Correlation between LDH, Liver Function, Platelets and Proteinuria in Preeclampsia with Severe Features

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Abstract
Objectives: To identify the relationship between LDH, bilirubin, SGPT, SGOT, and platelets with proteinuria in preeclampsia with severe features patients.
Method: This study is an observational analytical with a retrospective cross-sectional design. The samplings contain 70 patients from the medical records of patients who were diagnosed with preeclampsia with severe features at H. Adam Malik Hospital Medan from January 2020 to March 2023.
Results: It was found that 74.3% of the population had semiquantitative urine protein levels ≥+2. The average levels of LDH, total bilirubin, SGPT, SGOT, and platelets were 514.64 U/L, 0.9 mg/dL, 57.77 U/L, 64.01 U/L, and 197,585/mm^3, respectively. Statistical analysis showed a positive association between proteinuria and LDH (p=0.001). However, there was no meaningful association between liver and platelet function and proteinuria.
Conclusion: There is a relationship between LDH and proteinuria in severe preeclampsia patients.

Keywords: hemolysis, liver function, platelets, preeclampsia with severe features, proteinuria

Hubungan antara LDH, Fungsi Hati, Trombosit dengan Proteinuria pada Pasien Preeklamsia Berat

Abstrak
Tujuan: Untuk mengidentifikasi hubungan antara LDH, bilirubin, SGPT, SGOT, dan trombosit dengan proteinuria pada pasien preeklampsia dengan gejala berat.
Metode: Penelitian ini merupakan penelitian analitik observasional dengan desain potong lintang retrospektif. Sampel terdiri dari 70 pasien dari rekam medis pasien yang didiagnosis dengan preeklampsia berat di RSUP H. Adam Malik Medan pada periode Januari 2020 hingga Maret 2023.
Hasil: Ditemukan bahwa 74,3% dari populasi memiliki kadar protein urin semikuantitatif ≥+2. Kadar rata-rata LDH, bilirubin total, SGPT, SGOT, dan trombosit masing-masing adalah 514,64 U/L, 0,9 mg/dL, 57,77 U/L, 64,01 U/L, dan 197.585/mm3. Analisis statistik menunjukkan hubungan positif antara proteinuria dan LDH (p=0,001). Namun, tidak ada hubungan yang bermakna antara fungsi hati dan trombosit dengan proteinuria.
Kesimpulan: Terdapat hubungan antara LDH dan proteinuria pada pasien preeklampsia berat.

Kata kunci: hemolisis, fungsi hati, trombosit, preeklamsia berat, proteinuria

Introduction

One of the causes of morbidity and mortality in pregnant women is preeclampsia or hypertension in pregnancy, which is one of the complications of pregnancy. In 2019, there were around 278,300 deaths of pregnant women attributed to hypertensive disorders of pregnancy globally.[1] Preeclampsia ranks third as the cause of maternal death in Indonesia with 1,077 cases.[2] Data received for North Sumatra itself in 2021, the number of maternal deaths due to hypertension was in third place with 33 cases.[3] Preeclampsia is a disorder of pregnancy associated with hypertension, reduced organ perfusion due to vasospasm, and endothelial activation, which most commonly occurs after 20 weeks of gestation.[4]

Early detection of preeclampsia can be detected with a proteinuria test. The more significant the protein level in the urine, the more significant the risk for difficulties in outcomes for the baby delivered and mother. Several previous studies have pointed out that patients with preeclampsia should be alerted to the adverse symptoms when severe proteinuria occurs.[5,6]

Preeclampsia, based on its features, has two classifications: preeclampsia and preeclampsia with severe features (PE-SF), where PE-SF will increase the threat of maternal mortality and morbidities. Some of the morbidities that can occur in mothers with preeclampsia are hemolysis, increased liver function, and thrombocytopenia.[7] The parameters measured for these complications are lactate dehydrogenase (LDH), bilirubin, liver enzymes: serum glutamic oxaloacetic transaminase (SGOT) and serum glutamic pyruvic transaminase (SGPT), and platelets.[8]

Preeclampsia has shown associations with various complications for both the mother and the baby. These complications can be short-term or long-term. Short-term complications for the mother include HELLP syndrome, eclampsia, placental abruption, cerebrovascular bleeding, retinal detachment, and acute renal failure.[9] As mentioned earlier, for long-term complications that may occur for the mother, there is an increased risk of hypertension, ischemic heart disease, stroke, end-stage kidney disease, and death from cardiovascular events.[10] For the fetus, complications that can occur during pregnancy include fetal distress, intrauterine growth restriction (IUGR), and intrauterine fetal death (IUFD). After birth, complications for the baby may include low birth weight, often caused by preterm delivery.[11] In a study conducted by Sirenden et al,[11] they found a relationship between Apgar scores and the severity of preeclampsia; the more severe the symptoms experienced by the mother, the lower the Apgar score.

Several studies have shown a positive correlation between LDH and platelets with the incidence of proteinuria.[12–14] However, no studies have studied the effect of LDH, bilirubin, SGOT, SGPT, and platelets on proteinuria in PE-SF patients. Therefore, this study aims to determine the correlation between LDH, bilirubin, SGOT, SGPT, and platelets with the incidence of proteinuria in PE-SF patients at Haji Adam Malik Hospital Medan.

Method

This study is an analytic observational method using secondary data with a retrospective cross-sectional study approach. The study population consisted of 96 PE-SF patients from January 2020 to March 2023. Sampling according to inclusion and exclusion criteria using the total sampling method. Research samples were collected from 70 medical records that fulfilled the criteria. Inclusion criteria included pregnant women with PE-SF who had proteinuria and tested LDH, bilirubin, SGPT, SGOT, and platelets. The exclusion criteria were pregnant women

with preeclampsia, however, did not undergo tests for LDH, bilirubin, SGPT, SGOT, and platelets. Data obtained from the patient's medical records were then analyzed univariately to determine the frequency and bivariate method using the chi-square and Fisher exact tests using the IBM Statistical Program for Social Science (SPSS) Statistics 25, 32 bit edition.

Results

The age group of pregnant women with PE-SF found in this study was mainly in the 20-35 years category, with as many as 43 people (61.4%). According to Winasih[15], this age is considered an ideal period to start a pregnancy, so it becomes a reproductive age that has a higher pregnancy incidence rate compared to other age groups.

Gestational age was almost balanced with a difference of 2 people between categories, found in 20-33 weeks as many as 34 people (48.6%). Research done by Kinanti, Akbar, and Lestari reported that late-onset preeclampsia is often linked to a family history of hypertension, suggesting a potential association with genetic factors.[16]

The obstetric status of PE-SF mothers was mainly found in the multigravida category, with as many as 48 people (68.6%) with the rest being primigravida. This may happen because mothers who undergo pregnancy more than three times will encounter exaggerated stretching of the uterus, which can induce preeclampsia.[17]

Table 1 Maternal characteristics with PE-SF in Haji Adam Malik Hospital Medan

Characteristics	n	%
Age		
<20 years	2	2,9
20-35 years	43	61,4
>35 years	25	35,7
Gestasional Age		
20-33 weeks	34	48,6
≥ 34 weeks	36	51,4
Obstetric History		
Primigravida	22	31,4
Multigravida	48	68,6
Systolic BP		
<160 mmHg	11	15,7
≥160 mmHg	59	84,3
Diastolic BP		
<110 mmHg	41	58,6
≥110 mmHg	29	41,4
Proteinuria		
< +2	18	25,7
≥ +2	52	74,3

Severe hypertension was also found to be the most common in the results of this study, which was characterized by systolic blood pressure ≥160 mmHg, 59 people in total (84.3%) with the most diastolic blood pressure found in the <110 mmHg category as many as 41 people (58.6%). The most proteinuria levels found were ≥ +2 as many as 52 people (74.3%) and < +2 as many as 22 people (25.7%). These results are in line with the results reported in research by Permadi, Aditiawarman, and Lestari.[18]

Table 2 Statistical distribution of lab findings with PE-SF in Haji Adam Malik Hospital Medan

Laboratory	Mean±SD	Median	Min-Max
LDH (U/L)	514,64 ±506,88	406	120-3390
Total Bilirubin (mg/dL)	0,92±0,65	0,7	0,2-3,1
SGPT (U/L)	57,77 ±73,15	24	10-494
SGOT (U/L)	64,01 ±70,02	34	10-386
Platelet (/mm^3)	197.585 ±98.840	207.000	29.000-411.000

Table 3 The Relationship between LDH, Bilirubin, SGPT, SGOT, Platelets and Proteinuria in PE-SF

	Proteinuria		Total	*p*
	< +2	≥ +2	(n=70)	
LDH (U/L)				
< 400	15 (21,4%)	19 (27,1%)	34	0,001[a]
≥ 400	3 (4,2%)	33 (47,1%)	36	
Total Bilirubin (mg/dL)				
< 1,2	16 (22,9%)	40 (57,1%)	56	0,494[b]
≥ 1,2	2 (2,9%)	12 (17,1%)	14	
SGPT (U/L)				
< 60	14 (20%)	33 (47,1%)	47	0,265[a]
≥ 60	4 (5,7%)	19 (27,1%)	23	
SGOT (U/L)				
< 60	14 (20%)	30 (42,9%)	44	0,129[a]
≥ 60	4 (5,7%)	22 (31,4%)	26	
Platelets (/mm^3)				
< 100.000	15 (21,4%)	38 (54,4%)	53	0,529[b]
≥100.000	3 (4,2%)	14 (20%)	17	

[a] chi-square test [b] fisher's exact test

LDH levels were found to average 514.64 U/L with the most categories found in ≥ 400 U/L as many as 36 people (51.4%), then bilirubin levels were found to average 0.92 mg/dL with a category <1.2mg/dL as many as 54 people (80%). The average SGPT and SGOT levels were found to be 57.77 U/L and 64.01 U/L respectively, both of which were found mostly in the <60 U/L category, which were 57 people (67.1%) and 44 people (62.9%) respectively. Platelet levels were found to average 197,585/mm3 in this study with the most categories found in the >100,000/mm3 category, with 53 people (75.7%).

Based on table 3 of this study, only LDH influenced the incidence of proteinuria as evidenced by p=0.001 (p<0.05). The statistical results in this study showed no association between bilirubin (p=0.494), SGPT (p=0.265), SGOT (p=0.129), and platelets (p=0.529) with proteinuria in PE-SF.

Discussion

In this study, the LDH level in PE-SF increased from the normal limit. According to Ababio et al,[19] this occurs because hypoxia that occurs in preeclampsia will increase the process of glycolysis so that it can increase LDH activity. Research by Burwick et al,[20] found that when LDH levels ≥ 400 U/L, there is a risk for preeclamptic pregnant women to develop into PE-SF with poor outcomes.

This study showed no significant increase in PE-SF patients in total bilirubin. Some studies also proved no significant difference between preeclamptic mothers and normotensive mothers.[21] The liver releases bilirubin in a form called bile. If the liver is improperly functioning, bilirubin will not be released properly. For that reason, if bilirubin levels are higher than expected, this may mean that the liver is not functioning appropriately.[22]

This study showed an average increase in liver transaminase enzyme levels. This finding aligns with research conducted by Lodhi and Roy[23], which found an increase in SGPT and SGOT levels. This could be due to hepatocyte degeneration caused by hypoxia in the liver, leading to necrosis and subsequent release of enzymes into the bloodstream.[24]

Platelets in this study were not found to have a significant decrease. This is similar to the findings found by Nadeem et al[25], that no difference was found between preeclamptic women and normal pregnant women. However, in preeclampsia itself, there can be a decrease in platelet levels caused by injured endothelium. The wound will activate the coagulation system, which causes an increase in platelet consumption and production.[13]

It is believed that there is an association between LDH, liver function, platelets and proteinuria due to endothelial dysfunction that occurs in PE-SF patients. However, based on the results in this study, there was only an association between LDH and proteinuria in PE-SF patients.

Likewise, Cai et al,[12] found that hypertensive patients are comprehended to be more predisposed to endothelial dysfunction, which can simultaneously cause albuminuria. Hence, vascular endothelial injury and atherosclerosis may define the connection between LDH and albuminuria. In the results from Ma et al,[26] there was also a positive association between LDH and proteinuria. The study presented that LDH levels increased directly with the stringency of proteinuria.

Conclusion

This study found an association between LDH and proteinuria in PE-SF patients. However, there was no association between bilirubin, SGPT, SGOT, and platelets with proteinuria in PE-SF patients.

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Conflict of interest

The authors claim no conflict of interest.

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