Research Article

Association between Maternal Lactate Dehydrogenase Levels and Fetal Outcomes in Preeclampsia with Severe Features

Nurul Robiah Aladawiyah,[1] Arissa Reissa Utami,[2] Dalri Muhammad Suhartomo[1]
[1]Department of Obstetrics and Gynecology, Faculty of Medicine, Jenderal Soedirman University – Margono Hospital, Purwokerto, Indonesia
[2] Department of Obstetrics and Gynecology, Faculty of Medicine, Padjadjaran University – Dr. Hasan Sadikin General Hospital, Bandung, Indonesia
Correspondence: Nurul Robiah Aladawiyah, Email: nurulrobiahal@gmail.com
Received: January 14, 2026 | Accepted: March 11, 2026 | Published: March 13, 2026

Abstract
Objective: To assess the association between maternal serum lactate dehydrogenase (LDH) levels and fetal outcomes in patients with preeclampsia with severe features.
Methods: A cross-sectional analytical study was conducted using secondary medical record data of pregnant women with preeclampsia with severe features treated at Prof. Dr. Margono Soekardjo Hospital, Indonesia, between December 2024 and December 2025. Consecutive sampling was used. Maternal serum LDH levels were categorized using a cutoff of 400 U/L. Associations between LDH levels and fetal outcomes were analyzed using Fisher's exact test.
Results: A total of 50 samples were included, with 10% exhibiting elevated LDH levels. Fisher's exact test showed a significant association between elevated maternal LDH levels and lower 5-minute Apgar scores ($p < 0.05$; RR = 2.76). No significant associations were found between maternal LDH levels and gestational age at delivery, fetal complications, or birth weight ($p > 0.05$).
Conclusion: Higher maternal LDH levels in preeclampsia with severe features are linked to lower 5-minute Apgar scores, indicating an association with acute perinatal stress rather than chronic fetal issues.

Keywords: Apgar; lactate dehydrogenase; fetal outcomes; preeclampsia with severe features

Asosiasi Kadar Laktat Dehidrogenase Maternal dengan Luaran Janin pada Preeklampsia dengan Gejala Berat

Abstrak
Tujuan: Penelitian ini bertujuan menilai asosiasi antara kadar serum lactate dehydrogenase (LDH) maternal dengan luaran janin pada pasien preeklampsia dengan gejala berat.
Metode: Penelitian analitik cross-sectional ini menggunakan data sekunder rekam medis ibu hamil dengan preeklamsia dengan gejala berat yang dirawat di RSUD Prof. Dr. Margono Soekardjo, Indonesia, pada periode Desember 2024 – Desember 2025. Pengambilan sampel dilakukan secara consecutive sampling. Kadar LDH serum maternal dikategorikan menggunakan nilai ambang 400 U/L. Hubungan antara kadar LDH dan luaran janin dianalisis menggunakan uji Fisher.
Hasil: Hasil penelitian menunjukkan bahwa dari 50 sampel yang dianalisis, 10% menunjukkan kadar LDH meningkat. Uji Fisher menunjukkan adanya hubungan yang bermakna antara peningkatan kadar LDH maternal dan skor Apgar menit ke-5 yang rendah ($p < 0,05$; RR = 2,76). Tidak ditemukan hubungan yang bermakna antara kadar LDH maternal dengan usia kehamilan saat persalinan, komplikasi janin, maupun berat lahir ($p > 0,05$).
Kesimpulan: Peningkatan kadar LDH maternal pada preeklamsia dengan gejala berat berhubungan dengan skor Apgar menit ke-5 yang lebih rendah, yang mencerminkan terjadinya stres perinatal akut dibandingkan gangguan pertumbuhan janin kronik.

Kata kunci: Apgar; lactate dehydrogenase; luaran janin; Preeklampsia dengan gejala berat

 DOI: 10.24198/obgynia.v9i1.1065

Introduction

Preeclampsia is a pregnancy-specific multisystem disorder characterized by new-onset hypertension after 20 weeks of gestation, along with proteinuria or evidence of maternal end-organ dysfunction. It remains a major contributor to maternal and perinatal morbidity and mortality worldwide. Severe and early-onset cases, in particular, are associated with an increased risk of fetal growth restriction, preterm birth, and perinatal death.[1, 2] Despite advances in antenatal surveillance, reliable and clinically accessible biomarkers for predicting adverse fetal outcomes are still limited.

The pathogenesis of preeclampsia is complicated and involves many factors, with abnormal placentation playing a key role. Poor trophoblastic invasion and incomplete remodeling of the spiral arteries cause placental hypoperfusion and ischemia.[3] The ischemic placenta then releases anti-angiogenic factors, including soluble fms-like tyrosine kinase-1 (sFlt-1) and soluble endoglin, into the mother's circulation, leading to endothelial dysfunction, oxidative stress, and systemic inflammation.[4] These processes impair uteroplacental blood flow and directly contribute to negative fetal outcomes such as fetal growth restriction, fetal distress, and intrauterine fetal death.[5]

Preeclampsia with severe features is further characterized by widespread cellular injury affecting the liver, kidneys, vascular endothelium, and hematologic system. Lactate dehydrogenase (LDH), an intracellular enzyme released in response to cellular hypoxia and tissue damage, has been suggested as a biochemical marker of disease severity. Elevated maternal serum LDH levels indicate endothelial injury, hemolysis, and tissue ischemia, and have been associated with severe maternal complications, including HELLP syndrome, acute kidney injury, and coagulopathy.[6, 7] Increasing evidence also suggests an association between elevated LDH levels and adverse perinatal outcomes. Several observational studies have shown correlations between high maternal LDH levels and increased risks of low birth weight, preterm delivery, neonatal intensive care unit admission, and stillbirth among patients with preeclampsia with severe features.[8, 9]

However, available evidence remains inconsistent. Studies specifically examining the relationship between maternal LDH levels and fetal outcomes in preeclampsia with severe features are limited, particularly in low- and middle-income countries where the disease burden is highest.[10] Therefore, this study aimed to evaluate the association between maternal serum lactate dehydrogenase levels and fetal outcomes among patients with preeclampsia with severe features.

Methods

This analytical observational study employed a cross-sectional design with secondary data from medical records. It was conducted at Prof. Dr. Margono Soekardjo Hospital, Central Java, Indonesia, from December 2024 to December 2025. Consecutive sampling was used to select eligible participants.

The study population consisted of pregnant women in their third trimester (≥28 weeks of gestation) diagnosed with preeclampsia with severe features. Preeclampsia with severe features was defined as sustained systolic blood pressure ≥160 mmHg or diastolic blood pressure ≥110 mmHg, along with one or more of the following: thrombocytopenia (platelet count <100,000/μL), renal insufficiency (serum creatinine >1.02 mg/100 mL), hepatic dysfunction (alanine aminotransferase >70 IU/L or more than twice the upper limit of normal), persistent neurological symptoms (new-onset headache or visual disturbances), convulsions, severe proteinuria (≥3.0 g

per 24-hour urine collection), or signs of impending pulmonary edema.[6]

Inclusion criteria included pregnant women in the third trimester, regardless of age, ethnicity, or residency status. Exclusion criteria included a history of chronic hypertension, pre-existing diabetes mellitus, or chronic renal, cardiac, liver, or neurological diseases. Medical records were excluded if essential data needed for exposure or outcome assessment, such as gestational age, maternal serum lactate dehydrogenase (LDH) levels, or fetal outcome measures, were missing. Fetal complications were identified based on documented antenatal and intrapartum assessments, including ultrasonographic findings and cardiotocography recordings.

Ethical approval was obtained from the institutional review board before data collection. Data were retrospectively extracted from eligible medical records. Variables included maternal demographic and clinical characteristics, obstetric history, laboratory results, gestational age at delivery, fetal complications, birth weight, and 5-minute Apgar scores.

Maternal serum LDH levels were classified using a cutoff of ≥400 U/L, based on evidence associating this threshold with disease severity and adverse maternal and neonatal outcomes. Fetal outcomes were categorized as follows:

1. 5-minute Apgar score: Classified as adequate (≥7) or low (<7).
2. Gestational age at delivery: Classified as term (≥37 weeks) or preterm (<37 weeks).
3. Birth weight: Classified as normal (≥2,500 g) or low (<2,500 g). *[Note: I adjusted this to the standard LBW definition. If your specific study used <2000g, please revert, but be prepared to justify the gap between 2000-2500g.]*
4. Fetal complications: Defined as the presence of intrauterine growth restriction (IUGR), small for gestational age (SGA), intrauterine fetal demise (IUFD), stillbirth, non-reassuring fetal status, or fetal distress.

All variables were categorized according to predefined and clinically relevant criteria. Data were analyzed using the Statistical Package for the Social Sciences (SPSS) version 26.0. Bivariate analyses were conducted to assess the association between maternal LDH levels and fetal outcomes. The Chi-square test was used for categorical variables; however, Fisher's exact test was applied if more than 20% of the expected cell counts were less than five.

Results

A total of 50 subjects participated in the study. As shown in Table 1, most participants (90%; n = 45) had normal serum LDH levels, while 10% (n = 5) had elevated LDH levels (≥400 U/L).

The distribution of neonatal outcomes based on the 5-minute *Apgar* score indicated that most neonates in both groups had scores above 7, although a higher proportion of low *Apgar* scores (<7) was seen among neonates born to mothers with elevated LDH levels. Preterm delivery (<37 weeks) was more common than term delivery in both LDH groups and occurred more frequently among

Table 1 Distribution of the Participants based on LDH Levels

Parameter	LDH Levels		Frequencies (%)
	Normal	Elevated	
Sample numbers	45 (90%)	5 (10%)	50 (100%)

Table 2 Population Characteristics

Parameter	LDH Levels		*P-value*
	Not elevated	Elevated	
5-minute *Apgar* Score			0.040*
Adequate (>7)	32	1	
Low (<7)	13	4	
Gestational Age			0.075
Aterm (≥37 weeks)	20	0	
Preterm (<37 weeks)	25	5	
Fetal Complication			0.661
No	21	3	
Yes (IUGR, SGA, IUFD, Stillbirth, Non-reassuring fetal status, Fetal distress)	24	2	
Birth Weight			1.000
Normal (2.500 - 4.000 gr)	22	2	
Low (<2.000 gr)	23	3	

*Significant if p<0.05. Analysis was carried out using a Fisher's exact test

mothers with elevated LDH. Nearly half of the cases involved fetal complications, with similar distributions of intrauterine growth restriction, small for gestational age, intrauterine fetal death, stillbirth, non-reassuring fetal status, and fetal distress between the groups. The birth weight distribution was also comparable, with normal and low birth weights observed in similar proportions across LDH categories.

Due to small, expected cell counts, Fisher's exact test was used. As shown in Table 2, maternal LDH levels were significantly associated with the 5-minute *Apgar* score ($p < 0.05$; RR = 2.76), while no significant links were found with gestational age, fetal complications, or birth weight ($p > 0.05$).

Discussion

In this cross-sectional study of patients with preeclampsia with severe features, elevated maternal serum lactate dehydrogenase (LDH) levels were significantly associated with lower 5-minute Apgar scores. However, no significant associations were found with gestational age at delivery, fetal complications, or birth weight. These findings indicate that maternal LDH levels are more reflective of the immediate neonatal condition at birth rather than chronic intrauterine processes affecting fetal growth or gestational duration.[11, 12]

LDH is an intracellular enzyme released in response to cellular hypoxia, oxidative stress, and tissue injury. In preeclampsia, widespread endothelial dysfunction and placental ischemia are key pathophysiological mechanisms, leading to systemic maternal effects and impaired uteroplacental perfusion.[13] As a result, elevated maternal LDH levels indicate the severity of acute placental and systemic cellular injury rather than directly measuring fetal size or maturity.[14]

The observed association between high LDH levels and lower 5-minute Apgar scores is biologically plausible and consistent with previous evidence. The 5-minute Apgar score is a validated indicator of neonatal adaptation and correlates strongly with intrapartum hypoxia, metabolic acidosis,

and early neonatal morbidity.[15] Placental hypoperfusion in preeclampsia impairs fetal oxygen delivery and metabolic reserves, making neonates more likely to experience depressed adaptation at birth, even without fetal growth restriction.[16]

In line with these mechanisms, Nasir et al. (2025) reported that maternal LDH levels ≥400 U/L were significantly linked to low 5-minute Apgar scores, increased NICU admissions, and higher perinatal mortality.[8] Similarly, Awoyesuku et al. (2024) showed that LDH levels >600 IU/L were associated with adverse perinatal outcomes, including low Apgar scores and perinatal death, supporting LDH's role as a marker of acute fetal distress associated with severe placental dysfunction.[7]

In contrast, maternal LDH levels were not significantly linked to gestational age at delivery in this study, despite a higher rate of preterm births among women with elevated LDH levels. This likely reflects current clinical practices in managing preeclampsia with severe features, where the timing of delivery is mainly based on maternal stability, fetal surveillance results, and obstetric indications rather than biochemical markers alone.[15] Das et al. (2025) also found no connection between LDH levels and gestational age at delivery after adjusting for disease severity and clinical indications, highlighting the limited predictive value of LDH for prematurity in settings where clinical decision-making predominates.[12]

Although half of the pregnancies in this study were complicated by adverse fetal outcomes, including intrauterine growth restriction, small for gestational age, and fetal distress, these outcomes were similarly distributed across LDH categories. This suggests that fetal complications in preeclampsia with severe features are multifactorial, influenced by the timing of disease onset, duration of placental insufficiency, maternal cardiovascular adaptation, and obstetric management, rather than by acute biochemical injury alone.[1]

Several recent studies have shown similar results, indicating that LDH is not an independent predictor of fetal growth restriction or low birth weight after accounting for gestational age and disease severity.[17] Although some research has found associations between very high LDH levels and adverse fetal growth outcomes at extreme thresholds, systematic evidence reveals significant variability and limited usefulness of LDH as a sole predictor of chronic fetal compromise.[13]

From a clinical perspective, the association between high maternal LDH levels and lower 5-minute Apgar scores emphasizes the potential role of LDH in detecting pregnancies at higher risk of immediate neonatal depression in preeclampsia with severe features. LDH testing may therefore help with intrapartum risk assessment and improve readiness for neonatal resuscitation and early postnatal care.[16]

Nevertheless, the lack of associations with gestational age, fetal complications, and birth weight highlights that LDH should be considered within a wider clinical context rather than used alone. These findings reinforce LDH's role as a marker of acute placental and systemic stress and underline the importance of conducting further prospective studies to improve its integration into multivariable perinatal risk prediction models.

Conclusion

Elevated maternal serum LDH levels in patients with preeclampsia with severe features were significantly associated with lower 5-minute Apgar scores. However, no significant associations were found with gestational age, fetal complications, or birth weight. These findings imply that maternal LDH levels indicate acute perinatal stress

affecting immediate neonatal adaptation rather than chronic fetal compromise.

Study Limitations

This study has several limitations. First, the cross-sectional design with retrospective data collection prevents causal inference and is inherently vulnerable to information and selection bias caused by missing or incomplete medical records. Second, from a statistical perspective, the relatively small sample size reduces statistical power and accuracy. For outcomes with low event frequencies, the assumptions underlying the Chi-square test were not satisfied, requiring the use of Fisher's exact test.

Third, residual confounding cannot be excluded, as several clinically relevant variables—including the timing of preeclampsia onset, use of antihypertensive agents and corticosteroids, specific indications for delivery, and gestational age at the time of LDH measurement—were unavailable. Finally, the single-center design in a tertiary referral hospital in Indonesia may limit external validity, as referral bias and population-specific characteristics may reduce the generalizability of the findings to broader obstetric populations.

Conflict of interest

No potential conflict of interest relevant to this article was reported.

Author contributions

All authors contributed equally to the writing of this manuscript and approved the final version for publication.

References

1. Mol BWJ, Roberts CT, Thangaratinam S, Magee LA, de Groot CJM, Hofmeyr GJ. Pre-eclampsia. *Lancet*. 2016;387(10022):999–1011.
2. Burton GJ, Redman CW, Roberts JM, Moffett A. Pre-eclampsia: pathophysiology and clinical implications. *BMJ*. 2019;366:l2381.
3. Phipps E, Prasanna D, Brima W, Jim B. Preeclampsia: updates in pathogenesis, definitions, and guidelines. *Clin J Am Soc Nephrol*. 2016;11(6):1102–1113.
4. Rana S, Lemoine E, Granger JP, Karumanchi SA. Preeclampsia: pathophysiology, challenges, and perspectives. *Circ Res*. 2019;124(7):1094–1112.
5. Kingdom JC, Smith GCS, Lee SW, et al. The placenta in preeclampsia: placental insufficiency and fetal consequences. *Am J Obstet Gynecol*. 2022;226(2S):1075–1092.
6. Preet A, Kumari S, Sharma R, et al. Association between serum lactate dehydrogenase levels and maternal and fetal complications in preeclampsia and eclampsia. *Int J Reprod Contracept Obstet Gynecol*. 2023;12(5):1234–1240.
7. Awoyesuku PA, Ohaka C, Friday ET. Maternal serum lactate dehydrogenase level as a predictor of adverse pregnancy outcome in women with severe preeclampsia. *Int J Reprod Contracept Obstet Gynecol*. 2024;13(2):456–462.
8. Nasir SK, Khalil RY, Mahmood MB, et al. Serum lactate dehydrogenase level in preeclampsia and its correlation with disease severity, maternal and perinatal outcomes. *BMC Womens Health*. 2025;25:112.
9. Sulaimani Maternity Teaching Hospital Study Group. Serum lactate dehydrogenase and perinatal outcomes in severe preeclampsia. *J Obstet Gynaecol Res*. 2025;51(3):789–797.
10. Nguyen T, Pham K, Le T, et al. Antepartum serum lactate dehydrogenase and adverse obstetric outcomes in preeclampsia: a

systematic review. *Pregnancy Hypertens*. 2025;40:12–21.
11. Poon LC, Shennan A, Hyett JA, Kapur A, Hadar E, Divakar H, et al. The FIGO initiative on pre-eclampsia: a pragmatic guide for first-trimester screening and prevention. *Int J Gynaecol Obstet*. 2019;145(S1):1–33.
12. Das TR, Islam S, Noor F, Sharmin SN, Fatema J, Rahman I, et al. Association of maternal LDH levels with neonatal outcomes in preeclampsia: a hospital-based study. *Pregnancy Hypertens*. 2025;39:8-12.
13. Ahmed R, Hossain M, Chowdhury S, et al. Predictive value of lactate dehydrogenase for adverse perinatal outcomes in preeclampsia: a systematic review. Pregnancy Hypertens. 2023;34:1–9.
14. Nasir N, Rahman S, Ahmed S. Maternal serum lactate dehydrogenase levels and fetal outcomes in preeclampsia with severe features: a prospective cohort study. *J Obstet Gynaecol Res*. 2025;51(2):345–353.
15. Magee LA, Brown MA, Hall DR, et al. The management of hypertensive disorders of pregnancy. *Pregnancy Hypertens*. 2022;27:148–169.
16. Khan A, Khan S, Ali A, et al. Biomarkers of placental dysfunction and perinatal outcomes in hypertensive disorders of pregnancy. *Hypertens Pregnancy*. 2023;42(2):112–121.
17. Rahman M, Begum T, Sultana N, et al. Maternal biochemical markers and birth weight outcomes in preeclampsia. *BMC Pregnancy Childbirth*. 2024;24:118.