

Comparison of Maternal and Perinatal Outcomes between Severe Preeclampsia without Complications and with HELLP Syndrome

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Abstract

Introduction: Maternal and perinatal outcomes in severe preeclampsia conditions, without or accompanied by HELLP syndrome, are variable. There is currently a lack of research data in Indonesia comparing maternal and perinatal outcomes in both conditions. This study compares pregnancy outcomes between severe preeclampsia with no complications and severe preeclampsia with HELLP syndrome.

Methods: This study employs an observational analytical approach, utilizing a retrospective cross-sectional design. The samplings contain 92 patients from the medical records of patients who were diagnosed with preeclampsia without complications and severe preeclampsia with HELLP syndrome at Hasan Sadikin Hospital Bandung from January 2021 to December 2023.

Results: It was found that maternal with HELLP syndrome are five times more at risk for eclampsia compared to maternal with preeclampsia without complications. Maternal who have severe preeclampsia accompanied by HELLP are two times more at risk of having labor under 34 weeks or preterm compared to maternal with preeclampsia without complications. Other outcomes, including maternal mortality, DIC, acute renal failure, pulmonary edema, antepartum hemorrhage, as well as perinatal mortality, FGR, IUFD, and perinatal asphyxia, did not show a statistically significant difference in proportion ($p > 0.05$).

Conclusion: There is a relationship between maternal and perinatal outcomes in severe preeclampsia without complications or with HELLP syndrome.

Key words: Maternal Outcomes, Perinatal, HELLP Syndrome

Perbandingan Luaran Maternal dan Perinatal antara Preeklamsia Berat Tanpa Penyulit dan dengan Sindrom HELLP

Abstrak

Pendahuluan: Luaran maternal dan perinatal pada kondisi preeklamsia berat, tanpa dan dengan sindrom HELLP, tergolong bervariasi. Saat ini masih minim data penelitian di Indonesia yang membandingkan hasil luaran maternal dan perinatal pada kedua kondisi tersebut. Penelitian ini bertujuan untuk mengetahui perbandingan luaran kehamilan antara preeklamsia berat tanpa komplikasi dan preeklamsia berat dengan Sindrom HELLP.

Metode: Metode yang digunakan dalam penelitian ini adalah analitik observasional dengan desain potong lintang retrospektif. Sampel penelitian ini adalah 92 pasien dari rekam medis pasien yang didiagnosis preeklamsia tanpa komplikasi dan preeklamsia berat dengan Sindrom HELLP di Rumah Sakit Hasan Sadikin Bandung pada periode Januari 2021 hingga Desember 2023.

Hasil: Hasil penelitian menunjukkan bahwa ibu dengan sindrom HELLP berisiko lima kali lebih besar untuk mengalami eklampsia dibandingkan dengan ibu dengan preeklamsia tanpa komplikasi. Ibu yang mengalami preeklamsia berat disertai HELLP berisiko dua kali lebih besar untuk mengalami persalinan di bawah 34 minggu atau prematur dibandingkan dengan ibu yang mengalami preeklamsia tanpa komplikasi. Luaran lain seperti kematian ibu, DIC, gagal ginjal akut, edema paru, perdarahan antepartum dan juga kematian perinatal, FGR, IUFD, asfiksia perinatal tidak ada perbedaan proporsi yang bermakna secara statistik ($p > 0,05$).

Kesimpulan: Terdapat hubungan luaran maternal dan perinatal antara preeklamsia berat tanpa komplikasi atau dengan sindrom HELLP.

Kata kunci: Luaran Maternal, Perinatal, Sindrom HELLP

Introduction

Preeclampsia is a hypertensive disorder with proteinuria that can occur during pregnancy, usually identified after 20 weeks of pregnancy.¹ According to WHO, preeclampsia cases range between 2% and 10% of pregnancies worldwide. In Indonesia, based on data from the Sample Registration System (SRS) of the Indonesian Ministry of Health in 2016, the rate of preeclampsia reached 33%, ranked as the leading cause of maternal death. In addition to being life-threatening, complications that can arise in mothers with preeclampsia are placental ablation, kidney disorders, HELLP syndrome (hemolysis, elevated liver enzymes, and low platelets), convulsions, and pulmonary edema. Babies born to mothers with this condition may experience prematurity, low birth weight, or intrauterine fetal death (IUFD).² In severe preeclampsia (SPE), the risk of maternal complications increases if more signs can worsen the situation in pregnancy, such as the presence of HELLP syndrome.³

HELLP syndrome is characterized by erythrocyte rupture (hemolysis), elevated liver enzyme concentrations, and a decreased platelet count (thrombocytopenia).⁴ The incidence of HELLP syndrome in pregnancies with severe preeclampsia has been recorded at 10-12%.⁵ According to research conducted at Dr. Hasan Sadikin Hospital Bandung, West Java, the percentage of maternal deaths related to preeclampsia accompanied by HELLP syndrome in 2015–2022 reached 22%.⁶ In addition to death, perinatal outcomes that may occur are low birth weight (LBW), IUGR, asphyxia, fetal distress, and premature birth.⁷ Moreover, HELLP syndrome, which causes placental abruption, cesarean delivery, oligohydramnios, and fetal growth restriction, follows maternal outcomes with severe preeclampsia.⁸

Because maternal and perinatal

outcomes in severe preeclampsia conditions without or accompanied by HELLP syndrome are varied, coupled with the lack of research data in Indonesia comparing the results of maternal and perinatal outcomes in these two conditions, this study will further identify the comparison of pregnancy outcomes between severe preeclampsia without complications and severe preeclampsia with HELLP syndrome at Dr. Hasan Sadikin Hospital as a Health Service Center in Bandung in the period January 2021-December 2023.

Method

This study employs an observational analytical approach, utilizing a retrospective cross-sectional design. The samplings contain 92 patients from the medical records of patients who were diagnosed with severe preeclampsia without complications and severe preeclampsia with HELLP syndrome at Hasan Sadikin Hospital Bandung from January 2021 to December 2023. Subjects were selected using the random sampling method. The inclusion criteria were maternal, who were diagnosed with severe preeclampsia without complications and severe preeclampsia accompanied by HELLP syndrome, had complete data on maternal and perinatal labor outcomes, and were approved by the Research Ethics Committee of Padjadjaran University DP.04.03/D. XIV.4.4/654/2024 and the Research Ethics Committee of Dr. Hasan Sadikin Hospital DP.04.03/D.XIV.4.4/654/2024. Statistical analysis was performed with Microsoft® Excel 16.66.1 and IBM SPSS Statistics. Normality is tested using the Kolmogorov-Smirnov and Fisher's exact test with a confidence level of $p = 0.05$.

Results

Maternal characteristics of SPE and SPE with HELLP syndrome were homogeneous. In the

Table 1 Comparison of Maternal Characteristics in Severe Preeclampsia (SPE) with and without HELLP Syndrome

Characteristics	Diagnosis		P-value
	SPE	SPE + HELLP syndrome	
	N=46	N=46	
Age			1.000
≤ 20 years	3(6.5%)	1(2.2%)	
20-35 years	32(69.6%)	36(78.3%)	
>35 years	11(23.9%)	9(19.6%)	
Gravidity			0.263
Primigravida	19(41.3%)	12(26.1%)	
Multigravida	19(41.3%)	26(56.5%)	
Grandmultigravida	8(17.4%)	8(17.4%)	

*Chi-Square test, Kolmogorov Smirnov dan Exact Fisher

Table 2 Comparison of Maternal Outcomes in Severe Preeclampsia (SPE) with and without HELLP Syndrome

Maternal Outcomes	Diagnosis		P-value
	SPE	SPE + HELLP syndrome	
	N=46	N=46	
Mortality	0(0.0%)	0(0.0%)	1.000
DIC	0(0.0%)	1(2.2%)	1.000
Kidney Injury	2(4.3%)	2(4.3%)	1.000
Pulmonary Edema	1(2.2%)	4(8.7%)	0.361
Eclampsia	3(6.5%)	15(32.6%)	0.002*
Antepartum Hemorrhage	N=6	N=1	1.000
Placental abruption	4(66.7%)	1(100.0%)	
Placenta previa	2(33.3%)	0(0.0%)	
Postpartum Hemorrhage	0(0.0%)	0(0.0%)	1.000

*Chi-Square test, Kolmogorov Smirnov dan Exact Fisher

SPE and SPE with HELLP syndrome groups, the highest maternal age was between 20-35 years, with a percentage of SPE (69.6%) and SPE with HELLP syndrome (78.3%). While the highest type of gravidity in both conditions is multigravida, with a percentage of SPE (41.3%) and SPE with HELLP syndrome (56.5%).

The highest maternal outcome in the SPE group was antepartum hemorrhage (13.0%) in the placental abruption category

(66.7%), followed by eclampsia (6.5%), kidney injury (4.3%), pulmonary edema (2.2%), postpartum hemorrhage (0.0%) and DIC (0.0%). Meanwhile, in the SPE group with HELLP syndrome, the highest maternal outcome was eclampsia (32.6%), followed by pulmonary edema (8.7%), kidney injury (4.3%), DIC (2.2%), antepartum hemorrhage (2.2%) in the placental abruption category (100%) and postpartum hemorrhage (0.0%).

The results of statistical tests in the

Table 3 Comparison of Perinatal Outcomes in Maternal with Severe Preeclampsia (SPE) with and without HELLP Syndrome

Perinatal Outcomes	Diagnosis		P-value
	SPE N=46	SPE + HELLP syndrome N=46	
Gestational Age	N=46	N=46	0.0001***
≤ 34 weeks	18(39.1%)	37(80.4%)	
34 – 36 ⁺⁶ weeks	9(19.6%)	3(6.5%)	
≥ 37 weeks	19(41.3%)	6(13.0%)	
Intrauterine Fetal Death	7(15.2%)	11(23.9%)	0.293
Fetal Growth Restriction	2(4.3%)	3(6.5%)	1.000
APGAR Score	N=38	N=30	0.068
7 - 9	26(68.4%)	11(36.7%)	
4 - 6	9(23.7%)	15(50.0%)	
0 - 3	3(7.9%)	4(13.3%)	

*Chi-Square test, Kolmogorov Smirnov dan Exact Fisher

above study groups obtained $p > 0.05$ from the variables of mortality, DIC, kidney injury, pulmonary edema, antepartum, and postpartum hemorrhage in the diagnosis group of SPE and SPE with HELLP syndrome, so there is no statistically significant difference in proportion. While the P value on the Eclampsia variable is 0.002 (P-value < 0.05), which means there is a statistically significant difference in the proportion between the Eclampsia variable in the SPE and SPE diagnosis groups with HELLP syndrome.

Perinatal outcomes in the SPE group were mostly born at ≥ 37 weeks gestation (41.3%). The highest perinatal outcome was IUID (15.2%) followed by FGR (4.3%). The highest APGAR score in this condition was 7-9 (68.4%). Meanwhile, perinatal outcomes in the SPE with HELLP Syndrome group were mostly born at ≤ 34 weeks gestation (80.4%). The highest perinatal outcome was IUID (23.9%) followed by FGR (6.5%). The highest APGAR score in this condition was 4-6 (50%).

The results of statistical tests in the above study groups obtained $p > 0.05$ from

the variables of Intrauterine fetal death, fetal growth restriction, and asphyxia in the diagnosis group of SPE and SPE with HELLP syndrome, so there is no statistically significant difference in proportion. While the P value of the gestational age variable is smaller than 0.05 (P value < 0.05), which means that it is statistically significant in the SPE and SPE diagnosis groups with HELLP syndrome.

Discussion

A total of 92 mothers met the criteria of this study, where 46 mothers had severe preeclampsia without complications and 46 mothers had severe preeclampsia with HELLP syndrome. In both conditions, maternal age 20-35 years was the most common age. As for gravida, the multigravida category was the most common in both conditions for mothers with and without HELLP syndrome. The results of this study contradict the immunological theory that links gravida to the incidence of preeclampsia, suggesting that primigravidas have a higher risk of

preeclampsia compared to multigravidas.⁹ The difference between the results of this study and the theory is possible there are other factors such as the mother has prepared for pregnancy before pregnancy, antenatal care, care during pregnancy, nutritional intake during pregnancy, and lifestyle. So that gravida does not affect the incidence of preeclampsia.

This study showed that the incidence of maternal mortality, DIC, acute renal failure, pulmonary edema, and antepartum or postpartum hemorrhage in severe preeclampsia with HELLP syndrome was not significant. One of the factors influencing this is the improvement in maternal conditions after the administration of corticosteroids as a management of HELLP syndrome, thus reducing maternal morbidity and mortality. This is in line with research by Ahityadeva N T et al (2017) at Dr. Kariadi Hospital Semarang in 2016.¹⁰ Otherwise, it contradicts the findings found by Juwita Badani et al (2022) which showed that the incidence of postpartum hemorrhage increased 1.53 times in HELLP Syndrome.¹¹ The main causes of postpartum hemorrhage include uterine atony, placental remnants, and coagulopathy that commonly occurs in HELLP Syndrome.¹²

The results of the study on maternal outcomes with and without HELLP syndrome complication, in cases of eclampsia, were significant. Based on the results of statistical tests, maternal with severe preeclampsia accompanied by HELLP syndrome are five times more at risk for eclampsia compared to maternal with preeclampsia without complications. This is in accordance with research by Adhi Pribadi, et al in 2022 which showed that eclampsia cases were the highest number of cases at Dr. Hasan Sadikin Hospital in 2015-2022 compared to cases of gestational hypertension, preeclampsia, chronic hypertension, chronic hypertension superimposed. From the results of these data, it is concluded that eclampsia is 9 times

deadlier compared to preeclampsia which is only 1%.⁶ This can happen because HELLP syndrome is a severe development of preeclampsia that will increase the risk of obstetric complications such as eclampsia. Therefore, patients with HELLP syndrome should be treated prophylactically with magnesium sulfate to prevent seizures. Another study showed a similar result with the incidence of HELLP syndrome among women with eclampsia was higher than the women without HELLP syndrome ($P < 0.0008$).¹³

This study found that the incidence of perinatal mortality, FGR, and IUFD without complications and with HELLP syndrome complication was statistically insignificant. This is because the outcomes of infants with severe preeclampsia without complications and with HELLP syndrome have clinical conditions that are not much different. In maternal with severe preeclampsia without complications or with HELLP syndrome complication, infant outcomes are both decreased fetal heart rate, and weight loss and can cause fetal death in the womb, so both have conditions that are not much different.¹⁴⁻¹⁶ These results are similar to research by Ahityadeva N T et al (2017) at Dr. Kariadi Hospital Semarang in 2016 and also research by Sumarni (2019) at Margono Soekarjo Purwokerto Hospital, which showed that there is no relationship between IUFD and the incidence of HELLP syndrome in maternal with severe preeclampsia.¹⁷ However, it contradicts the research of Nurokhim & Widyarningsih, (2019) which showed a significant relationship between severe preeclampsia and fetal growth restriction¹⁹¹⁸

The results of the study on perinatal gestational age found that the value of $p = 0.0001 > 0.05$ which means there is a significant relationship between HELLP syndrome in maternal preeclampsia with perinatal gestational age. Perinatal with gestational age below 34 weeks or preterm is

more common in maternal who have severe preeclampsia accompanied by HELLP syndrome. Maternal with HELLP syndrome are two times more at risk of having labor under 34 weeks or preterm compared to maternal with preeclampsia without complications. This result is similar to Ali Sungkar et al. (2020) research in Dr. Cipto Mangunkusumo Hospital from 2015-2017 that the median gestational age of neonates with HELLP Syndrome is 30 weeks, which is preterm birth. Therefore, severe preeclampsia with HELLP syndrome is more dangerous because the potential to cause preterm is higher. Some studies reported that prematurity was consistent between gestational age and neonatal morbidity and mortality. Based on the high risk for preterm birth in HELLP syndrome, management and delivery of these cases should be performed at tertiary centers equipped with highly trained neonatal and adult intensive care unit personnel and facilities. It is essential to improve both maternal and neonatal outcomes.

The results of the study on the APGAR score found that maternal with HELLP syndrome has perinatal outcomes with lower APGAR scores that are considered asphyxia than maternal without HELLP syndrome but it is statistically insignificant. This contradicts research by Sumarni (2019), which shows there is a relationship between neonatal asphyxia and the incidence of HELLP syndrome in maternal with preeclampsia.¹⁷ Prematurity, which is a condition that gestational age <34 weeks and commonly occurs in maternal with HELLP syndrome, causes incomplete lung maturity, resulting in a low Apgar score.

The study's limitation is the lack of HELLP syndrome cases in RSRS between January and December 2022. So the duration range is longer, between January 2022 and December 2023. In addition, the data from medical records pertaining to maternal and perinatal outcomes is incomplete.

Conclusion

This study found an association in maternal and perinatal outcomes between severe preeclampsia without complications or with HELLP syndrome at RSUP Dr. Hasan Sadikin. Maternal with HELLP syndrome had a 5-fold higher risk of developing eclampsia. Furthermore, perinatal outcomes in maternal with HELLP syndrome are 2-fold higher risk of being born less than 34 weeks or preterm birth. Apart from that, there is no difference in maternal mortality, DIC, acute renal failure, pulmonary edema, antepartum hemorrhage, and also perinatal mortality, FGR, IUFD, perinatal asphyxia in maternal with preeclampsia without complications, or with HELLP syndrome.

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