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The impact of biochemical marker levels in pregnant patients diagnosed with HELLP syndrome on predicting the progression and recovery timelines

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ABSTRACT

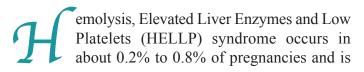
Objectives: This study investigates the role of biochemical markers in predicting the clinical course of pregnant women with Hemolysis, Elevated Liver Enzymes and Low Platelets (HELLP) syndrome, aiming to correlate marker levels with disease progression and recovery timelines for improved prognostic assessment and therapeutic strategies.

Methods: A retrospective analysis was conducted on 50 pregnant patients (aged 18-45) diagnosed with HELLP syndrome between October 2022 and November 2023. Data on demographics, vital signs, clinical symptoms, and laboratory markers (platelets, liver enzymes, lactate dehydrogenase [LDH], and bilirubin) were examined. Outcomes measured included complications, intensive care unit needs, and recovery time.

Results: The mean age was 30.74 ± 5.27 years and body mass index of 29.76 ± 5.88 kg/m2. The gestational age was 31.97 ± 4.45 weeks. Significant cut-off values were identified for urea at 27.50 (sensitivity: 100%, specificity: 73%, 82=0.553, 82=0.

Conclusions: The study highlights the importance of renal and hematological markers (urea, creatinine, LDH, bilirubin, platelets) in predicting HELLP outcomes. Renal markers showed high sensitivity, while hematological markers correlated with hospital stay duration, supporting their integration into clinical protocols to optimize treatment and patient management.

Keywords: Biomarkers, HELLP syndrome, hospital stay, predictive value



associated with increased risks of complications for both the mother and the fetus [1]. While hypertension is commonly observed, the symptoms of preeclampsia

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[2] can be either subtle or absent [3]. Prompt and precise diagnosis is crucial for effective management. Furthermore, the maternal symptoms can be non-specific and may be confused with other medical or obstetric issues, necessitating differential diagnosis [4]. HELLP syndrome is defined by two primary diagnostic frameworks. The more commonly used Tennessee classification defines the condition by the presence of microangiopathic hemolytic anemia, which is indicated by an abnormal blood smear, reduced serum haptoglobin, and increased levels of lactate dehydrogenase (LDH) (above 600 IU/L, more than twice the normal upper limit) and aspartate aminotransferase (AST) (above 70 IU/L). Additionally, bilirubin levels greater than 1.2 mg/dL and a platelet count below 100×10⁹ are required for diagnosis [5]. A less severe variant, known as "HELLP," meets only two of these criteria. Additionally, the Mississippi Triple-class classification system differentiates the syndrome based on the lowest platelet count observed [6].

HELLP syndrome is often associated with preeclampsia, a condition characterized by the onset of high blood pressure (≥140/90 mmHg after 20 weeks of gestation) that resolves after delivery, along with notable proteinuria (≥300 mg/day or a spot urine-to-creatinine ratio ≥30 mg/mmol) [2]. PE is about ten times more common than HELLP syndrome. When preeclampsia and HELLP occur before 28 weeks of gestation, which accounts for roughly 20-30% of cases, they are usually associated with more severe complications [7, 8]. The clinical presentation of HELLP can progress rapidly and may indicate severe complications [9].

The main goal of this study is to assess how biochemical markers can predict the clinical progression and recovery in pregnant patients diagnosed with HELLP syndrome. By examining the levels of these markers, the study seeks to identify correlations with the severity and trajectory of the syndrome.

METHODS

This retrospective cohort study sought to explore how the levels of biochemical markers in pregnant women diagnosed with HELLP syndrome influence the prediction of their progression and recovery timelines. Our study was commenced after the consent of Ankara Etlik City Hospital No. 1 Clinical Research Ethics Committee with the number: AEŞH-EK1-2023-728 on 06/12/2023. Our analysis was carried out following the ethical guidelines set forth in the Declaration of Helsinki. The study was conducted at the Department of Obstetrics and Gynecology and included patients treated between October 1st, 2022, and November 1st, 2023. The study cohort included all individuals diagnosed with HELLP syndrome within the designated study timeframe. To be included in the study, patients had to have a confirmed diagnosis of HELLP syndrome based on clinical and laboratory criteria and have completed treatment for the condition at our centre. Individuals were excluded from the study if they were younger than 18 years, had a history of systemic health conditions, were carrying multiple fetuses, had a previous diagnosis of cancer prior to pregnancy, were engaged in active smoking, alcohol consumption, or illicit drug use, were diagnosed with infectious diseases such as HIV, HCV, or HBV, had any chronic hepatic pathology, or had undergone liver transplantation in the past.

Data for the study was collected retrospectively from the medical records of eligible patients. This included demographic data such as maternal age, gravidity, parity, history of abortions, number of living children, and any documented chronic illnesses. Vital signs such as blood pressure, heart rate, respiratory rate, and body temperature were monitored during the patients' entire hospital admission. Detailed information regarding patients' clinical symptoms, including headache, epigastric pain, visual disturbances, nausea, and vomiting, was retrieved from their medical records. Comprehensive laboratory data was collected, including platelet count, hemoglobin levels, liver enzymes (Alanine aminotransferase [ALT] and AST), LDH levels, bilirubin levels, uric acid levels, creatinine (Cr) levels, and proteinuria levels. Documentation regarding the patients' clinical course, including duration of hospitalization, development of HELLP syndrome-related complications (e.g., disseminated intravascular coagulation (DIC), placental abruption, acute renal failure, eclampsia, cerebral hemorrhage, acute respiratory distress syndrome (ARDS), liver hematoma), need for intensive care unit admission, and requirement for blood product transfusions was meticulously reviewed and recorded. Postoperative laboratory values at 2 hours, 6 hours, and 24 hours

were also collected to assess the trajectory of biochemical markers.

The collected data was analyzed to investigate potential correlations between the initial levels of key biochemical markers (platelet count, ALT and AST, LDH, and bilirubin) and various aspects of HELLP syndrome. These aspects included the severity of the syndrome, the likelihood of developing complications, the overall recovery timeline, the duration of hospitalization, and the time required for blood pressure and other clinical parameters to normalize. This in-depth analysis sought to offer a broader insight into the prognostic significance of these biochemical markers in HELLP syndrome, with the potential to enhance clinical management of this severe pregnancy complication.

Statistical Analysis

Statistical analysis was conducted using the SPSS software (Version 27, SPSS Inc., Chicago, IL, USA). The normality of the distributions of biochemical markers (platelet count, ALT and AST, LDH, and bilirubin) was evaluated using the Kolmogorov-Smirnov test, Shapiro-Wilk test, and histograms. The relationship between the initial levels of these markers and the clinical parameters, including the duration of hospitalization, time to normalization of blood pressure, and the occurrence of HELLP syndrome-related complications was assessed. Spearman's correlation analysis was used to assess the association between the initial levels of biochemical markers and the severity of HELLP syndrome, as reflected by factors such as hospitalization duration, time to blood pressure normalization, and the occurrence of complications. A Pvalue of less than 0.05 was considered statistically significant for all analyses.

RESULTS

In our study, demographic and clinical characteristics of patients diagnosed with HELLP syndrome were presented (Table 1). Hematologic and biochemical parameters in patients with HELLP syndrome are summarized in Table 1. Patients demonstrated significant abnormalities in several markers. The mean systolic blood pressure was elevated at 164.8±18.1 mmHg, and the mean diastolic blood pressure was 104.1±12.5

mmHg, indicating prominent hypertension. Lactate dehydrogenase (LDH) levels were markedly increased, with a mean value of 730.3±589.3 U/L, consistent with hemolysis. Total bilirubin averaged 1.1±1.3 mg/dL, and direct bilirubin was elevated at 0.6±0.8 mg/dL, reflecting liver dysfunction. Other notable findings included a mean neutrophil count of 10.883±3,743/mm³, a neutrophil-to-lymphocyte ratio (NLR) of 6.75±4.73, and reduced platelet counts averaging 137.3±92.4 ×10³/mm³. Elevated liver enzymes were also observed, with alanine aminotransferase (ALT) at 177.4±225.0 IU/L and aspartate aminotransferase (AST) at 276.0±367.7 IU/L.

The white blood cell count was notably elevated, especially in neutrophils, which contributed to a high neutrophil-to-lymphocyte ratio (NLR), a key indicator of systemic inflammation. Platelet counts were significantly reduced, a hallmark of thrombocytopenia in HELLP syndrome. Additionally, elevated ALT and AST further supported the diagnosis of hepatic involvement. Renal function was also impacted, as evidenced by elevated blood urea nitrogen (BUN) and creatinine levels, suggesting some degree of renal compromise. These findings reflect the complex nature of HELLP syndrome, involving significant hemolysis, liver dysfunction, and renal involvement.

Maternal and neonatal outcomes in patients diagnosed with HELLP syndrome were thoroughly evaluated (Table 2). Eclampsia occurred in 16% of cases, representing a significant complication. Thrombocytopenia was observed in 8% of patients with varying severity, while the majority (92%) had platelet counts that did not require extensive transfusion. Fibrinogen levels remained within normal ranges in 96% of patients. Maternal admission to the intensive care unit was required in 16% of cases, though no maternal deaths were reported. Postpartum hemorrhage was noted in 6% of patients.

Neonatal outcomes in HELLP syndrome revealed significant complications (Table 2). Intrauterine growth restriction (IUGR) was observed in 38.8% of pregnancies, while preterm birth or preterm premature rupture of membranes (PPROM) occurred in 82% of cases. External cephalic version was frequently performed (data not explicitly provided but implied by interventions). Fetal distress was noted in 16% of pregnancies. Neonatal intensive care unit (NICU) admission was required for 83.7% of neonates, with 52%

Table 1. Demographic, clinical characteristics, hematological, and biochemical parameters of patients with HELLP syndrome

| Characteristics | Data |
|--|---------------------------------------|
| Gestational age (weeks) | 31.9±4.5 |
| Age (years) | 30.7±5.3 |
| BMI (kg/m^2)) | 29.8±5.9 |
| Parity | |
| 0 | 24 (48%) |
| 1 | 18 (36%) |
| 2 | 4 (8%) |
| 3 | 1 (2%) |
| 4 | 2 (4%) |
| 7 | 1 (2%) |
| Smoke | |
| No | 48 (96%) |
| Yes | 2 (4%) |
| IVF | |
| No | 47 (94%) |
| Yes | 3 (6%) |
| GDM | 45 (01 00/) |
| No | 45 (91.8%) |
| Yes | 4 (8.2%) |
| Delivery | 2 ((0/) |
| Normal spontaneous delivery | 3 (6%) |
| Cesarean section | 47 (9%4) 164.8±18.1 |
| Systolic blood pressure (mmHg) Diastolic blood bressure (mmHg) | 104.6±18.1 104.1±12.5 |
| ζ Θ, | 730.3±589.29 |
| LDH (U/L) Total bilimbin (mg/dL) | 730.3±389.29 1.1±1.3 |
| Total bilirubin (mg/dL) Direct bilirubin (mg/dL) | 0.6±0.8 |
| White blood cell (/mm³) | 14035±4309.1 |
| Neutrophil (/mm³) | 10883.2±3742.99 |
| Lymphocyte (/mm³) | 2261.8±1530.44 |
| NLR | 6.75±4.73 |
| Monocyte (/mm³) | 762.4±289.6 |
| Haematocrit (%) | 37.65±5.97 |
| MPV (fL) | 11.21±1.07 |
| Platelets (×1000/mm³) | 137.32±92.37 |
| PLR | 137.32 ± 92.37 0.08 ± 0.07 |
| Haemoglobin (g/dL) | 12.39±1.9 |
| ALT (IU/L) | 12.39 ± 1.9 177.38 ± 225.01 |
| AST (IU/L) | 275.98±367.66 |
| BUN (mg/dL) | 273.98±307.00 29.21±19.83 |
| , , , | |
| Creatinine (mg/dL) | 1.12±2.5 |

Data are shown as mean±standard deviation or n (%). BMI=Body Mass Index, IVF=In-vitro Fertilisation, GDM=Gestational Diabetes Mellitus, HELLP=Hemolysis, Elevated Liver Enzymes and Low Platelets, LDH=lactate dehydrogenase, NLR=Neutrophil-to-Lymphocyte Ratio, MPV=Mean Platelet Volume, PLR=Platelet-to-lymphocyte ratio, ALT=Alanine Aminotransferase, AST=Aspartate aminotransferase, BUN=Blood Urea Nitrogen

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Table 2. Maternal and neonatal outcomes in HELLP syndrome

| | Frequency of Occurrence / Application | Data |
|-------------------------------------|---------------------------------------|------------|
| Erythrocyte suspension fransfusion | 0 | 43 (86%) |
| | 2 | 4 (8%) |
| | 3 | 1 (2%) |
| | 4 | 2 (4%) |
| Transfusion of FFP | 0 | 45 (90%) |
| | 2 | 4 (8%) |
| | 20 | 1 (2%) |
| Platelet (×1000/mm³) | 0 | 46 (92%) |
| , , | 1 | 1 (2%) |
| | 2 | 2 (4%) |
| | 3 | 1 (2%) |
| Fibrinogen | 0 | 48 (96%) |
| | 1 | 2 (4%) |
| Maternal intensive care unit) | 0 | 42 (84%) |
| | 1 | 8 (16%) |
| Maternal death | 0 | 50 (100%) |
| Postpartum haemorrhage | 0 | 47 (94%) |
| ostpurtum nucmorr nuge | 1 | 3 (6%) |
| UGR | 0 | 30 (61.2%) |
| con | 1 | 19 (38.8%) |
| Preterm/ PPROM | 0 | 9 (18%) |
| Teterm, 11 KOM | 1 | 41 (82%) |
| ntrauterine ex fetus | 0 | 49 (98%) |
| inti autei me ex ietus | 1 | 1 (2%) |
| Fetal distress | 0 | 42 (84%) |
| retai distress | 1 | 8 (16%) |
| Neonatal intensive care unit | 0 | 8 (16.3%) |
| Neonatal intensive care unit | | 41 (83.7%) |
| Description districts and districts | 0 | |
| Respiratory distress syndrome | 0 | 24 (48%) |
| AT | 1 | 26 (52%) |
| Neonatal sepsis | 0 | 43 (86%) |
| NT | 1 | 7 (14%) |
| Neonatal pneumonia | 0 | 44 (88%) |
| o.Clbl/DOD | 1 | 6 (12%) |
| Retinal hemorrhage/ ROP | 0 | 39 (78%) |
| [mtmaxamtularlar harranilar | 1 | 11 (22%) |
| Intraventricular hemorrhage | 0 | 47 (94%) |
| | 1 | 3 (%6) |
| Hypoxic-ischemic encephalopathy | 0 | 50 (100%) |
| Necrotizing enterocolitis | 0 | 46 (92%) |
| | 1 | 3 (6%) |
| | 10 | 1 (2%) |
| Early neonatal death | 0 | 45 (90%) |
| | 1 | 5 (10%) |

Data are shown as n (%). FFP=fresh frozen plasma, IUGR=intrauterine growth retardation, HELLP=Hemolysis, Elevated Liver Enzymes and Low Platelets, PPROM=preterm premature rupture of membranes, ROP=retinopathy of prematurity

Table 3. Hospital stay duration and neonatal outcomes

| | Data |
|------------------------------------|-------------------|
| Before birth hospital stay (hours) | 29.12±67.11 |
| After birth hospital stay (hours) | 147.54±91.37 |
| Birth weight (gram) | 1705.3 ± 876.02 |
| APGAR 1 | 5.92 ± 2.51 |
| APGAR 5 | 7.8 ± 2.06 |
| Hospitalization (day) | 22.98±26.63 |

Data are shown as mean±standard deviation.

experiencing respiratory distress syndrome (RDS). Neonatal sepsis and pneumonia affected 14% and 12% of neonates, respectively. Additionally, retinopathy of prematurity (ROP) occurred in 22%, and intraventricular hemorrhage (IVH) in 6% of neonates. Hypoxic-ischemic encephalopathy (HIE) was universal among the cohort, with 100% requiring intervention, often including therapeutic hypothermia. Necrotizing enterocolitis

affected 8% of neonates, while early neonatal death occurred in 10%, underscoring the severe neonatal morbidity and mortality associated with HELLP syndrome.

Data on the duration of hospitalization and neonatal outcomes related to HELLP syndrome are presented in Table 3. The average duration of hospitalization before birth was relatively short, measured at 29.12±67.11 hours, while the post-birth hospital stay was substantially longer, averaging 147.54±91.37 hours. Neonatal outcomes revealed a high prevalence of low-birth-weight infants, with a mean birth weight of 1705.3±876.02 grams. The mean APGAR score at 1 minute was 5.92±2.51, indicating that many infants required initial resuscitative support; however, the 5-minute APGAR score improved significantly to 7.8±2.06, suggesting stabilization shortly after birth. Neonatal hospitalization duration averaged 22.98±26.63 days, with variability suggesting prolonged NICU stays in some cases. These findings underscore the critical importance of intensive neonatal care and close monitoring in pregnancies affected by

Table 4. Diagnostic accuracy of biomarkers in eclampsia* and related complications in posterior reversible encephalopathy syndrome (PRES)

| Eclampsia | AUC | SD | P value | 95% CI | | Cut-off | Sensitivity | Specificity |
|------------------|-------------|-------------|-------------|-------------|-------------|------------|-------------|-------------|
| | | | | Lower | Upper | | | |
| Total bilirubin | 0.728^{*} | 0.079^{*} | 0.022* | 0.573* | 0.884^{*} | 0.49* | 0.82^{*} | 0.69* |
| | 0.689 | 0.090 | 0.044 | 0.513 | 0.866 | 0.49 | 0.77 | 0.70 |
| Direct bilirubin | 0.760^{*} | 0.075^{*} | 0.009^{*} | 0.613* | 0.907^{*} | 0.19^{*} | 0.73* | 0.77^{*} |
| | 0.715 | 0.088 | 0.022 | 0.543 | 0.888 | 0.19 | 0.69 | 0.78 |
| WBC | 0.702^{*} | 0.106^{*} | 0.043* | 0.493^{*} | 0.910^{*} | 16120* | 0.64^{*} | 0.82^{*} |
| | 0.713 | 0.092 | 0.023 | 0.533 | 0.893 | 14755 | 0.69 | 0.73 |
| Lymphocyte | 0.797^{*} | 0.084^{*} | 0.003^{*} | 0.633^{*} | 0.961^{*} | 2245* | 0.73* | 0.77^{*} |
| | 0.686 | 0.100 | 0.048 | 0.489 | 0.883 | 2245 | 0.62 | 0.76 |
| NLR | 0.732^{*} | 0.082^{*} | 0.020^* | 0.571^{*} | 0.893^{*} | 4.67* | 0.64^{*} | 0.72^{*} |
| Platelets | 0.852^{*} | 0.054^{*} | <0.001* | 0.746^{*} | 0.958^{*} | 165.5* | 0.82^{*} | 0.79^{*} |
| | 0.772 | 0.081 | 0.004 | 0.614 | 0.931 | 134.5 | 0.85 | 0.73 |
| ALT | 0.825^{*} | 0.087^* | 0.001^* | 0.655^{*} | 0.995^{*} | 73.5* | 0.82^{*} | 0.79^{*} |
| | 0.794 | 0.096 | 0.002 | 0.605 | 0.983 | 73.5 | 0.77 | 0.81 |
| AST | 0.791^{*} | 0.087^* | 0.003* | 0.621* | 0.962^{*} | 68* | 0.73* | 0.85^{*} |
| | 0.756 | 0.098 | 0.007 | 0.564 | 0.947 | 68 | 0.69 | 0.86 |

WBC=white blood cell, NLR=Neutrophil-to-Lymphocyte Ratio, ALT=Alanine aminotransferase, AST=aspartate aminotransferase, AUC=Area Under Curve, SD=Standart Deviation, CI= Confidence Interval, *Statistically significant difference or result

Table 5. Biomarkers for hepatic ischemia and rupture

| Hepatic ischemia- rupture | AUC | SD | P value | 95% CI | | Cut-off | Sensitivity | Specificity |
|------------------------------|-------|-------|---------|--------|-------|---------|-------------|-------------|
| | | | | Lower | Upper | | | |
| LDH | 0.710 | 0.078 | 0.011 | 0.558 | 0.863 | 572 | 0.74 | 0.74 |
| Total bilirubin | 0.729 | 0.075 | 0.006 | 0.582 | 0.875 | 0.59 | 0.78 | 0.74 |
| Direct bilirubin | 0.733 | 0.072 | 0.005 | 0.592 | 0.875 | 0.28 | 0.70 | 0.70 |
| Lymphocyte | 0.709 | 0.074 | 0.011 | 0.564 | 0.855 | 1765 | 0.74 | 0.70 |
| PLatelets | 0.665 | 0.078 | 0.046 | 0.512 | 0.818 | 94 | 0.70 | 0.63 |
| ALT | 0.870 | 0.055 | <0.001 | 0.762 | 0.977 | 100 | 0.87 | 0.85 |
| AST | 0.845 | 0.059 | <0.001 | 0.729 | 0.962 | 146 | 0.87 | 0.81 |

LDH=Lactate dehydrogenase, ALT=Alanine aminotransferase, AST=Aspartate aminotransferase, AUC=Area Under Curve, SD=Standart Deviation, CI= Confidence Interval

HELLP syndrome.

The diagnostic accuracy of various biomarkers for eclampsia and related complications, including Posterior Reversible Encephalopathy Syndrome (PRES), was assessed. Among the biomarkers evaluated, platelet count exhibited the highest discriminatory power, with an AUC of 0.852 (P<0.001), sensitivity of 82%, and specificity of 79% at a cut-off value of 165.5 ×10³/mm³, suggesting strong clinical relevance as a diagnostic tool. ALT also demonstrated excellent predictive value with an AUC of 0.825 (P=0.001), sensitivity of 82%, and specificity of 79% at a cut-off of 73.5 U/L. Both platelet count and ALT were identified as reliable and statistically significant indicators for the diagnosis of eclampsia, with high sensitivity and specificity values that support their integration into clinical risk assessment models (Table 4).

In women with PRES, ALT and AST demonstrated strong predictive abilities for cerebral edema and stroke related to eclampsia. ALT was a strong predictor, with a high sensitivity and specificity, while AST also showed notable diagnostic performance. Platelet, while moderately predictive, still proved use-

ful in identifying eclampsia-related complications, with a reasonable balance between sensitivity and specificity. These findings suggest that a combination of specific biomarkers - particularly platelets (AUC= 0.852, P<0.001), ALT (AUC 0.825, P=0.001), AST (AUC=0.791, P=0.003), and lymphocyte count (AUC=0.797, P=0.003) - may serve as highly valuable clinical tools for the diagnosis and management of eclampsia and its associated complications, including PRES. These markers demonstrated strong diagnostic performance with high sensitivity (up to 85%) and specificity (up to 86%) (Table 4).

The evaluation of biomarkers for hepatic ischemia and rupture revealed significant findings. ALT demonstrated the strongest predictive value, with high sensitivity and specificity, making it a reliable indicator for diagnosing hepatic ischemia and rupture. AST also exhibited strong predictive performance, although slightly lower than ALT, providing valuable diagnostic insights. LDH, total bilirubin, and direct bilirubin showed moderate predictive value, highlighting their potential utility in the diagnosis of hepatic complications. Lymphocyte count and platelet count were less

Table 6. Association of biomarkers with hospital stays after birth

| | | β | t | P value | R^2 |
|----------------------------|-----|-------|-------|---------|-------|
| Hospital stays after birth | NLR | 0.303 | 2.730 | 0.009 | 0.427 |
| | BUN | 0.553 | 4.987 | <0.001 | |

NLR=Neutrophil-to-Lymphocyte Ratio, BUN=Blood Urea Nitrogen

effective in predicting hepatic ischemia and rupture, demonstrating lower sensitivity and specificity. These findings suggest that ALT and AST are particularly valuable biomarkers for predicting hepatic ischemia and rupture, demonstrating the highest diagnostic performance with AUC values of 0.870 (P<0.001) and 0.845 (P<0.001), respectively. In contrast, biomarkers such as LDH (AUC= 0.710, P=0.011), total bilirubin (AUC= 0.729, P=0.006), direct bilirubin (AUC= 0.733, P=0.005), and lymphocyte count (AUC=0.709, P=0.011) showed moderate predictive value and may serve as supplementary diagnostic tools (Table 5).

The analysis of factors influencing hospital stays after birth revealed significant correlations with various biomarkers. The NLR showed a moderate positive correlation with the duration of hospital stays, indicating that higher NLR values are associated with longer stays. However, the relatively modest correlation suggests that NLR alone accounts for only a limited portion of the variability in hospital stay duration. In contrast, BUN demonstrated a stronger positive correlation with the length of hospital stay, suggesting that elevated BUN levels are a more substantial predictor of longer hospitalizations. These findings highlight BUN as a significantly more reliable marker than NLR for predicting the length of post-birth hospital stay, with a higher standardized beta coefficient (β = 0.553, P<0.001) compared to NLR (β =0.303, P=0.009), as shown in Table 6. The model explained 42.7% of the variance in hospital stay duration $(R^2=0.427)$.

DISCUSSION

Our most significant finding was that elevated levels of liver enzymes—particularly ALT and AST—demonstrated strong predictive value not only for the development of HELLP syndrome but also for specific complications such as eclampsia, cerebral edema, hepatic ischemia, and extended postpartum hospitalization. HELLP syndrome, a serious pregnancy disorder marked by hemolysis, increased liver enzyme levels, and thrombocytopenia, presents considerable risks to both the mother and the fetus. It is often associated with adverse outcomes such as eclampsia, placental abruption, acute kidney injury, pulmonary edema, and maternal and fetal death [10, 11]. While the exact

pathophysiology of HELLP syndrome remains unclear, systemic inflammation and endothelial dysfunction are believed to play key roles [12]. Predicting the progression of HELLP syndrome and its associated complications is crucial for timely intervention and improved patient management. This study is the first to thoroughly assess the predictive significance of various biochemical markers for specific complications of HELLP syndrome, such as eclampsia, cerebral edema and stroke, hepatic ischemia, and the length of postpartum hospital stay.

Prior research has identified that factors such as genetics, immune function, inflammation, metabolism, and coagulation processes play integral roles in the development of HELLP syndrome [13]. The pathogenesis of this condition involves a complex interplay of factors, where inflammatory processes and immune reactions are critical. In these reactions, cells such as neutrophils, lymphocytes, and platelets are actively involved, secreting inflammatory cytokines that contribute to the syndrome's onset [13]. This study corroborates our findings regarding the association between elevated neutrophil and monocyte counts and HELLP syndrome. Both studies observed significantly higher levels of these cells in HELLP patients at the time of delivery compared to low-risk pregnancies. However, while this study focuses on the predictive value of various inflammatory indices derived from these cell counts in the first trimester, our research highlights the significance of liver enzymes, particularly ALT and AST, not just for predicting HELLP development but also for prognosticating specific complications [14]. Our findings suggest that routine monitoring of ALT and AST throughout pregnancy could offer valuable insights into HELLP progression, potentially beyond the predictive capacity of early pregnancy inflammatory indices. This difference in focus stems from our study's broader exploration of biochemical markers and their association with specific HELLP-related complications, offering a more comprehensive understanding of the syndrome's prediction and prognosis.

Sisti *et al.* [15] also investigated the role of inflammatory markers in HELLP syndrome, focusing on NLR and Platelet-to-lymphocyte ratio (PLR). Like our findings, they observed a significantly higher NLR and lower PLR in women with HELLP compared to healthy controls. However, their study primarily fo-

cused on these ratios as potential diagnostic markers for HELLP syndrome, while our research delved deeper into the predictive capacity of a broader range of biochemical markers, including liver enzymes, for specific HELLP-related complications. By evaluating outcomes like eclampsia, cerebral edema, hepatic ischemia, and postpartum hospital stay duration, our research offers a more extensive understanding of the prognostic value of these markers beyond their diagnostic potential.

Strengths and Limitations

This research offers important perspectives on the predictive significance of different biochemical markers for complications associated with HELLP syndrome. Nevertheless, it is crucial to recognize the study's limitations. Being a retrospective analysis, it is prone to inherent biases linked to data gathering and patient selection. The limited sample size may also restrict the ability to generalize the findings. Furthermore, the study design does not allow for definitive conclusions regarding causality between the observed biomarkers and specific HELLP syndrome complications.

Despite these limitations, our study has several strengths. It is the first to comprehensively evaluate a wide range of biochemical markers in relation to specific HELLP syndrome complications, providing a more nuanced understanding of their prognostic value. The study also highlights the importance of monitoring liver enzymes throughout pregnancy, potentially offering a valuable tool for identifying patients at higher risk for specific complications. These findings warrant further investigation in larger prospective studies to confirm the identified associations and elucidate the underlying mechanisms.

CONCLUSION

This study highlights the significant predictive value of biochemical markers in HELLP syndrome, particularly ALT and AST, renal markers (urea and creatinine), and inflammatory indices (NLR). Routine monitoring of these markers can offer valuable insights into disease progression and guide clinical management, ultimately improving maternal and fetal outcomes. Additional studies with larger sample sizes and prospective designs are necessary to confirm these

results and investigate the underlying mechanisms of HELLP syndrome.

Ethics Approval and Consent to Participate

This study was approved by the Ankara Etlik City Hospital No. 1 Clinical Research Ethics Committee (Decision No: AEŞH-EK1-2023-728; date: 06.12.2023). All procedures were conducted in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki Declaration and its later amendments. Informed consent was waived because of the retrospective nature of the study and the analysis used anonymous clinical data.

Data Availability

All data generated or analyzed during this study are included in this published article. The data that support the findings of this study are available on request from the corresponding author, upon reasonable request.

Authors' Contribution

Study Conception: MAS, AK; Study Design: MP, SE; Supervision: kky; Funding: RTA, AK; Materials: N/A; Data Collection and/or Processing: RTA, AK; Statistical Analysis and/or Data Interpretation: RTA, AK; Literature Review: DSK; Manuscript Preparation: MAS; and Critical Review: MP, SE.

Conflict of Interest

The author(s) disclosed no conflict of interest during the preparation or publication of this manuscript.

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Generative Artificial Intelligence Statement

The author(s) declare that no artificial intelligence-based tools or applications were used during the preparation process of this manuscript. The all content of the study was produced by the author(s) in accordance with scientific research methods and academic ethical principles.

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