Research Article

Correlation between Maternal Lactate Dehydrogenase Levels and APGAR Scores in Preeclampsia Patients at Margono Soekarjo Hospital from 2022–2024

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Abstract
Objective: This study aims to investigate the correlation between maternal lactate dehydrogenase (LDH) levels and neonatal APGAR scores in preeclamptic patients.
Methods: This is an observational analytic study with a cross-sectional design conducted at Margono Soekarjo Hospital from January 2022 to May 2024, involving 78 women with preeclampsia who underwent cesarean delivery. Participants were categorized into early-onset (<34 weeks) and late-onset (≥34 weeks) preeclampsia groups. LDH levels and APGAR scores were analyzed using Spearman's correlation and ROC analysis.
Results: This study showed that elevated LDH levels were significantly associated with lower one-minute APGAR scores, showing moderate correlations in both groups, and were related to five-minute APGAR scores. The LDH cut-off points predicting poor one-minute APGAR outcomes were 284 IU/L (sensitivity 82.1%, specificity 66.7%) for early-onset and 491.5 IU/L (sensitivity 44.4%, specificity 96.2%) for late-onset preeclampsia.
Conclusion: Elevated maternal LDH levels are associated with lower one-minute APGAR scores in preeclamptic patients, especially in early-onset cases, indicating they may serve as an early marker for fetal hypoxia and asphyxia risk.

Keywords: APGAR score; lactate dehydrogenase; preeclampsia

Korelasi antara Level Laktat Dehidrogenase Maternal dan Skor APGAR pada Pasien Preeklamsia di Rumah Sakit Margono Soekarjo Tahun 2022–2024

Abstrak
Tujuan: Penelitian ini bertujuan untuk meneliti hubungan antara kadar laktat dehidrogenase (LDH) maternal dan skor APGAR neonatus pada pasien preeklampsia.
Metode: Penelitian ini merupakan studi analitik observasional dengan desain potong lintang yang dilakukan di RSUD Margono Soekarjo pada Januari 2022 hingga Mei 2024, melibatkan 78 wanita dengan preeklampsia yang menjalani persalinan melalui seksio sesarea. Peserta dibagi menjadi dua kelompok, yaitu preeklampsia onset dini (<34 minggu) dan onset lambat (≥34 minggu). Kadar LDH dan skor APGAR dianalisis menggunakan korelasi Spearman dan analisis ROC.
Hasil: Hasil penelitian ini menunjukkan bahwa peningkatan kadar LDH berhubungan signifikan dengan skor APGAR satu menit yang lebih rendah, menunjukkan korelasi sedang pada kedua kelompok, serta menandai adanya kaitan dengan skor APGAR lima menit. Titik potong kadar LDH yang memprediksi hasil APGAR satu menit yang buruk adalah 284 IU/L (sensitivitas 82,1%, spesifisitas 66,7%) untuk preeklampsia onset dini dan 491,5 IU/L (sensitivitas 44,4%, spesifisitas 96,2%) untuk onset lambat.
Kesimpulan: Kadar LDH maternal yang meningkat berhubungan dengan penurunan skor APGAR satu menit pada pasien preeklampsia, terutama pada kasus onset dini. Hal ini menunjukkan bahwa LDH dapat berfungsi sebagai penanda dini risiko hipoksia dan asfiksia janin.

Kata kunci: Laktat dehidrogenase; preeklamsia; skor APGAR

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Introduction

Hypertension during pregnancy is defined as high blood pressure that develops after 20 weeks of gestation, without protein in the urine or other signs of organ damage. In contrast, preeclampsia is a pregnancy-specific hypertensive disorder characterized by multi-system involvement and can occur with or without proteinuria. The blood pressure criterion for defining hypertension in pregnancy is a systolic blood pressure of ≥140 mmHg and/or a diastolic blood pressure of ≥90 mmHg, confirmed by two separate measurements. Hypertensive disorders during pregnancy are a leading cause of maternal and perinatal morbidity and mortality, with preeclampsia affecting approximately 2–10% of pregnancies worldwide.[1] It is estimated that preeclampsia causes around 50.000 maternal deaths and over 500.000 perinatal deaths worldwide. The prevalence of preeclampsia is significantly higher in developing countries compared to developed nations.[2] In Indonesia, the reported incidence was about 5.3% in 2016.[3]

Lactate dehydrogenase (LDH) is an intracellular oxidoreductase enzyme that plays a role in anaerobic metabolism and is present in almost all tissues throughout the body. Its presence in the bloodstream usually results from cellular damage and cytoplasmic leakage. Depending on the type of tissue affected, LDH levels can stay elevated in the blood for up to seven days.[4,5] Among various clinical conditions, preeclampsia has been associated with increased LDH levels. Several studies have reported significantly higher LDH concentrations in preeclamptic patients compared to normotensive pregnant women, with levels rising according to disease severity. Elevated LDH may serve as a marker of disease progression and potential complications in preeclampsia, as the condition often affects multiple organ systems, including the cardiovascular, renal, nervous, and hematologic systems.[6–8]

The APGAR score is a quick clinical assessment tool used to evaluate a newborn's condition, particularly in establishing effective respiration, within the first minute and then reassessed at five minutes. It includes five parameters: skin color, heart rate, reflex irritability, muscle tone, and respiratory effort—each assigned a score from 0 to 2. A total score of 7–10 is considered normal, 4–6 indicates moderate distress, and 0–3 is classified as severely depressed, especially in term and late preterm infants. Although it is somewhat subjective in assessing asphyxia or hypoxia, changes in the APGAR score at five and ten minutes are recognized as predictive indicators of neonatal outcomes.[9,10] Previous studies have shown that neonates born to mothers with preeclampsia have lower APGAR scores compared to those from normotensive pregnancies, with further decreases seen in cases of severe disease.[11,12]

The severity and timing of preeclampsia are crucial factors affecting both maternal and fetal outcomes.[1,13] While previous studies have established an association between elevated transaminase levels—including lactate dehydrogenase (LDH)—and lower APGAR scores in cases of hepatic injury due to perinatal asphyxia, there is still a lack of data specifically examining this correlation in the context of preeclampsia. Therefore, this study aims to explore the relationship between maternal LDH levels and neonatal APGAR scores in preeclamptic pregnancies.

Methods

This study was an observational analytic study with a cross-sectional design. Data were retrospectively collected from medical records as secondary data within a defined timeframe, without follow-up of the observed variables. Data were obtained from the parity census at Margono Soekarjo Hospital by identifying patients with preeclampsia and SC delivery

methods. Additional data such as LDH levels and APGAR scores were also extracted from existing medical records. Laboratory samples, including liver function tests and LDH levels, were obtained from blood samples taken on the first day of admission, using 10 cc of cubital venous blood. Each patient then received appropriate management for preeclampsia before delivery. Patients were categorized into early and late preeclampsia groups based on delivery timing, with cases ending before 34 weeks classified as early onset preeclampsia. The 1- and 5-minute APGAR scores were assessed by a pediatric specialist and grouped into good and poor scores. Maternal age was divided into low-risk and high-risk groups based on preeclampsia risk. Body mass index was categorized according to the WHO Asia Pacific BMI standards. LDH levels were classified as elevated or normal. The minimum sample size was calculated using the correlation coefficient formula, resulting in a required sample of 24 subjects. Subjects were recruited using a non-probability, consecutive sampling method.

The population in this study consisted of pregnant women diagnosed with preeclampsia who received care at the Department of Obstetrics and Gynecology, Margono Soekarjo Hospital, between January 2022 and May 2024. Subjects who underwent cesarean section were included if their medical records contained complete data on maternal age, body mass index (BMI), parity status, lactate dehydrogenase (LDH) levels, and one- and five-minute APGAR scores. Exclusion criteria included vaginal delivery, a documented history of pre-existing cardiovascular, hepatic, renal, hematologic, autoimmune diseases, or malignancies prior to pregnancy. The data were categorized based on the onset of preeclampsia. In cases of severe preeclampsia, pregnancy termination was performed at 34 weeks of gestation according to current clinical guidelines.

The collected data were analyzed using univariate and bivariate statistical methods. Univariate analysis was performed to describe each variable's characteristics, with results shown in tables that include frequency distributions and percentages. Descriptive statistics summarized the data. Bivariate analysis was carried out to explore the relationships between variables. Since the variables were measured on an ordinal scale, Spearman's rank correlation test was considered suitable. This analysis aimed to assess the statistical significance, strength, and direction of the correlation between LDH levels and APGAR scores. The Youden index was used to identify the optimal cut-off point of LDH levels as a predictor of APGAR scores. A p-value of less than 0.05 was considered statistically significant. All statistical analyses were performed using IBM SPSS Statistics version 25.0.

Results

A total of 133 subjects with preeclampsia were collected in this study. Among the data collected, 35 subjects had incomplete medical records, 17 subjects had a vaginal delivery method, two subjects had a history of cardiovascular disease, and one subject had an autoimmune disease. Therefore, 78 subjects were included in this study and were divided into two groups based on gestational age. Group one consists of subjects with early-onset preeclampsia (< 34 weeks of gestation), while group two includes subjects with late-onset preeclampsia (≥ 34 weeks of gestation). The baseline characteristics of the subjects are presented in Table 1. The subjects in this study are mostly in the lower-risk age group, with multiple parity statuses and obesity. LDH levels were normal in most subjects. The one-minute APGAR scores were mostly poor, but the five-minute APGAR scores were generally higher.

Spearman's test was conducted in this study to evaluate the correlation between

Table 1 Baseline Characteristics

	Group 1 (n = 34)		Group 2 (n = 44)	
	n	**%**	**n**	**%**
Maternal				
Age				
Low risk (20 – 35 years old)	23	29.5	25	32.1
High risk (< 20 or ≥ 36 years old)	11	14.1	19	24.3
Parity Status				
Nullipara (0)	11	14.1	6	7.7
Primipara (1)	5	6.4	12	15.4
Multipara (≥ 2)	18	23.1	26	33.3
Body Mass Index (BMI)				
Underweight (<18.5 kg/m^2)	5	6.4	4	5.1
Normoweight (≥18.5 - <23.0 kg/m^2)	12	15.4	12	15.4
Overweight (≥23.0 and <27.5 kg/m^2)	11	14.1	12	15.4
Obese (≥27.5 kg/m^2)	6	7.7	16	20.5
Lactate Dehydrogenase (LDH) Level				
Elevated (> 600 IU/L)	19	24.3	5	6.4
Normal (≤ 600 IU/L)	15	19.2	39	50
Neonatal				
One-minute APGAR Score				
Poor (1-6)	28	35.9	18	23.1
Good (7-10)	6	7.7	26	33.3
Five-minute APGAR Score				
Poor (1-6)	5	6.4	5	6.4
Good (7-10)	29	37.2	39	50.0

LDH levels and APGAR scores (Table 2). For the one-minute APGAR score, results showed a positive (+) correlation between the two variables, as indicated by the r value. The correlation is classified as moderate, with r values of 0.366 and 0.285 in groups 1 and 2, respectively. The five-minute APGAR score also showed a positive correlation with LDH levels, with statistical significance (Table 3). The ROC curve results for group 1 indicate an area under the curve (AUC) of 0.762. The optimal cutoff point according to the Youden Index is an LDH of 284 IU/L, with 82.1% sensitivity and 66.7% specificity (Figure 1a). For group 2, the AUC is 0.718, with a cutoff of 491.5 IU/L, yielding 44.4% sensitivity and 96.2% specificity (Figure 1c). Both groups showed a strong correlation, as indicated by the AUC values.

Table 2 Spearman's *Rank* Test Results of LDH Levels and One-Minute APGAR Score

	***Correlation Coefficient* (r)**	***p-value***
Group 1	0.366	0.033
Group 2	0.285	0.061

Table 3 Spearman's *Rank* Test Results of LDH Levels and Five-Minute APGAR Score

	Correlation Coefficient (r)	*p-value*
Group 1	-0,406	0,001
Group 2	-0,116	0.444

ROC curve analysis was also conducted to examine the relationship between LDH levels and the five-minute APGAR score. For group 1, the AUC is 0.152, with a critical LDH value of 934 IU/L, showing 3.4% sensitivity and 100% specificity (Figure 1b). For group 2, the AUC is 0.056, with an LDH cutoff of 798.5 IU/L, resulting in 2.6% sensitivity and 100% specificity (Figure 1d).

Discussion

This study examined the relationship between LDH levels and APGAR scores in women with preeclampsia, which was divided into two groups based on the disease's onset. The exact cause of preeclampsia remains unknown. However, both maternal and placental factors are believed to play a role in their development. In cases of early-onset preeclampsia, the underlying pathophysiological mechanisms

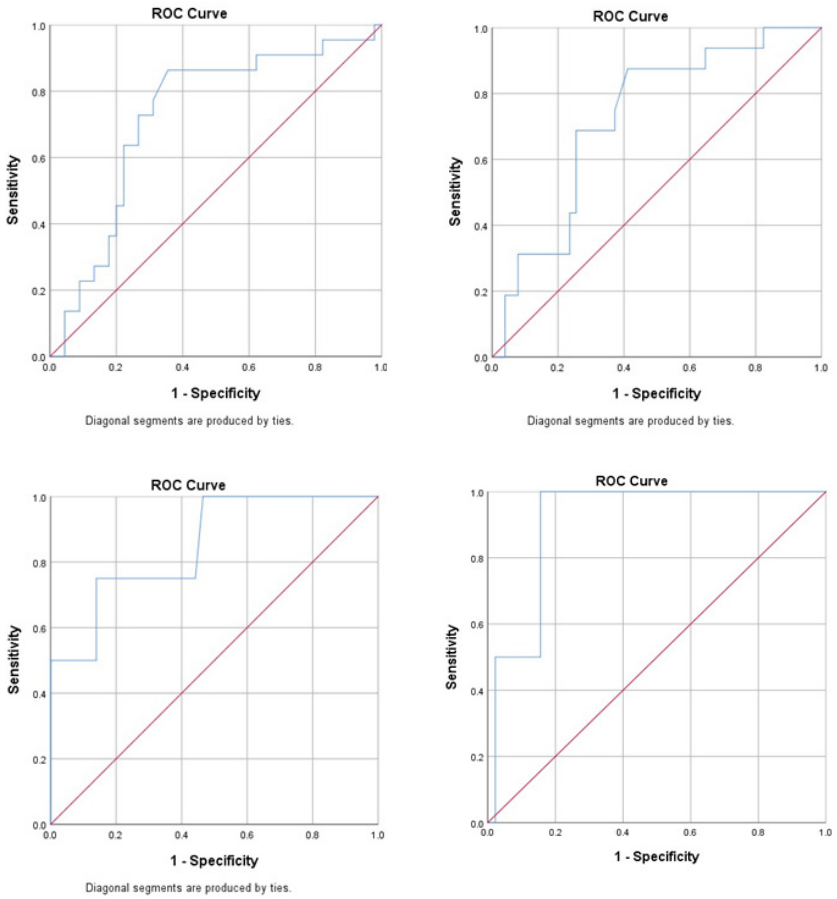

Figure 1 LDH Cut-off Point and One-Minute APGAR to Predict Neonatal Hypoxia with ROC Curve. (A) LDH and APGAR1' in Preterm, (B) LDH and APGAR5' in Preterm, (C) LDH and APGAR1' in Term, and (D) LDH and APGAR5' in Term

are thought to mainly stem from intrinsic placental abnormalities. Conversely, late-onset preeclampsia is more closely linked to pre-existing maternal risk factors, with the condition potentially resulting from complex interactions between the placenta and maternal predispositions to cardiovascular and metabolic disorders.[14,15] Although other risk factors—such as extremes of maternal age, chronic hypertension, and diabetes mellitus—are more commonly linked to early-onset presentations, research indicates that early-onset preeclampsia is more frequently associated with fetoplacental complications. A study conducted in Poland suggested that these complications may result from defective trophoblastic invasion and impaired spiral artery remodeling. Thus, placental hypoxia could trigger an inflammatory cascade by releasing anti-angiogenic factors, which leads to maternal endothelial dysfunction and further increases inflammation.[14,16] Another study in Ethiopia reported that both maternal and fetal adverse outcomes were significantly more severe in early-onset preeclampsia. Poor fetal outcomes include lower first and fifth-minute APGAR scores.[15,16]

Most subjects in this study belonged to the lower-risk age group of 20 to 35 years old. Pregnancies in adolescents (<20 years) are more likely to have elevated blood pressure and a higher incidence of eclamptic seizures. In contrast, women of advanced maternal age (>35 years) are at greater risk for hypertensive disorders during pregnancy. Older age has also been consistently linked to adverse perinatal outcomes, including increased chances of preterm birth, low APGAR scores, fetal growth restriction (FGR), small-for-gestational-age (SGA) neonates, and intrapartum asphyxia. The link between maternal age and the development of preeclampsia is believed to involve vascular changes such as arterial stiffness, progressive endothelial dysfunction, and impaired maternal hemodynamic adaptation during pregnancy.[13,17,18]

A study conducted by Zhu et al. reported that a higher maternal body mass index (BMI ≥25 kg/m²) was significantly associated with lower APGAR scores. Elevated maternal BMI indicates increased fat accumulation, especially visceral fat, which predisposes the placenta to lipid buildup. This lipotoxic environment triggers inflammatory responses and boosts oxidative stress, possibly impairing placental structure, cellular growth, and blood vessel formation.[19] Grand multiparity has been reported to be significantly associated with lower APGAR scores compared to women with lower parity.[20] Meanwhile, another study by Abukari et al. found that APGAR scores were less likely to be low in women with multiparity, primarily through vaginal delivery.[21]

A low APGAR score is strongly linked to a higher risk of neonatal asphyxia, long-term developmental delays, cerebral palsy, and neonatal death.[21,22] However, consistently low scores at five minutes are considered a more reliable predictor of mortality and cerebral palsy.[9] Preeclampsia is a significant risk factor for neonatal asphyxia, which can be reflected in lower APGAR scores. The underlying pathophysiology involves degenerative changes in the placental villi caused by sustained maternal arteriole vasospasm, leading to chronic intrauterine hypoxia. A study by Wang et al. further supported this link, showing that complicated preeclampsia is more often associated with reduced APGAR scores. Among the factors influencing neonatal outcomes in preeclamptic pregnancies, gestational age stands out as a key determinant. The study identified an optimal gestational age of 28.5 weeks for predicting low APGAR scores, with a sensitivity of 77.3% and a specificity of 69.9%.[11,12,23]

As far as we know, this is the first study to examine the relationship between LDH levels and one- and five-minute APGAR

scores in preeclampsia, separated by early and late onset. Our results showed a positive correlation between higher LDH levels and lower one-minute APGAR scores in both early- and late-onset preeclampsia groups. This indicates that higher LDH levels are correlated with lower one-minute APGAR scores. The early-onset group had a sensitivity of 82.1% and a specificity of 66.7%, while the late-onset group had values of 44.4% and 96.2%, respectively. These findings are consistent with previous studies in India, which found that increased LDH levels were linked to greater maternal and fetal complications, including lower APGAR scores.[15] However, our study further clarified this relationship by dividing preeclampsia into early and late onset, showing a statistically significant positive correlation ($p = 0.033$) only in the early-onset group. This supports existing evidence that early-onset preeclampsia is generally associated with more severe fetomaternal outcomes.

A significant positive correlation was also observed between elevated LDH levels and five-minute APGAR scores in both groups. However, unlike the findings for the one-minute APGAR score, the five-minute scores showed 100% specificity but very low sensitivity across both groups. These findings suggest that LDH levels may have limited utility as a predictive biomarker for five-minute APGAR scores. This contrasts with previous studies, which have indicated that both one- and five-minute APGAR scores are useful indicators of neonatal outcomes, with the five-minute score often considered more predictive.[24,25]

The discrepancy might be due to our focus on the association between LDH levels and APGAR scores, while earlier studies mainly examined the link between APGAR scores and long-term neonatal outcomes. It is important to recognize that the five-minute APGAR score may reflect the success of immediate neonatal resuscitation efforts, which could lead to higher scores regardless of the initial fetal condition. Thus, further research is needed to understand the mechanisms behind these differing findings. Despite these limitations, our results indicate that elevated LDH levels could be an early biomarker for compromised neonatal health, as shown by the significant correlation with one-minute APGAR scores.

Conclusion, this study showed a strong positive link between higher lactate dehydrogenase (LDH) levels and lower one-minute APGAR scores in preeclamptic patients, especially in the early-onset preeclampsia group. These results indicate that increasing LDH levels might be an early sign of poor neonatal outcomes as reflected by the one-minute APGAR score.

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