. ($p=0.00$) (Table 10). These results were in line with those found in Faiza et al. study which indicated that mothers with severe preeclampsia had a risk of 3.303 times and 4.5 times for preterm childbirth compared to women without severe preeclampsia. It has been recognized that in severe preeclampsia premature



birth can occur due to vasospasm of blood vessels which will reduce blood flow to the placenta, so that there was impaired placental function. If vasospasm lasts for a long time, then it will interfere with fetal growth. If there is an increase in uterine tone and sensitivity to stimulation, it can result in premature childbirth.²¹

Table 11. Perinatal death

Variables	No Perinatal Death N=210 (%)	Perinatal Death N = 6 (%)	<i>p</i>
Degree of preeclampsia			
Without severe symptoms	103 (47.69)	1 (0.46)	0.21
With severe symptoms	107 (49.54)	5 (2.31)	

In this study, there was no significant relationship between preeclampsia without severe symptoms or with severe symptoms in relations to perinatal mortality (p=0.21) (Table 11). These findings were also in line with those of Faiza et al. which indicated that mothers with severe preeclampsia did not have a significant relationship with perinatal mortality or Intra Uterine Fetal Death (IUFD). Although the finding in this study was not statistically significant, there was a tendency for infants born to mothers with severe preeclampsia to experience complications in the form of perinatal death clinically, in this case IUFD and severe asphyxia. There were other factors affect the occurrence of Intra Uterine Fetal Death (IUFD) such as placental abruption, DM, breech position, congenital abnormalities.²¹

The occurrence of perinatal death in mothers with preeclampsia is supported by a notion that there are four causalities of maternal, fetal and neonatal death from an obstetric perspective, ie. hemorrhagic, sepsis and infection, high blood pressure and preeclampsia or eclampsia and obstructed childbirth. The occurrence of spasm in the arteriolar blood vessels in preeclampsia will then cause compensation as a way to overcome the increase in peripheral pressure so that oxygen can still reach all tissues adequately. As a result, blood flow to the placenta will decrease and cause in disturbances in fetal growth and due to lack of oxygen, it can cause fetal distress or fetal distress.^{1,22}

Table 12. Asphyxia neonatorum

Variables	No Asphyxia Neonatorum N=188 (%)	Asphyxia Neonatorum N = 28 (%)	<i>p</i>
Degree of preeclampsia			
Without severe symptoms	93 (43.06)	11 (5.09)	0.31
With severe symptoms	95 (43.98)	17 (7.87)	

In this study, there was no significant relationship between preeclampsia with or without severe symptoms on the incidence of asphyxia neonatorum (p=0.31),

although it was not statistically significant but there was a tendency for infants born to mothers with severe preeclampsia to have severe preeclampsia complications in the form of asphyxia neonatorum clinically (Table 12). The results in this study were in line with a previous study by Heriyanti that there were no statistically significant relationship found between severe preeclampsia and neonatorum asphyxia at Dr. Moewardi Hospital, Surakarta, Indonesia.²³ According to Sunarsih's research (2014) preeclampsia mothers tended to give birth to asphyxia babies, although statistically it was not significant.⁴ Asphyxia can occur in infants with pre-eclampsia mothers due to preeclampsia, and spiral artery spasms occur which cause disruption of uteroplacental circulation so that fetal hypoxia occurs and continues to be asphyxia neonatorum.^{23,24}

CONCLUSION

There is a significant relationship between preeclampsia with or without severe symptoms and maternal outcome, namely the childbirth process, while there is a non-significant relationship between preeclampsia with or without severe symptoms on maternal outcomes, namely antepartum hemorrhage, postpartum hemorrhage, eclampsia, HELLP syndrome, and maternal death. There is a significant relationship between preeclampsia with or without severe symptoms and perinatal outcomes, ie. Intra Uterine Growth Restriction (IUGR), Low Birth Weight (LBW), and preterm birth, while there is a non-significant relationship between preeclampsia with or without severe symptoms on perinatal outcomes of perinatal mortality and neonatal asphyxia. Precautions for maternal and perinatal outcomes must still be carried out, considering some outcomes do not have a significant relationship to the severity of preeclampsia, meaning that these outcomes can still occur even in preeclampsia without severe symptoms.

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