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Original Research

Evaluation of Hematological Inflammatory Indices and Aspartate Aminotransferase to Platelet Ratio Index in Relation to Diagnosis and Length of Hospital Stay in Patients with Hyperemesis Gravidarum

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ABSTRACT

Objective: This study aimed to evaluate the diagnostic and prognostic value of systemic inflammatory indices and the Aspartate Aminotransferase-to-Platelet Ratio Index (APRI) score in patients diagnosed with hyperemesis gravidarum (HG) and to investigate their association with the length of hospital stay.

Methods: A total of 210 pregnant women were included, comprising 105 patients with HG and 105 healthy controls, matched based on maternal age, gravida, parity, number of previous abortions, and gestational age. Inflammatory indices including the neutrophil-to-lymphocyte ratio (NLR), monocyte-to-lymphocyte ratio (MLR), systemic immune-inflammation index (SII), systemic inflammation response index (SIRI), pan-immune-inflammation value (PIV), and Aspartate Aminotransferase-to-Platelet Ratio Index (APRI) were compared between groups. Receiver operating characteristic (ROC) analysis, univariable, and multivariable logistic regression were performed to assess diagnostic performance and predictors of prolonged hospitalization (≥2 days).

Results: All inflammatory indices were significantly elevated in the HG group ($p < 0.001$). NLR showed the highest diagnostic performance (area under the curve [AUC] = 0.83). MLR remained statistically significant in the multivariable model ($p = 0.023$), although the effect size was small and the confidence interval wide. Although several indices were associated with HG diagnosis, none independently predicted prolonged hospitalization. Ketonuria was the only variable significantly associated with a hospital stay of ≥2 days (odds ratio [OR] = 1.862, 95% CI: 1.077–3.220, $p = 0.026$). APRI was also significantly elevated in HG patients; this represents its first evaluation in this context.

Conclusion: Systemic inflammatory indices may assist in the diagnostic evaluation of HG but appear to have limited prognostic value for hospital stay duration. Ketonuria remains a more reliable indicator of disease severity. The observed elevation of APRI should be interpreted with caution, as supporting hepatic imaging and biochemical markers were not included, and requires further validation in future prospective studies.

Keywords: aspartate aminotransferases, hyperemesis gravidarum, inflammatory markers, neutrophil-to-lymphocyte ratio

INTRODUCTION

Nausea and vomiting are frequent complaints during early pregnancy, yet the intensity and duration of these symptoms can vary substantially across different stages of gestation [1]. Hyperemesis gravidarum (HG) represents the most severe end of this spectrum and is associated with unfavorable maternal and fetal outcomes [2]. Although a universally accepted diagnostic definition is lacking, HG is widely acknowledged as a debilitating form of pregnancy-related nausea and vomiting, with its prevalence reported to range between 0.3% and 10.8% [3]. In cases where the condition becomes unmanageable, patients may experience dehydration, imbalances in electrolytes, and profound nutritional deficiencies, collectively contributing to notable maternal morbidity. In such scenarios, oral intake is typically not tolerated, prompting the need for inpatient care to provide intravenous hydration, electrolyte stabilization, and symptomatic relief [4].

The underlying pathophysiological mechanisms of HG are yet to be fully clarified. Nevertheless, available evidence points to a multifaceted etiology, including genetic predisposition, hormonal influences, and potential infectious triggers [5]. Inflammatory processes are also suspected to play a role, supported by findings of altered inflammatory biomarkers in affected pregnant individuals. Specifically, reductions in antioxidant defenses and elevations in inflammatory markers indicate that immune and inflammatory pathways may contribute to the pathogenesis of HG [6].

Main Points

- Inflammatory indices including NLR, PLR, SII, SIRI, and APRI were significantly elevated in patients with hyperemesis gravidarum.
- NLR showed the highest diagnostic performance among all indices (AUC = 0.83).
- In multivariable analysis, only MLR remained an independent predictor of hyperemesis gravidarum.
- Ketonuria was the sole factor associated with prolonged hospital stay.
- These findings suggest that ketonuria may serve as a practical indicator of disease burden and need for hospitalization.

Hematological markers such as the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), systemic immune-inflammation index (SII), systemic inflammation response index (SIRI), pan-immune-inflammation value (PIV), and the aspartate aminotransferase-to-platelet ratio index (APRI) are regarded as surrogate indicators of systemic inflammation. These indices have been widely studied across a variety of medical conditions, including obstetric pathologies, where they serve as accessible tools for evaluating inflammatory activity, estimating clinical prognosis, and anticipating adverse pregnancy outcomes [7–11].

This study aimed to investigate whether these inexpensive and easily measurable hematologic indices—specifically NLR, PLR, SII, SIRI, PIV, and APRI—demonstrate significant differences between pregnant women requiring hospitalization for hyperemesis gravidarum and healthy pregnant individuals, and whether these markers are associated with the duration of hospitalization.

MATERIAL AND METHODS

Patient Selection

The HG group consisted of 105 patients who were diagnosed during hospitalization based on clinical symptoms, laboratory findings, and physician evaluation. The control group included 105 healthy pregnant women who presented for routine antenatal follow-up during the same period. These individuals had no symptoms of nausea, vomiting, or dehydration and showed no signs of systemic inflammation or infection. Control group participants were matched 1:1 with the HG group using propensity score nearest-neighbor matching with replacement, based on maternal age, gravida, parity, number of previous abortions, and gestational age. A comprehensive review of the patients' medical records was conducted to gather clinical data, patient characteristics, and follow-up information. The study was conducted in accordance with the ethical standards of the Declaration of Helsinki. This retrospective study was approved by the Gaziantep City Hospital Clinical Research Ethics Committee (Approval No: 176/2025, Date: 16.04.2025), and the requirement for written informed consent was waived due to the retrospective design of the study.

Exclusion criteria for both groups included fever, preeclampsia, multiple pregnancy, fetal anomalies, gestational diabetes, thyroid disorders, autoimmune or rheumatologic diseases, coagulopathies, malignancy, or the use of anti-inflammatory or immunomodulatory medications. All participants had singleton pregnancies and were not receiving any medication at the time of data collection.

All patients in the HG group were hospitalized based on clinical assessment at the time of admission. The diagnosis of hyperemesis gravidarum was established in accordance with an international consensus that proposes four simplified criteria: onset of symptoms before 16 weeks of gestation, severe nausea and/or vomiting, inability to maintain adequate oral intake, and substantial impairment of daily functioning [12]. Patients who fulfilled these criteria and required supportive therapy—including intravenous hydration, nutritional supplementation, or antiemetic treatment—were admitted for inpatient care.

Data Collection and Inflammatory Indices

All demographic and clinical data were obtained retrospectively from patient records and the hospital information management system. Gestational age was determined based on the first day of the last menstrual period and confirmed by ultrasonographic measurements.

The following demographic variables were recorded: age (years), gravida, parity, number of abortions, and gestational age (weeks). Laboratory parameters including hemoglobin (g/dL), white blood cell count (WBC, $10^3/\mu L$), neutrophils (NEU, $10^3/\mu L$), lymphocytes (LYM, $10^3/\mu L$), monocytes (MON, $10^3/\mu L$), platelets (PLT, $10^3/\mu L$), and aspartate aminotransferase (AST, U/L) were extracted from initial blood tests performed at admission. All hematologic measurements were performed using the Beckman Coulter DxH 800 hematology analyzer. Serum AST levels were measured using the Beckman Coulter AU5800 clinical chemistry analyzer (Beckman Coulter, Brea, CA, USA). Systemic inflammatory indices were calculated using complete blood count and biochemical values obtained at the time of hospital admission. The NLR was calculated by dividing the absolute neutrophil count by the lymphocyte count. The MLR was defined as the monocyte count divided by the lymphocyte count. The SII was calculated by multiplying the platelet count by the neutrophil count and dividing the result by the lymphocyte count. The PIV was derived by multiplying the SII by the monocyte count. The SIRI was computed as the product of neutrophil and monocyte counts divided by the lymphocyte count. Lastly, the APRI was calculated using the formula: (AST / 35) × 100 / platelet count.

Statistical Analysis

All statistical analyses were performed using R (version 4.5.0, R Foundation for Statistical Computing, Vienna, Austria). The normality of continuous variables was assessed using the Shapiro–Wilk test and histogram inspection. Continuous variables were summarized as median (25th–75th percentile, IQR), and categorical variables were presented as counts and percentages. Group comparisons were performed using the Mann–Whitney U test, and U statistics with corresponding p-values were reported.

To assess the diagnostic performance of inflammatory indices—including the NLR, MLR, SII, PIV, SIRI, and APRI—receiver operating characteristic (ROC) curve analysis was conducted, and area under the curve (AUC) values were calculated.For each index, the optimal cut-off value was determined using the Youden index. Based on these thresholds, sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated. Additionally, odds ratios (ORs), 95% confidence intervals (CIs), and p-values were calculated using univariate logistic regression to estimate the likelihood of HG above versus below the cut-off. For the analysis of prolonged hospital stay (≥2 days), candidate predictors were first assessed using LASSO (L1-penalized logistic regression). All eight predictors (abortus, lymphocyte count, hematocrit, BUN, ketonuria, urine pH, urine specific gravity, AST) retained non-zero coefficients and were included in the final multivariable logistic regression model. Model calibration was evaluated using the Hosmer–Lemeshow goodness-of-fit test, explanatory power was assessed with Nagelkerke R^2, and collinearity was examined using VIF.

A two-tailed p-value of <0.05 was considered statistically significant.

RESULTS

After 1:1 propensity score matching, the final analytic sample included 105 patients with HG and 105 matched controls. The two groups were comparable with respect to maternal age, gravidity, parity, abortion history, and gestational age, with no statistically significant differences detected between them ($p > 0.05$ for all comparisons) (Table 1).

In the evaluation of hematologic and biochemical parameters, the HG group exhibited notably higher white blood cell and neutrophil counts, accompanied by reduced lymphocyte levels.

Additionally, AST and alanine aminotransferase (ALT) levels were significantly elevated in HG patients relative to controls ($p < 0.05$). Urinary findings revealed significantly increased ketonuria and urine specific gravity in the HG group, while other urinalysis parameters remained similar between groups (Table 1).

All assessed inflammatory markers—NLR, MLR, SII, SIRI, PIV, and APRI—were significantly elevated in patients with HG compared to healthy pregnant controls ($p < 0.001$ for all), as presented in Table 2. Of these markers, NLR demonstrated the highest discriminative capability with an area under the curve (AUC) of 0.83, followed by SII and SIRI (both AUC = 0.79), whereas APRI yielded the lowest discriminative value (AUC = 0.65) (Figure 1).

Univariate logistic regression indicated that each inflammatory index was significantly associated with HG diagnosis. However, when adjusted for confounding variables in multivariate analysis, only MLR remained an independent predictor of HG (adjusted OR = 0.009, 95% CI: 0.000–0.525, p = 0.023), while the predictive value of the other indices diminished (Table 3).

Receiver operating characteristic (ROC) analysis was employed to determine optimal cut-off points for HG prediction. Among all indices, NLR $\geq$ 4.071 demonstrated the most favorable diagnostic performance (sensitivity 72%, specificity 84%, OR = 13.57), followed by SIRI and SII. Despite APRI showing high sensitivity (83%), its low specificity (44%) limited its clinical applicability (Table 4).

Finally, within the HG cohort, multivariate logistic regression identified ketonuria as the sole independent predictor of prolonged hospitalization ($\geq$2 days) (OR = 1.862, 95% CI: 1.077–3.220, p = 0.026). In contrast, none of the hematologic indices or biochemical parameters were significantly associated with the duration of hospital stay (Table 5).

Table 1. Comparison of Demographic, Hematologic, Biochemical, and Urine Parameters Between Patients With Hyperemesis Gravidarum and Healthy Pregnant Controls

Variables	HG (n: 105)	Control (n: 105)	p-value
Age (years)	26.0 (22.0–29.0)	27.0 (24.0–31.0)	0.204
Gravidity	1.0 (1.0–3.0)	1.0 (1.0–2.0)	0.455
Parity	0.0 (0.0–1.0)	0.0 (0.0–1.0)	0.730
Abortus	0.0 (0.0–0.0)	0.0 (0.0–0.0)	0.661
Gestational Age (weeks)	10.71 (8.86–12.43)	11.14 (8.57–12.43)	0.992
White Blood Cell (×10³/μL)	10.3 (8.3–12.5)	8.8 (7.8–10.2)	**<0.001**
Neutrophils (×10³/μL)	7.9 (6.3–10.4)	5.9 (4.9–7.6)	**<0.001**
Lymphocytes (×10³/μL)	1.6 (1.2–1.9)	2.1 (1.8–2.3)	**<0.001**
Monocytes (×10³/μL)	0.5 (0.5–0.7)	0.6 (0.5–0.7)	0.399
Hemoglobin (g/dL)	12.7 (12.1–13.2)	12.5 (11.8–13.5)	0.898
HCT (%)	37.7 (36.0–39.6)	37.5 (35.5–39.6)	0.798
Platelets (×10³/μL)	258.0 (226.0–303.0)	264.0 (215.0–322.0)	0.492
AST (U/L)	22.0 (17.0–25.0)	18.0 (16.0–24.0)	**0.006**
ALT (U/L)	18.0 (14.0–28.0)	14.0 (11.0–20.0)	**0.001**
Ketonuria (semi-quantitative, score 0–4)	2.0 (1.0–3.0)	0.0 (0.0–0.0)	**<0.001**
Urine PH	6.0 (5.5–6.5)	5.5 (5.5–6.5)	0.223
Urine specific gravity	1024 (1017–1030)	1019 (1010–1024)	**<0.001**

Abbreviations: HG: Hyperemesis gravidarum; HCT: Hematocrit; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; pH: Potential of hydrogen (urine pH).

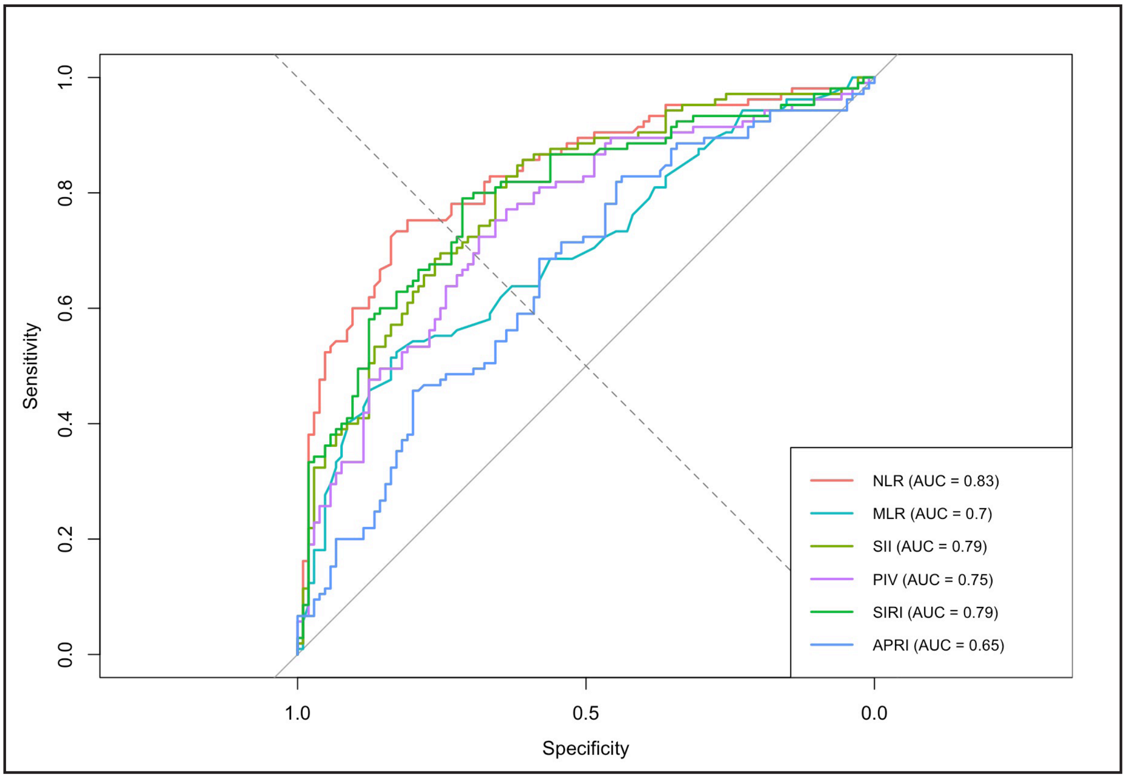

Figure 1. ROC curve analysis of inflammatory indices for predicting HG.

Receiver operating characteristic (ROC) curves for neutrophil-to-lymphocyte ratio (NLR), monocyte-to-lymphocyte ratio (MLR), systemic immune-inflammation index (SII), systemic inflammation response index (SIRI), pan-immune-inflammation value (PIV), and aspartate aminotransferase-to-platelet ratio index (APRI) in the diagnosis of hyperemesis gravidarum (HG). NLR demonstrated the highest diagnostic accuracy with an area under the curve (AUC) of 0.83, followed by SII and SIRI (AUC = 0.79). APRI showed the lowest predictive performance (AUC = 0.65).

Table 2. Comparison of Inflammatory Indices Between Patients With Hyperemesis Gravidarum and Healthy Pregnant Controls

Indices	HG (n=105)	Control (n=105)	U statistic	p-value
NLR	5.20 (3.87–7.15)	2.92 (2.45–3.84)	9008.5	< 0.001
MLR	0.37 (0.26–0.50)	0.28 (0.23–0.34)	7617.5	< 0.001
SII	1327.68 (975.00–1802.25)	715.96 (536.00–1116.17)	8486.0	< 0.001
PIV	742.74 (546.74–1172.37)	427.21 (282.46–681.77)	7911.0	< 0.001
SIRI	2.73 (2.06–4.60)	1.57 (1.22–2.50)	8403.0	< 0.001
APRI	0.23 (0.19–0.29)	0.18 (0.15–0.25)	6992.5	< 0.001

Abbreviations: NLR: Neutrophil-to-Lymphocyte Ratio, MLR: Monocyte-to-Lymphocyte Ratio, SII: Systemic Immune-Inflammation Index, PIV: Pan-Immune-Inflammation Value, SIRI: Systemic Inflammation Response Index, APRI: AST-to-Platelet Ratio Index, HG: Hyperemesis Gravidarum. Data are presented as median (IQR). Mann–Whitney U test was performed for all comparisons.

Table 3. Univariable and Multivariable Logistic Regression Analyses for Predicting Hyperemesis Gravidarum Based on Inflammatory Indices

Predictor	Univariable Analysis			Multivariable Analysis		
	OR	95% CI	p-value	Adjusted OR	95% CI	p-value
NLR	1.705	1.411 – 2.061	**< 0.001**	3.6	0.952 – 13.611	0.059
MLR	86.159	9.908 – 749.231	**< 0.001**	0.009	0.000 – 0.525	**0.023**
SII	1.001	1.001 – 1.002	**< 0.001**	0.997	0.992 – 1.002	0.201
PIV	1.002	1.001 – 1.002	**< 0.001**	1.004	0.996 – 1.011	0.380
SIRI	1.95	1.522 – 2.498	**< 0.001**	0.703	0.087 – 5.691	0.741
APRI	10.47	1.245 – 88.073	**0.030**	1.738	0.109 – 27.622	0.695

Abbreviations: NLR = Neutrophil-to-Lymphocyte Ratio, MLR = Monocyte-to-Lymphocyte Ratio, SII = Systemic Immune-Inflammation Index, PIV = Pan-Immune-Inflammation Value, SIRI = Systemic Inflammation Response Index, APRI = AST-to-Platelet Ratio Index, OR = Odds Ratio, CI = Confidence Interval.

Table 4. Diagnostic Performance and Risk Estimates of Inflammatory Indices for Predicting Hyperemesis Gravidarum

Indices	Cut-off	Sensitivity	Specificity	PPV	NPV	OR	95% CI	p-value
NLR	4.071	0.72	0.84	0.82	0.75	13.57	6.92–26.58	**<0.001**
MLR	0.364	0.52	0.83	0.75	0.64	5.12	2.71–9.66	**<0.001**
SII	914.66	0.83	0.64	0.7	0.79	7.98	4.22–15.08	**<0.001**
PIV	514.8	0.77	0.64	0.68	0.74	5.95	3.25–10.90	**<0.001**
SIRI	2.016	0.79	0.71	0.73	0.77	9.43	5.01–17.76	**<0.001**
APRI	0.182	0.83	0.44	0.6	0.72	3.53	1.88–6.62	**<0.001**

Abbreviations: NLR = neutrophil-to-lymphocyte ratio; MLR = monocyte-to-lymphocyte ratio; SII = systemic immune-inflammation index; PIV = pan-immune-inflammation value; SIRI = systemic inflammation response index; APRI = AST-to-platelet ratio index; PPV = positive predictive value; NPV = negative predictive value; OR = odds ratio; CI = confidence interval.

Table 5. Multivariable Logistic Regression Analysis for Predicting Prolonged Hospital Stay (≥2 Days) Among Patients With Hyperemesis Gravidarum

Predictor	OR	95% CI	p-value
Abortus	0.693	0.319 – 1.509	0.356
Lymphocyte count (×10³/µL)	0.771	0.339 – 1.754	0.535
Hematocrit (%)	1.086	0.917 – 1.285	0.339
Blood urea nitrogen (mg/dL)	1.058	0.906 – 1.234	0.476
Ketonuria (semi-quantitative)	1.862	1.077 – 3.220	**0.026**
Urine pH	1.608	0.727 – 3.558	0.241
Urine specific gravity	1.05	0.991 – 1.113	0.095
APRI	103.383	0.349 – 30667.707	0.110

Abbreviations: OR = Odds Ratio, CI = Confidence Interval, BUN = Blood Urea Nitrogen, HCT = Hematocrit, HG = Hyperemesis Gravidarum. APRI = AST-to-platelet ratio index. Model diagnostics: Hosmer–Lemeshow goodness-of-fit test indicated excellent calibration (χ^2=2.87, p=0.94). The model explained 22% of the variance in prolonged hospital stay (Nagelkerke R^2=0.22). No significant multicollinearity was observed among predictors (all VIF values <1.3). Candidate variables were selected using LASSO (L1-penalized logistic regression), which retained all eight predictors for inclusion in the final model.

DISCUSSION

This study investigated the clinical relevance of several hematological inflammatory markers—namely NLR, MLR, SII, SIRI, PIV, and APRI—in pregnant individuals diagnosed with HG, with a particular focus on their potential association with hospitalization duration. All indices examined were significantly elevated in the HG group compared to healthy controls. In multivariable logistic regression, only MLR remained independently associated with HG, although with a small effect size. Furthermore, ketonuria was the sole variable significantly correlated with prolonged hospital stay. These findings suggest that systemic inflammation may play a role in the pathogenesis of HG and that selected blood-based indices could provide supportive, albeit limited, information in the clinical assessment of these patients.

In a prior investigation by Yıldırım et al. [13], systemic inflammatory markers such as NLR, PLR, SII, SIRI, and AISI were reported to be significantly elevated in patients diagnosed with HG, with positive correlations noted between these indices and the severity of the condition. Among the evaluated markers, SIRI demonstrated the strongest predictive utility for both the diagnosis and severity of HG, with cut-off values of 3.14 (AUC = 0.695, sensitivity 54%, specificity 75%) for diagnosis and 2.74 (AUC = 0.785, sensitivity 82%, specificity 68%) for severity assessment. Consistent with those findings, the current study also identified SIRI as a useful discriminative marker for HG, yielding a cut-off point of 2.016 (AUC = 0.79, sensitivity 79%, specificity 71%). Nonetheless, in multivariable logistic regression, SIRI failed to maintain independent statistical significance, whereas MLR emerged as the only index independently associated with HG.

In a case-control study comparing 54 patients with HG and 58 healthy pregnant women, significantly higher NLR levels were reported in the HG group (median: 3.2, range: 1.6–7.1) compared to controls (median: 2.1, range: 1.0–4.7), along with a strong positive correlation between NLR and C-reactive protein (CRP) ($r = 0.872$, $p < 0.001$), supporting the utility of NLR as a marker of subclinical inflammation in HG [14].Similarly, another study evaluating the role of NLR, PLR, and plateletcrit in the diagnosis and severity of HG identified a cut-off value of 3.9 for NLR (AUC = 0.64), indicating limited discriminatory capacity [15]. A prospective analysis conducted in the emergency setting found elevated NLR and PLR levels among HG patients, although CRP was the only marker associated with severity [16]. Consistent with prior studies, NLR levels were also significantly higher in the HG group in our cohort (median: 5.20 vs. 2.92, $p < 0.001$), and the marker showed good diagnostic performance with a cut-off of 4.071 (AUC = 0.83, sensitivity 72%, specificity 84%, OR = 13.57, 95% CI: 6.92–26.58, $p < 0.001$). However, NLR did not retain independent significance in the multivariable logistic regression model. These findings suggest that while NLR may serve as a valuable indicator in the initial evaluation of HG, its predictive utility may diminish when adjusted for other clinical and laboratory parameters.

Soysal et al. [17] examined the relationship between inflammatory markers and ketonuria severity in patients with HG, reporting significantly higher NLR, MLR, and PLR levels in the HG group compared to healthy controls (all $p < 0.001$). These markers were found to increase in parallel with ketonuria severity, and strong positive correlations were observed between ketonuria and NLR (rho = 0.80, $p < 0.001$), MLR (rho = 0.67, $p < 0.001$), and PLR (rho = 0.67, $p < 0.001$), highlighting a potential link between systemic inflammation and metabolic stress. In our study, both NLR and MLR were significantly elevated among HG patients. NLR demonstrated the strongest diagnostic performance (AUC = 0.83), but it did not remain an independent predictor in the multivariable analysis, which contrasts with several prior reports. Adıgüzel et al. [18] also reported significantly higher NLR and MLR levels in HG patients compared with controls (median NLR: 4.37 vs. 3.52, AUC = 0.648; median MLR: 0.34 vs. 0.32, AUC = 0.585), both showing only modest discriminative ability. In our study, MLR showed a somewhat higher discriminative performance (AUC = 0.70), but although it remained statistically significant in the multivariable model, the effect size was small and the confidence interval wide, limiting its clinical applicability. These differences may reflect variations in study design, sample size, or patient characteristics. Taken together, these results suggest that while NLR and MLR may reflect the inflammatory burden of HG, their role as reliable standalone diagnostic or prognostic markers remains limited and requires validation in larger, multicenter studies.

Çintesun et al. [19] investigated the diagnostic performance of subclinical inflammatory markers in HG and their association with ketonuria grade. Significantly increased NLR and PLR levels were observed in the HG group (both $p < 0.05$), but only red cell distribution width (RDW) showed a significant correlation with ketonuria severity ($p < 0.05$). No meaningful relationship was identified between NLR and ketonuria grade.

In the current study, NLR was again significantly elevated in the HG group; however, ketonuria was the sole marker that independently predicted a longer duration of hospitalization (≥2 days) in multivariable analysis. This observation suggests that ketonuria may have utility not only as a diagnostic marker, but also as a practical indicator of disease burden and the anticipated need for inpatient management.

Aslan et al. [20] investigated the relationship between hematological markers and both the diagnosis of HG and the severity of ketonuria. Their findings indicated significantly elevated NLR and PLR values in patients with HG compared to healthy individuals. Moreover, these indices, along with neutrophil counts, showed a stepwise increase in parallel with higher ketonuria levels. In multivariable analysis, NLR, PLR, and mean corpuscular hemoglobin (MCH) were identified as independent predictors of both HG and the extent of ketonuria positivity. Consistent with these findings, our study also demonstrated significantly elevated NLR levels in the HG group. However, NLR did not retain statistical significance in the multivariable logistic regression model, whereas ketonuria emerged as the only independent predictor of extended hospitalization. These results imply that although inflammatory markers like NLR may provide insights into the underlying pathophysiology of HG, ketonuria may serve as a more clinically relevant indicator for anticipating disease burden and hospitalization needs.

Doğru et al. [21] examined the predictive value of SII and other hematological parameters in HG, particularly in relation to hospital stay duration and the risk of readmission. Their analysis revealed a significant association between SII and hospitalization lasting longer than two days ($p = 0.001$), although SII did not significantly predict the likelihood of rehospitalization. Additionally, a positive correlation between ketonuria and hospital stay length was noted. In our cohort, SII was likewise elevated in patients with HG and demonstrated acceptable diagnostic utility; however, it did not remain independently associated with prolonged hospitalization in multivariable analysis.

In our study, APRI levels were significantly higher in patients with HG compared to healthy controls. This finding suggests a possible link between systemic inflammation in HG and subclinical hepatic involvement. Supporting this, Worede et al. [22] recently demonstrated that nearly half of women with HG exhibited elevated AST and ALT levels, indicating that hepatic dysfunction may frequently accompany the condition. Similarly, Tolunay et al. [23] showed that first-trimester APRI scores were significantly higher in women who subsequently developed intrahepatic cholestasis of pregnancy, further highlighting the potential relevance of APRI as a marker of hepatic stress during pregnancy. Nevertheless, as our study did not include liver imaging or comprehensive hepatic function testing, the interpretation of APRI elevation in HG should be made with caution. Prospective studies integrating biochemical panels and imaging are warranted to clarify whether APRI can serve as a reliable adjunctive marker in the clinical evaluation of HG.

Limitations

This study has several limitations that should be acknowledged. One of the study's limitations is that external validation has not been performed, and the generalizability of the results to different populations is limited due to the single-center, retrospective study design. Future multicenter prospective studies are warranted to confirm and expand upon these findings. Although strict exclusion criteria were applied to ensure that patients with any signs or suspicion of infectious diseases were excluded, the lack of systematic infectious disease screening could be considered another limitation. Moreover, due to the retrospective nature of the study, important potential confounders such as baseline nutritional status, BMI, smoking habits, and subclinical infections could not be fully controlled, and these factors may independently affect hematological and inflammatory indices. Furthermore, while multiple inflammatory indices were evaluated, no serial measurements were obtained to monitor their changes during hospitalization. The study also did not assess how these markers vary across different gestational stages, which could have provided insights into temporal inflammatory patterns. Lastly, liver function was not directly assessed through imaging or elastographic methods, limiting the interpretation of elevated APRI levels in relation to hepatic status. Future studies incorporating hepatic imaging and additional biochemical markers are warranted to validate these observations.

CONCLUSION

Systemic inflammatory indices were significantly elevated in patients with HG and may serve as supportive tools in the diagnostic evaluation. However, none of these indices demonstrated independent predictive value for the length of hospital stay. Ketonuria was the only parameter found to be significantly associated with prolonged hospitalization. Although APRI levels were higher in the HG group, this finding should be interpreted with caution because direct liver imaging and more comprehensive liver function tests were not performed. Future prospective studies including hepatic imaging and additional biochemical markers are warranted to validate these observations. These results indicate that, although inflammatory markers may contribute to the diagnostic assessment of HG, ketonuria appears to be a more reliable indicator for estimating disease severity and guiding inpatient management decisions.

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Informed Consent: A comprehensive review of the patients' medical records was conducted to gather clinical data, patient characteristics, and follow-up information. Due to the retrospective design of the study, the requirement for informed consent was waived by the ethics committee.

Data Availability Statement: All data generated or analyzed during this study are included in this published article. No additional datasets were generated. Further information is available from the corresponding author upon reasonable request.

Conflict of Interest: The authors declare no conflict of interest.

Funding: No external funding was received for this study.

Ethical Approval: This study was approved by the Ethics Committee of Gaziantep City Hospital (Approval No: 176/2025, Date: 2025-04-16).

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