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MATERNAL AND PERINATAL OUTCOMES OF EARLY AND LATE ONSET PREECLAMPSIA WITH SEVERE FEATURES IN MUHAMMADIYAH PALEMBANG HOSPITAL

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ABSTRACT

Background: Preeclampsia is a condition characterized by new-onset hypertension during pregnancy, which can lead to various complications for both the mother and baby. It is categorized into early-onset preeclampsia (EO-PE) and late-onset preeclampsia (LO-PE) based on the timing of onset, each having distinct pathophysiologies and complications. Pre-eclampsia complicates 2-8% of all pregnancies worldwide. **Objective**: This study aims to evaluate maternal and perinatal outcomes in patients with early and late-onset severe preeclampsia. **Methods**: An analytic observational study with a cross-sectional design was conducted at a secondary healthcare facility. The study included 554 women with severe preeclampsia who delivered at the facility, categorized into EO-PE and LO-PE groups. Maternal characteristics and outcomes, as well as perinatal outcomes, were analyzed. **Results**: Out of the total cases, 40 (7.22%) were EO-PE and 514 (92.78%) were LO-PE. Maternal outcomes such as HELLP syndrome, visual impairment, placental abruption, oliguria, ICU admission, and eclampsia were significantly higher in the EO-PE group. Additionally, perinatal outcomes including birth weight and APGAR scores were notably worse in the EO-PE group. **Conclusion**: Adverse maternal and perinatal outcomes were significantly more prevalent in early-onset preeclampsia compared to late-onset preeclampsia.

BACKGROUND

Preeclampsia is a pregnancy-related disorder that typically occurs after 20 weeks of gestation, characterized by the onset of hypertension (systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg) and either proteinuria or signs of significant end-organ dysfunction in a previously normotensive woman. There is a more critical form of the condition, marked by more pronounced hypertension (systolic blood pressure ≥160 mmHg or diastolic blood pressure ≥110 mmHg) and significant organ damage, such as kidney impairment, liver dysfunction, neurological symptoms, or hematological abnormalities and it is called preeclampsia with severe feture.[1]

In Indonesia, the estimated prevalence of preeclampsia and eclampsia is 8.6% and 2.5%, respectively, while the maternal mortality rate due to these conditions ranges from 9.8% to 25%.

Preeclampsia can be classified based on its timing: Early-Onset Preeclampsia (EO-PE), which occurs before 34 weeks of gestation, and Late-Onset Preeclampsia (LO-PE), which occurs after 34 weeks. While both forms share some symptoms, they differ significantly in terms of maternal and perinatal outcomes, prognosis, and complications. Early-onset and late-onset preeclampsia have distinct causes and should be treated as separate conditions. [4]

Few studies show more severe morbidity and mortality in EO-PE[4,5,6,7,8]. However, these studies conducted research in tertiary health care, which were complicated cases referred to. This can cause an uneven distribution of cases.

This research aims to identify the differences in characteristics as well as maternal and perinatal

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outcomes in patients with early-onset and late-onset severe preeclampsia at a secondary healthcare hospital, allowing us to analyze data from a well-distributed set of cases.

METHODS

This cross-sectional study was conducted at Muhammadiyah Palembang Hospital, utilizing data extracted from medical records. The sample consisted of women who gave birth with severe preeclampsia at this hospital between January 2018 and December 2021.

The study included patients with a singleton pregnancy who were diagnosed with severe preeclampsia based on the criteria set by the American College of Obstetricians and Gynecologists (ACOG). To be included, patients had to have a gestational age of at least 20 weeks, with a systolic blood pressure of 160 mmHg or higher, or a diastolic blood pressure of 110 mmHg or higher, along with other severe features.

Exclusion criteria in the study were multiple pregnancies, hypertension due to causes other than preeclampsia (chronic hypertension, chronic kidney disease, lupus erythematosus, antiphospholipid syndrome, and diabetes mellitus), as well as incomplete medical record data.

Our institute bioethics and Humaniora committee approved this study. We collect the data from patient history, clinical exams, laboratory exams, radiology exams, medical treatment, and nursing reports.

Samples were grouped as EO-PE at 20 to 33 weeks and LO-PE at at least 34 weeks gestation. Maternal outcomes included in this study were pulmonary edema, visual disturbances, placental abruption, oliguria, postpartum hemorrhage, ICU admission, death, eclampsia, and HELLP syndrome. Indicator of oliguria is urine output with a volume of less than 15 mL/hour for six consecutive hours with/without the use of diuretic drugs.

The study evaluated perinatal outcomes by assessing various birth weight categories: very low birth weight (<1,000 grams), low birth weight (1,000-2,499 grams), normal birth weight (2,500-3,999 grams), and high birth weight (>3,999 grams). Additionally, the APGAR score was used to evaluate the presence or absence of stillbirth and asphyxia.

The subjects' characteristics were analyzed using a descriptive univariate method presented as a frequency table. A further comparison within each characteristics between the two groups was then done, with categoric data analyzed using chi-square and numeric data analyzed using the Mann Whitney U test, due to the abnormal spread of numeric data. Then, maternal and perinatal outcomes were analyzed using a cross-sectional bivariate manner with chi-square. The value is significant if the test results produce a p-value of less than 0.05.

RESULT

In the study, 554 patients met the inclusion criteria and were divided into two groups: the early-onset preeclampsia (EO-PE) group, which consisted of 40 patients diagnosed before 34 weeks of gestation, and the late-onset preeclampsia (LO-PE) group, which included 514 patients diagnosed at or after 34 weeks of gestation.

The mothers' ages ranged from 15 to 50 years, with both the median and average age being 32 years. The lowest gestational age recorded was 21 weeks, which involved a stillbirth and severe complications such as HELLP syndrome and ICU admission, while the highest gestational age was 42 weeks. The highest gravida status recorded was 11. In the EO-PE group, the average gestational age at diagnosis was between 30 and 31 weeks, with the highest frequency of cases occurring between 33 and 34 weeks. Analysis showed that the only factor significantly associated with the timing of preeclampsia onset was gestational age ($p < 0.001$). Detailed characteristics of the research subjects are provided in Table 1.

Table 1. Maternal demographic characteristics

Characteristics	EO-PE (40)	LO-PE (514)	P-Value
Age (years)			
<20	2 (5%)	16 (3%)	0,664
20 – 35	25 (62,5%)	314 (61%)	
>35	13 (32,5%)	184 (36%)	
Gestational age (weeks)			
20-36	40 (100%)	36 (7,00%)	<0,001*
37-40	0 (0%)	419 (81,52%)	
>40	0 (0%)	59 (11,48%)	
Education			
Elementary	14 (35%)	144 (28%)	0,689
Middle school	9 (20%)	118 (23%)	
High school	17(42,5%)	209 (40,5)	
Diploma	1 (2,5%)	13 (2,5%)	
Bachelor	0 (0%)	30 (6%)	

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Occupation			
Civil servant	0 (0%)	10 (1,95%)	0,639
Private employe	4 (10%)	43 (8,37%)	
House wife	36 (90%)	461 (89,7%)	
Gravida			
Primigravida	10 (25%)	121 (23,5)	0,834
Multigravida	30 (75%)	393 (76,5)	
Delivery Methode			
Sectio caesarea	25 (62,5%)	376 (73,2%)	
Vaginal delivery	15 (37,5%)	138 (26,8%)	0,147
Spontaneous	15 (37,5%)	132 (25,7%)	
Vacum	0 (0%)	6 (1,2%)	

#Median (min—max) because normality shows abnormal spread of data
**Significant when p <0.05*

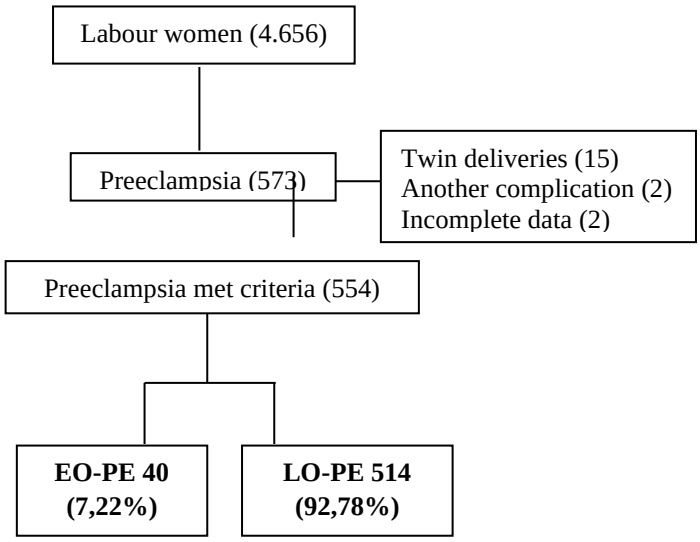

Fig 1. Sample size chart

Based on the analysis of maternal outcomes, it was found that the most frequent maternal outcome was oliguria, which occurred in 53 subjects (9.57%). The next most frequent maternal outcomes in order were ICU admission (3.61%), eclampsia (3.07%), visual impairment (2.71%), and HELLP syndrome (1.8%). It was also found that all patients who experienced placental abruption came to the hospital with complaints of bleeding. Of the total 20 patients undergoing treatment in the ICU, three patients had HELLP syndrome, eight patients had eclampsia, and one patient had pulmonary oedema. Bivariate analysis tests showed the significance of the outcomes of HELLP syndrome, visual disturbances, placental dissolution, oliguria, ICU care, and eclampsia in EO-PE patients compared to LO-PE. This analysis can be seen further in Table 2.

Tabel 2. Maternal outcomes in early- and late-onset preeclampsia

Maternal Outcomes	EO-PE (40)	LO-PE (514)	P-Value
Pulmonary edema	0 (0%)	1 (0,2%)	0,777
HELLP syndrome	7 (17%)	3 (0,6%)	**< 0,001***
Visual impairment	6 (14,6%)	9 (1,8%)	**< 0,001***
Placental abruption	2 (4,9%)	1 (0,2%)	**< 0,001***
Oliguria	10 (24,4%)	43 (8,4%)	**0,001***
Postpartum hemorrhage	1 (2,4%)	7 (1,4%)	0,318
ICU admission	7 (17%)	13 (2,6%)	**< 0,001***
Mortality	0 (0%)	1 (0,2%)	0,777
Eclampsia	4 (9,8%)	13 (2,5%)	**0,01***

**Significant when p <0.05*
f Fischer test

Analysis of perinatal outcomes showed that 77.98% of all neonates born had normal birth weights. The birth weight range was 700-4.930gr. Apart from that, the majority (94.77%) of babies born did not experience asphyxia. However, 8 (1.44%) babies experienced asphyxia, and 21 (3.79%) neonates were stillborn. It is known that birth weight and APGAR score at 5 minutes have a significant correlation in cases of EO-PE compared with LO-PE. This analysis is presented in Table 3.

Tabel 3. Perinatal outcomes in early- and late-onset preeclampsia

Perinatal Outcomes	EO-PE (40)	LO-PE (514)	P-Value
Birth weight			
< 1.000 gram	2 (5%)	0 (0%)	
1.000-2.499 gram	33 (82,5%)	65 (12,5%)	**< 0,001[f*]**
2.500-3.999 gram	5 (12,5%)	427 (83%)	
>3.999 gram	0 (0%)	22 (4,5%)	
APGAR score minute 5			
Stillborn	12 (30%)	9 (2%)	**< 0,001***
Asphyxia	1 (2,5%)	7 (1,5%)	
No asphyxia	27 (67,5%)	498 (97%)	

**Significant when p <0.05*

DISSCUSION

This research was conducted on 554 EO-PE and LO-PE patients, and then we analyzed characteristics including age, gestational age, education, occupation, and gravida. This study found that the most common age group was patients aged 20-35 years, which was similar to Gustiani in 2018, which reported that the incidence of severe preeclampsia was more common in pregnant women of productive age 20-34 years.[2] Then another study by Lisonkova and Joseph in 2013 also reported the same thing, that pregnant women of productive age (20 -34 years old) have a higher risk

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of experiencing late-onset severe preeclampsia compared to other age groups. However, the study showed no significant difference between the ages of the two groups of preeclampsia, the same as the results of this research.[9]

Management of severe preeclampsia includes termination of pregnancy regardless of gestational age. Based on the NICE guidelines for Hypertension in Pregnancy, termination of preeclampsia can be carried out based on gestational age and other accompanying conditions. If one of the signs of an emergency or complication of preeclampsia already exists, then an active treatment or termination of pregnancy must be carried out immediately, either vaginally or by cesarean section.[10] Most clinical reports indicate that cesarean section is preferred for termination of pregnancy, and therefore the rate of Caesarean section was significantly higher than the rate of vaginal delivery, both in LO-PE and EO-PE.[11] This is why Caesarean section was this study's most common delivery method, as such there is no significant difference between the two groups due to the Caesarean section being the main modality of management in patients with preeclampsia.

This study also found that educated mothers, at least high school graduates, were almost equal in number to pregnant women with elementary and high school education. This finding is consistent with the research by Hutabarat et al. in 2016, which indicated that mothers with both high and low education levels had the same likelihood of developing preeclampsia, demonstrating no significant difference between the LO-PE and EO-PE groups.[12]

Based on research by Nuning and Mardiana in 2014, maternal employment does not have a significant relationship with the incidence of preeclampsia. This research states that work is more related to stress levels, so pregnant women who do not work are also at risk of experiencing preeclampsia in pregnancy because, as housewives, they also experience stress.[13] This was proven in this study, where 89.7% of the subjects were housewives, and also the insignificance of maternal job to the presence of EO-PE compared to LO-PE.

The gravida is controversial about the incidence of preeclampsia. Studies by Djannah in 2010 and Langelo in 2013 stated that primigravida pregnancies are more dominant in the incidence of preeclampsia[14,15] . In this study, it was found that multigravida mothers were more common than primigravidas in cases of PEB. Hutabarat's research in 2016 also found that preeclampsia patients were more commonly found in multigravida (61%) compared to primigravida (39%).[12] This result could be due to the possibility of the multigravida women experiencing recurrent preeclampsia.

However, there is one outcome that is significant to correlate with the presence of EO-PE compared to LO-PE, which is the gestational age. Per definition, the two groups are named based on the onset of the preeclampsia, which was early onset on earlier gestational age compared to late onset on a later gestational age.[10]

Most research found that LO-PE cases are more frequently found than EO-PE. Madazli, in 2018, examined the prevalence of EO-PE and LO-PE, which showed that EO-PE occurred in 5-20% of preeclampsia cases and LO-PE occurred in 75-80% of preeclampsia cases.8 In addition, in the research of Gomathy, et al. in 2018 showed similar results with PEB occurring more frequently in the late-onset group (72.4%) than early onset (27.6%).[4] Similar to these studies, this study also showed more cases of LO-PE (92, 78%) compared to EO-PE (7.22%).

In this study, various maternal outcomes were significantly associated with EO-PE compared with LO-PE. HELLP syndrome significantly correlates with its occurrence in EO-PE compared with LO-PE. This condition occurred in 1.8% of all preeclampsia cases in this study. In Amorim et al.'s study in 2014, the majority of cases of HELLP syndrome underwent cesarean delivery. According to theory, women with preeclampsia and HELLP syndrome usually have worse outcomes than preeclamptic mothers without HELLP syndrome.[16]

In this study, visual impairment was one of the outcomes that were significantly related to EO-PE subjects compared to LO-PE this result also found in Pooja Wadhwani research in 2020.[5] Placental abruption is where the placenta separates, which should be implanted in the uterus after the 20th week of pregnancy. This condition can occur especially in cases of hypertension during pregnancy, including severe preeclampsia. In one study, it was found that placental abruption in gestational hypertension occurred in 10-21% of all cases.[17] This study have the same result with Pooja Wadhwani in 2020 which

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placental abruption are moe common in EO-PE than LO-PE.

In general, EO-PE has a higher risk of causing worse perinatal outcomes compared with LO-PE. This includes lower newborn Apgar scores and longer hospital stays, and it can even increase neonatal mortality and morbidity.[18] In a study by Aziz et al. in 2016, it was found that there was a significant relationship between birth weight and the baby's Apgar score. Which was lower with the incidence of EO-PE compared with the incidence of LO-PE.6 The findings found in this study were also similar to the results of that study, with a significant relationship between birth weight and Apgar scores in infants with EO-PE mothers compared with LO-PE. In the occurrence of EO-PE, there can be fetal consequences in the form of growth restriction compared to fetuses born at term gestation.[19] In contrast, a study by Soliman et al. in 2020 found that respiratory morbidity, including asphyxia associated with a low Apgar score, was more common in neonates born to EO-PE mothers compared to those born to LO-PE mothers. This occurs because fetal lungs that are not yet fully developed are required for birth as a termination in the preeclampsia condition, so the fetus is more susceptible to experiencing respiratory disorders and other comorbidities.[20]

CONCLUSION

The research results showed that maternal and fetal complications in severe preeclampsia were more common in early onset compared to late onset. Suggestions for future researchers who are interested in this research are to look for relationships between other factors that have not been discussed in this research to better recognize the effects of severe preeclampsia on pregnant women and their fetuses.

ETHICAL APPROVAL

Approved by our Institutional Bioethics Committee, Faculty of Medicine Muhamadiyah Palembang University, (No.019/EC/KBHKI/FK-UMP/XI/2022)

CONFLICTS OF INTEREST

The authors declare no conflict of interest.

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AUTHOR CONTRIBUTIONS

Conceptualization, Aryani Aziz,; methodology, Aryani Aziz and Uqbah Abdul Salam,; software, Uqbah Abdul Salam; validation, Aryani Aziz and Uqbah Abdul Salam; formal analysis, Uqbah Abdul Salam; investigation, Aryani Aziz; resources, Aryani Aziz and Uqbah Abdul Salam; data curation, Aryani Aziz and Uqbah Abdul Salam; writing original draft preparation, Abdul Salam; writing review and editing, Aryani Aziz and Uqbah Abdul Salam; visualization, Uqbah Abdul Salam; supervision, Aryani Aziz; project administration, Aryani Aziz and Uqbah Abdul Salam; funding acquisition, Aryani Aziz and Uqbah Abdul Salam.

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