Clinical and Experimental Obstetrics & Gynecology

Clin. Exp. Obstet. Gynecol. **2026**; 53(7): 52190
https://doi.org/10.31083/CEOG52190

Original Research

Association Between the Naples Prognostic Score and Ketonuria Severity in Patients With Hyperemesis Gravidarum

Mehmet Faruk Olcenoglu[1,*], Merve Olcenoglu[1], Gamze Savci[1]

[1]Department of Gynecology and Obstetrics, Karamanoglu Mehmetbey University Faculty of Medicine, 70200 Karaman, Turkiye
*Correspondence: farukolcenoglu@hotmail.com (Mehmet Faruk Olcenoglu)

Academic Editor: Michael H. Dahan
Submitted: 23 March 2026 Revised: 7 May 2026 Accepted: 15 May 2026 Published: 17 July 2026

Abstract

Background: Hyperemesis gravidarum (HG) is a clinical condition characterized by systemic inflammation and maternal malnutrition. However, the role of a composite index integrating both inflammatory and nutritional parameters for identifying the degree of metabolic stress, as reflected by ketonuria severity, has not been investigated. This study aimed to evaluate the association between the Naples Prognostic Score (NPS), a composite index on inflammatory and nutritional biomarkers, and ketonuria severity in patients with HG. **Methods:** This retrospective cross-sectional study included 241 pregnant women hospitalized with a diagnosis of HG between October 2022 and October 2025. Patients were stratified into mild-to-moderate (n = 134) and severe (n = 107) ketonuria groups based on urine ketone levels. The NPS was calculated using the neutrophil-to-lymphocyte ratio (NLR), lymphocyte-to-monocyte ratio (LMR), serum albumin, and total cholesterol levels. Group comparisons, correlation analyses, receiver operating characteristic (ROC) curve analysis, and multivariable logistic regression analyses were performed. **Results:** Age, body mass index (BMI), and obstetric history were comparable between groups. Neutrophil count, NLR, and NPS were significantly higher in the severe ketonuria group. In contrast, lymphocyte count, LMR, serum albumin, and total cholesterol were significantly lower, reflecting a greater inflammatory and nutritional burden in patients in the severe ketonuria group. Among all variables tested, NPS demonstrated the strongest correlation with ketonuria severity ($r = 0.845$; $p < 0.001$). ROC curve analysis revealed that NPS had excellent discriminatory performance in identifying severe ketonuria (area under the ROC curve [AUC] = 0.939; sensitivity 90.65%, and specificity 93.28% at a cutoff value ≥3). In the multivariable logistic regression analysis, an NPS ≥3 (odds ratio [OR] = 110.261; 95% confidence interval [CI]: 42.724–284.560; $p < 0.001$) and total cholesterol level (OR = 0.981; $p = 0.037$) were independently associated with severe ketonuria. The wide CI reflects model instability and shared variance between the NPS and its components; therefore, the point estimate should not be interpreted as a stable measure of effect size. **Conclusions:** At admission, NPS demonstrated a strong cross-sectional association with the severity of ketonuria and excellent discriminatory performance for identifying severe ketonuria. However, because both measures were obtained simultaneously, these findings should be interpreted as reflecting a concurrent association rather than true prospective prediction.

Keywords: hyperemesis gravidarum; ketonuria; neutrophil-to-lymphocyte ratio; albumin; prognosis

1. Introduction

Hyperemesis gravidarum (HG) refers to the severe form of nausea and vomiting during pregnancy. It is characterized by intractable nausea and vomiting leading to dehydration, electrolyte disturbances, and weight loss exceeding 5% of pre-pregnancy body weight. Ketonuria is a frequent biochemical finding but is best understood as a marker of starvation-induced ketogenesis rather than a defining diagnostic feature [1,2]. HG affects approximately 0.3% to 3.6% of pregnancies. It is the most common cause of hospitalization in the first trimester and among the leading indications for antenatal hospitalization overall [3,4]. Diagnosis is typically made by exclusion. Gastrointestinal, endocrine, and infectious conditions that may present with a similar clinical picture should be systematically evaluated and excluded [2,4]. The need for intravenous hydration and close biochemical monitoring due to impaired oral intake imposes a significant healthcare burden and cost [4,5]. Maternal malnutrition and vitamin deficiencies can predispose to serious complications. HG may also be associated with adverse perinatal outcomes, including low birth weight and preterm birth [6]. Therefore, HG should not be addressed solely at the symptomatic level but should instead be considered a biological process whose underlying mechanisms require clarification [4,7].

The pathophysiology of HG cannot be explained solely by hormonal signals. Increased oxidative stress and accompanying subclinical inflammation may contribute to the clinical phenotype through depletion of antioxidant reserves and disruption of redox homeostasis. This response may sustain disease persistence and inform potential therapeutic targets [8,9]. Hemogram-derived parameters may help quantify this burden. Meta-analyses and case-control studies have reported that neutrophil-to-lymphocyte ratio (NLR) is higher in affected patients than in healthy pregnant women, and in some series; however, lymphocyte-to-monocyte ratio (LMR) is lower. This pattern has been interpreted as consistent with increased neutrophil activa-

Copyright: © 2026 The Author(s). Published by IMR Press.
This is an open access article under the CC BY 4.0 license.

Publisher's Note: IMR Press stays neutral with regard to jurisdictional claims in published maps and institutional affiliations.

tion and relative lymphocyte depletion, but its relationship with disease severity is inconsistent across studies [10,11]. Prolonged fasting and recurrent vomiting lead to depletion of maternal stores. In hospitalized cases, malnutrition, low prealbumin levels, and deterioration in albumin-based inflammatory nutritional indices have been reported [12,13,14]. Reductions in total cholesterol and lipoprotein fractions suggest suppression of lipid metabolism. These findings support that HG may be better understood as an immunonutritional disorder, with implications for patient monitoring and risk classification [14,15].

In clinical practice, HG severity is primarily monitored using scales such as the Pregnancy-Unique Quantification of Emesis and Nausea (PUQE). However, these tools rely on patient-reported subjective symptom assessment and do not directly reflect biochemical or immunological burden [16]. Ketonuria is a routinely available admission biomarker; however, it primarily reflects starvation-induced ketogenesis rather than dehydration, and contemporary evidence indicates no consistent relationship between admission ketonuria and validated symptom severity, weight loss, or readmission risk [17]. As such, ketonuria should be considered a marker of acute metabolic stress at presentation rather than a surrogate for overall HG severity. Reliance on a single parameter, such as NLR alone or albumin alone, oversimplifies the interaction between inflammation and malnutrition. No single marker therefore adequately captures the full clinical burden of HG [18]. The Naples Prognostic Score (NPS), developed by Galizia and colleagues [19] for colorectal cancer, was designed to address this need. It integrates NLR, LMR, serum albumin, and total cholesterol [19]. The simultaneous capture of inflammatory and nutritional domains by NPS has been associated with survival outcomes across multiple malignancy cohorts and with the prediction of adverse outcomes in coronary artery disease [20,21].

In HG, inflammation and malnutrition often coexist in most patients. Low serum albumin and total cholesterol levels, along with biomarkers associated with oxidative stress, are considered findings supportive of this dual burden [22]. However, the applicability of the NPS in HG, which combines immune activation via NLR and LMR with nutritional status via serum albumin and total cholesterol within the same framework, has not yet been established [19]. This study aimed to investigate the association between NPS and ketonuria severity, as well as to evaluate its discriminatory performance in predicting severe HG, with the goal of providing a practical and objective triage tool for clinical use.

2. Materials and Methods

2.1 Study Design

This retrospective cross-sectional study was conducted at the Department of Obstetrics and Gynecology, Karamanoğlu Mehmetbey University Education and Research Hospital. The study covered a three-year period from October 2022 to October 2025. The study protocol was designed in accordance with the principles of the Declaration of Helsinki.

2.2 Study Population

HG was defined, in accordance with current American College of Obstetricians and Gynecologists (ACOG) guidance [6], as persistent nausea and vomiting beginning in the first trimester (≤14 weeks of gestation) accompanied by at least two of the following: documented loss of ≥5% of pre-pregnancy body weight, dehydration requiring intravenous fluid replacement, ketonuria of ≥+1 on urine dipstick, and electrolyte disturbances, in the absence of an alternative cause. Pregnant women hospitalized with a diagnosis of HG due to persistent nausea and vomiting, impaired oral intake, and dehydration symptoms between the 7th and 14th weeks of pregnancy within the specified date range were included in the study. Inclusion criteria were defined as follows: positive urinary ketones (+1 or higher) on urinalysis, availability of complete blood count and biochemistry (serum albumin, total cholesterol) results obtained prior to treatment at the time of admission, and spontaneous singleton pregnancy. Cases with other gastrointestinal or systemic conditions that could cause ketonuria or nausea and vomiting (including diabetic ketoacidosis, gastroenteritis, appendicitis, pancreatitis, and urinary tract infection), multiple and molar pregnancies, known chronic systemic diseases (including chronic hypertension, diabetes mellitus, and renal or hepatic insufficiency), a history of autoimmune disease or malignancy, and evidence of active infection findings were excluded from the study. During the study period, 254 pregnant women were admitted to our institution for first-trimester nausea and vomiting; 241 of these met all inclusion criteria for HG and formed the analytic cohort. Aggregate institutional denominators for total pregnancies registered during the study period could not be reliably retrieved from the legacy electronic record system, which is acknowledged as a limitation.

2.3 Data Collection and Grouping

Patient data were retrospectively retrieved from the hospital electronic information management system. Demographic variables (age, gravida, parity, history of abortion, body mass index [BMI]), obstetric history, and laboratory parameters at admission (neutrophil, lymphocyte, and monocyte counts; serum albumin; and total cholesterol levels) were recorded. All data were anonymized prior to analysis. Patients with incomplete admission laboratory data (complete blood count, serum albumin, or total cholesterol) or missing urine ketone results were excluded at the inclusion stage. The final analytic dataset (n = 241) contained complete data for all study variables, and no imputation was required.

Patients were stratified into two groups based on urine ketone levels at presentation: mild-to-moderate ketonuria

(+ or ++) and severe ketonuria (+++ or ++++). At our institution, these levels are interpreted as indicating a higher metabolic burden and typically require more aggressive fluid and nutritional support. Earlier HG studies have used similar cutoffs when ketonuria has been treated as a severity marker. Urine dipstick testing is not precise. However, it reflects routine clinical practice and the information available at the time of admission.

Although composite severity measures such as the PUQE score, percentage of weight loss, electrolyte disturbances, length of hospital stay, and need for parenteral nutrition would offer a more multidimensional construct of severity, these variables were not consistently and systematically documented in the electronic medical records during the study period. Urine ketonuria was therefore selected as the most uniformly available, time-anchored, semi-quantitative biochemical indicator at admission, recognizing that it reflects acute metabolic stress rather than overall HG severity.

2.4 Calculation of the NPS

The NPS was calculated according to the original method defined by Galizia et al. [19]. The score comprises four components: NLR, LMR, serum albumin, and total cholesterol levels. One point was assigned for each parameter exceeding its specified threshold value: NLR >2.96, LMR <4.44, albumin <4.0 g/dL, and total cholesterol <180 mg/dL. The total score ranges from 0 to 4.

2.5 Statistical Analyses

A formal *a priori* sample size calculation was not performed due to the retrospective nature of the study; all eligible cases within the predefined three-year period were included to maximize statistical efficiency. With 107 severe ketonuria events and 2 predictors retained in the primary multivariable model (NPS ≥3 and total cholesterol; events-per-variable ratio = 53.5), and 6 predictors in the secondary clinically adjusted model (events-per-variable ratio = 17.8), both models exceeded the conventional minimum threshold of 10 events per variable required to limit overfitting.

Statistical analyses were conducted using IBM SPSS Statistics for Windows, Version 27 (IBM Corp., Armonk, NY, USA). Two-tailed *p*-values of less than 0.05 ($p < 0.05$) were considered statistically significant. The normal distribution assumption was assessed using histograms and quantile-quantile (Q-Q) plots. Descriptive statistics were presented using mean ± standard deviation (SD) for normally distributed continuous variables, median (minimum – maximum) for non-normally distributed continuous variables, and frequency (percentage) for categorical variables. Continuous variables were analyzed using Student's *t*-test or Mann-Whitney U test depending on the normality of distribution. Categorical variables were analyzed using the chi-square test, Fisher's exact test, or the Fisher-Freeman-Halton test, as appropriate. Spearman correlation coefficients were calculated to evaluate associations between ketonuria level and other continuous variables. Performance of the NPS in predicting severe ketonuria was evaluated using receiver operating characteristic (ROC) curve analysis. The optimal cutoff point was determined using Youden's index. Multivariable logistic regression analysis (forward conditional selection method) was performed to determine significant factors independently associated with severe ketonuria. Statistically significant variables identified in the univariable analysis results were included in the multivariable logistic regression model. In addition, a separate multivariable logistic regression analysis was performed to assess the associations between total cholesterol, NPS, and severe ketonuria after adjustment for clinically relevant covariates by including all variables simultaneously. Variance inflation factors (VIFs) were calculated to assess potential multicollinearity in both regression models.

Variables included in the multivariable model were not selected solely on the basis of univariable significance. Covariates were prespecified based on *a priori* clinical relevance to the inflammatory–nutritional axis of HG (gestational week, neutrophil count, lymphocyte count, NLR, LMR, serum albumin, total cholesterol, and NPS ≥3). Forward conditional entry was used as the variable retention method within this prespecified covariate pool, balancing the limited number of events with the need to control for confounding. Given the exploratory and hypothesis-generating nature of this study, no formal correction for multiple comparisons was applied. Reported *p*-values for univariable group comparisons and correlations should therefore be interpreted as exploratory rather than confirmatory, and the strongest signals (NPS, serum albumin, total cholesterol) should be considered candidate associations requiring prospective validation.

3. Results

A total of 241 pregnant women with ketonuria were included in the study; mild-to-moderate ketonuria was detected in 134 (55.6%), and severe ketonuria was detected in 107 (44.4%). There were no significant differences between the two groups in basic demographic characteristics, obstetric history, or baseline clinical characteristics (Table 1).

Inflammatory and nutritional parameters showed marked differences between the groups. Neutrophil count and NLR values were higher in the severe ketonuria group, whereas lymphocyte count, LMR, serum albumin, and total cholesterol levels were significantly lower compared with the mild-to-moderate group. Furthermore, NPS was significantly higher in the severe ketonuria group ($p < 0.001$) (Table 1).

In the correlation analysis, NPS showed the strongest correlation with ketonuria level among all variables examined ($p < 0.001$). NLR, neutrophil count, and gestational week showed a positive correlation, whereas total choles-

Table 1. Summary of variables according to ketonuria severity.

Variables	Total (n = 241)	Mild-to-moderate (n = 134)	Severe (n = 107)	*p*-value
Age, years	28.05 ± 4.40	28.50 ± 4.22	27.50 ± 4.58	0.078†
BMI, kg/m^2	25.73 ± 2.94	26.01 ± 2.97	25.37 ± 2.88	0.093†
Gestational week	9.86 ± 2.07	9.63 ± 2.00	10.15 ± 2.13	0.054†
Comorbidity	0 (0.00%)	0 (0.00%)	0 (0.00%)	N/A
Gravidity	2 (1–6)	2 (1–6)	2 (1–5)	0.261‡
Parity	0 (0–3)	0.5 (0–3)	0 (0–3)	0.220‡
Abortion	0 (0–3)	0 (0–3)	0 (0–2)	0.669‡
Living children	0 (0–3)	0.5 (0–3)	0 (0–3)	0.180‡
History of intrauterine fetal demise	1 (0.41%)	1 (0.75%)	0 (0.00%)	1.000#
History of ectopic pregnancy	1 (0.41%)	1 (0.75%)	0 (0.00%)	1.000#
Cesarean history	47 (19.50%)	25 (18.66%)	22 (20.56%)	0.836§
Neutrophil, ×10^3	7.14 ± 2.37	6.73 ± 2.24	7.65 ± 2.43	**0.002**†
Lymphocyte, ×10^3	1.71 ± 0.66	1.85 ± 0.65	1.54 ± 0.64	**<0.001**†
Monocyte, ×10^3	0.43 ± 0.18	0.41 ± 0.15	0.46 ± 0.21	0.089†
NLR	3.88 (1.06–78.00)	3.59 (1.06–55.00)	4.68 (1.47–78.00)	**<0.001**‡
LMR	4.38 ± 1.99	4.91 ± 2.14	3.71 ± 1.54	**<0.001**†
Albumin (g/dL)	4.04 ± 0.35	4.15 ± 0.31	3.92 ± 0.35	**<0.001**†
Total cholesterol	178.39 ± 26.78	187.60 ± 27.45	166.86 ± 20.90	**<0.001**†
NPS	2 (0–4)	2 (0–4)	3 (1–4)	**<0.001**‡
0	6 (2.49%)	6 (4.48%)	0 (0.00%)	
1	47 (19.50%)	46 (34.33%)	1 (0.93%)	
2	82 (34.02%)	73 (54.48%)	9 (8.41%)	**<0.001**¶
3	77 (31.95%)	8 (5.97%)	69 (64.49%)	
4	29 (12.03%)	1 (0.75%)	28 (26.17%)	

Descriptive statistics are presented using mean ± standard deviation (SD) for normally distributed continuous variables, median (minimum – maximum) for non-normally distributed continuous variables, and frequency (percentage) for categorical variables.

† Student's *t*-test, ‡ Mann-Whitney U test, § Chi-square test, # Fisher's exact test, ¶ Fisher-Freeman-Halton test. N/A, not applicable. Statistically significant *p*-values are shown in bold.

BMI, body mass index; NLR, neutrophil-to-lymphocyte ratio; LMR, lymphocyte-to-monocyte ratio; NPS, Naples Prognostic Score.

terol, LMR, serum albumin, and lymphocyte count showed a negative correlation ($p < 0.001$). No significant correlation was observed between ketonuria level and demographic or obstetric variables (Table 2).

ROC curve analysis demonstrated that NPS exhibits excellent discriminatory power in predicting severe ketonuria and achieves high sensitivity, specificity, and overall accuracy at an optimal cutoff value ≥3 (Fig. 1, Table 3).

According to multivariable logistic regression analysis, low total cholesterol (odds ratio [OR]: 0.981, 95% confidence interval [CI]: 0.964–0.999, $p = 0.037$, VIF = 1.526) and high (≥3) NPS (OR: 110.261, 95% CI: 42.724–284.560, $p < 0.001$, VIF = 2.800) were independently associated with severe ketonuria. Other variables included in the analysis, such as gestational week ($p = 0.503$, VIF = 1.138), neutrophil count ($p = 0.896$, VIF = 1.514), lymphocyte count ($p = 0.327$, VIF = 2.105), NLR ($p = 0.607$, VIF = 1.703), LMR ($p = 0.830$, VIF = 2.056), and serum albumin ($p = 0.756$, VIF = 1.498) were nonsignificant. The highest VIF was 2.800 (for NPS), indicating no evidence of multicollinearity in the model (Table 4).

In addition, an additional multivariable logistic regression model was constructed to evaluate the associations between total cholesterol, NPS, and severe ketonuria after adjustment for clinically relevant covariates. High (≥3) NPS (OR: 125.160, 95% CI: 44.716–350.325, $p < 0.001$, VIF = 1.283) remained independently associated with severe ketonuria, whereas total cholesterol (OR: 0.982, 95% CI: 0.964–1.000, $p = 0.052$, VIF = 1.218) was not statistically significant after adjustment for age ($p = 0.320$, VIF = 1.208), BMI ($p = 0.900$, VIF = 1.025), gestational week ($p = 0.533$, VIF = 1.073) and gravidity ($p = 0.661$, VIF = 1.246). The highest VIF was 1.283 (for NPS), indicating no evidence of multicollinearity in the model (Table 5).

4. Discussion

In this study, 241 pregnant women hospitalized with HG were classified as having mild-to-moderate ketonuria (n = 134) or severe ketonuria (n = 107) based on urine ketone

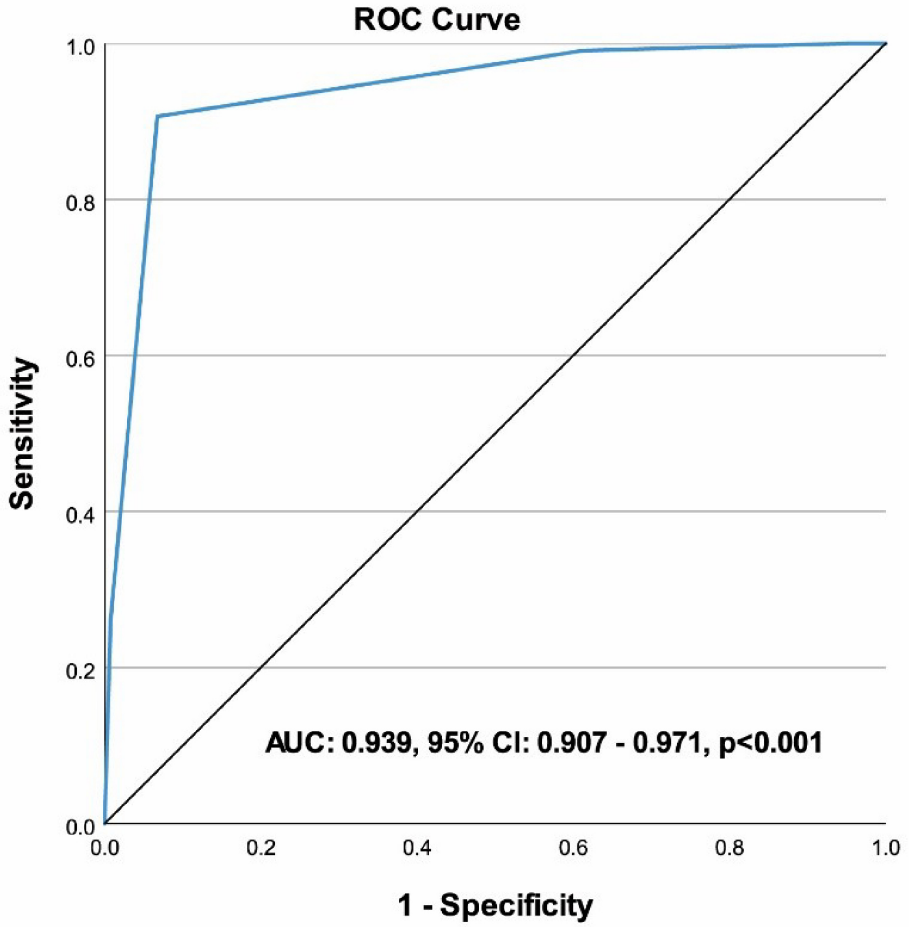

Fig. 1. ROC curve of the NPS for predicting severe ketonuria. ROC, receiver operating characteristic; AUC, area under the ROC curve; CI, confidence interval.

Table 2. Correlations between variables and ketonuria levels.

Variables	r	*p*-value
Age	–0.077	0.235
BMI, kg/m^2	–0.092	0.154
Gestational week	0.163	**0.011**
Gravidity	–0.067	0.297
Parity	–0.059	0.363
Abortion	–0.052	0.420
Living children	–0.071	0.276
Neutrophil, ×10^3	0.233	**<0.001**
Lymphocyte, ×10^3	–0.290	**<0.001**
Monocyte, ×10^3	0.095	0.140
NLR	0.385	**<0.001**
LMR	–0.390	**<0.001**
Albumin	–0.375	**<0.001**
Total cholesterol	–0.396	**<0.001**
NPS	0.845	**<0.001**

r: Spearman correlation coefficient. Statistically significant *p*-values are shown in bold.

Table 3. Performance of NPS in predicting severe ketonuria: ROC curve analysis.

Cutoff	≥3
Sensitivity	90.65%
Specificity	93.28%
Accuracy	92.12%
PPV	91.51%
NPV	92.59%
AUC (95% CI)	0.939 (0.907–0.971)
p-value	<0.001

PPV, positive predictive value; NPV, negative predictive value.

levels. No significant differences were observed between the groups in age, BMI, and basic obstetric characteristics. Inflammatory activity was more pronounced in the severe ketonuria group, with higher neutrophil counts, NLR, and NPS. Nutritional impairment was also more pronounced in this group, with lower lymphocyte counts, LMR, serum albumin, and total cholesterol levels. In the correlation analysis, the strongest association between ketonuria level and the variables examined was observed for NPS (r = 0.845; $p < 0.001$). In ROC analysis, NPS demonstrated excellent discriminatory performance (area under ROC curve [AUC]

Table 4. Significant factors independently associated with severe ketonuria: multivariable logistic regression analysis.

	β-coefficient	Standard error	*p*-value	Exp(β)	95% CI for Exp(β)	
Total cholesterol	–0.019	0.009	**0.037**	0.981	0.964	0.999
NPS, ≥3	4.703	0.484	**<0.001**	110.261	42.724	284.560
Constant	0.932	1.634	0.568	2.541		

Nagelkerke $R^2 = 0.761$. Statistically significant *p*-values are shown in bold.

Table 5. Associations between total cholesterol, NPS, and severe ketonuria after adjustment for clinically relevant covariates: multivariable logistic regression analysis.

Variables	β-coefficient	Standard error	*p*-value	Exp(β)	95% CI for Exp(β)	
Age	–0.062	0.062	0.320	0.940	0.833	1.062
BMI, kg/m^2	–0.010	0.083	0.900	0.990	0.841	1.164
Gestational week	–0.077	0.124	0.533	0.926	0.727	1.180
Gravidity	0.115	0.262	0.661	1.122	0.672	1.873
Total cholesterol	–0.018	0.009	0.052	0.982	0.964	1.000
NPS, ≥3	4.830	0.525	**<0.001**	125.160	44.716	350.325
Constant	3.229	3.096	0.297	25.253		

Nagelkerke $R^2 = 0.764$. Statistically significant *p*-values are shown in bold.

= 0.939; 95% CI: 0.907–0.971), and at a cutoff value of 3, sensitivity was 90.65% and specificity was 93.28%. The median NPS was 3 (1–4) in the severe ketonuria group and 2 (0–4) in the mild-to-moderate ketonuria group. Overall accuracy was 92.12%, and the positive predictive value (PPV) was 91.51%. In multivariable logistic regression analysis, an NPS ≥3 emerged as the strongest independent predictor of severe ketonuria (OR = 110.261; 95% CI: 42.724–284.560; $p < 0.001$). This study is the first to evaluate NPS in the context of HG. It should be acknowledged that ketonuria, as assessed by urine dipstick, is not a validated surrogate for overall HG severity. Koot et al. [17] reported no significant association between ketonuria levels at presentation and symptom severity scores, weight loss, or rehospitalization rates. In the present study, ketonuria was therefore not used as a proxy for clinical severity per se but rather as an objective, routinely available indicator of acute metabolic and nutritional stress at the time of admission.

NPS may add value beyond a simple urine ketone dipstick, as ketonuria reports a single downstream biochemical consequence of fasting, whereas NPS integrates upstream inflammatory burden (NLR, LMR) with nutritional reserve status (albumin, total cholesterol) that together contribute to the clinical course of HG. The two measures are conceptually complementary rather than competitive: ketonuria reflects the immediate metabolic state, whereas NPS captures the underlying inflammatory and nutritional substrate from which it arises. Whether NPS provides incremental triage value beyond PUQE score, ketonuria, and weight loss cannot be determined by the present cross-sectional design and remains the central rationale for prospective validation studies.

Oxidative stress and systemic inflammation are recognized features of HG. Tumor necrosis factor alpha (TNF-α) levels have been reported to rise with disease severity. This may partly explain why hematological markers shift more markedly in severe cases [23,24]. In our data, neutrophil counts and NLR were higher in the severe group, whereas lymphocyte counts and LMR showed the opposite trend. In the correlation analysis, NLR showed a positive correlation with ketonuria severity, whereas LMR showed a negative correlation, suggesting that ketonuria may parallel inflammatory activity. The literature reports that NLR is elevated in HG compared with control pregnancies, may increase with clinical severity, and may reflect a higher inflammatory burden when combined with high-sensitivity C-reactive protein [25,26]. Some studies have also reported that specific NLR threshold values may be associated with the presence of HG or more severe clinical presentations [27]. However, pregnancy is a dynamic state of adaptation characterized by neutrophil mobilization and functional redistribution of lymphocytes in the peripheral immune system [28,29]. The fact that a wide physiological reference range for NLR has been defined according to trimesters suggests that a single cutoff value may not achieve comparable specificity across all pregnant women [30]. Clinical variables such as dehydration and hemoconcentration, concomitant infections, and sampling timing can affect both absolute cell counts and ratio-based indices. Indeed, although NLR and platelet-to-lymphocyte ratio have been reported as elevated in HG in emergency department cohorts, they did not correlate with severity scores, and some prospective series found no between-group differences in NLR and reported no association between ketonuria and inflammatory indices [31,32,33]. These inconsistencies suggest that individual inflammatory markers may reflect disease burden, but are insufficient for reliable clinical decision-making when used in isolation. Composite scores combining inflammatory and nutritional parameters may therefore offer more consistent clinical information in this setting [34,35].

Prolonged vomiting and a marked decrease in oral intake in HG increase the risk of maternal malnutrition through negative energy balance and weight loss [18,36]. Therefore, with increasing severity of ketonuria, a more pronounced decrease in albumin and total cholesterol levels is expected, reflecting a more pronounced catabolic state with increased use of protein and lipid stores. In our study, both parameters were significantly lower in the severe ketonuria group and showed a moderate negative correlation with ketonuria levels. Total cholesterol remained an independent predictor in the multivariable model. The literature reports that total cholesterol and low-density lipoprotein (LDL) cholesterol, as well as apolipoprotein A (apo A) and apo B levels, are reduced in hyperemetic pregnancies compared with healthy pregnancies, and that the lipid profile can undergo significant alterations in HG [15,37]. A recent prospective study also showed that serum albumin was lower in the HG group and that several hematological indices changed with disease severity [14]. Total cholesterol does not solely reflect energy reserves biologically. Circulating LDL cholesterol is considered the primary substrate for placental progesterone synthesis [38,39]. Therefore, significant hypocholesterolemia, especially in early pregnancy, may be associated with processes such as hormone biosynthesis and fetal growth. Cohort studies have reported an association between low maternal total cholesterol and preterm birth as well as lower birth weight [40,41]. On the other hand, serum albumin shows a physiological decrease during pregnancy depending on gestational age, and may also decrease in the presence of inflammation due to being a negative acute phase protein. Therefore, its interpretation as a standalone marker of malnutrition is limited [42,43]. Although total cholesterol was independently associated with severe ketonuria in our data, this finding should be interpreted with caution and does not establish causality. Overall, these findings support an integrated assessment of inflammatory and nutritional together rather than evaluating them separately.

Since the NPS is a composite score that integrates inflammation and malnutrition within the same framework, it is expected to provide stronger predictive performance than individual markers by capturing both pathophysiological dimensions of HG. The NPS integrates serum albumin and total cholesterol with NLR and LMR, thereby covering both nutritional reserves and systemic inflammatory response within a single score [20]. In our study, NPS correlated strongly with ketonuria severity ($r = 0.845$) and showed excellent discriminatory performance in ROC analysis (AUC = 0.939). In the multivariable model, an NPS ≥ 3 was the strongest independent predictor of severe ketonuria (OR = 110.261), and the overall explanatory power of the model was high (Nagelkerke $R^2 = 0.761$). The prognostic value of NPS in settings where inflammation and malnutrition coexist has been demonstrated across multiple clinical contexts [44]. In colorectal cancer, the NPS outperformed the NLR, LMR, Prognostic Nutritional Index, and Controlling Nutritional Status in predicting overall survival, and similar findings have been reported in gastric and metastatic pancreatic cancer [45,46]. Data also indicate that the NPS may be an independent predictor of long-term mortality in heart failure [47]. Recent meta-analyses in gastrointestinal cancers further show that high NPS is consistently associated with poorer survival [48]. However, the NPS has not yet been validated in pregnancy populations, and a significant proportion of the thresholds used are derived from oncology cohorts. Pregnancy-specific hemodilution and leukocyte dynamics may require different cutoff values. Clinically, the fact that the NPS can be rapidly and inexpensively calculated from routine hemogram and biochemistry results suggests that it could be a practical tool for early triage of high-risk HG cases and for planning more aggressive hydration and early nutritional support in resource-limited settings.

The OR of 110.261 observed for NPS ≥ 3 in the multivariable model warrants methodological consideration. Such a high point estimate typically raises concerns about overfitting or multicollinearity, particularly when a composite score and its constituent variables are included simultaneously into the same regression model. In the present analysis, NPS components (NLR, LMR, albumin, and total cholesterol) were included alongside the NPS itself in the univariable screening step; however, in the final multivariable model, only NPS ≥ 3 and total cholesterol emerged as independent predictors, whereas the individual components did not reach statistical significance. This pattern is consistent with NPS reflecting the shared variance of its constituents, which may have inflated the point estimate while rendering the individual components redundant. The wide CI (42.724–284.560), despite statistical significance, reflects this instability and should be interpreted with caution. The high Nagelkerke R^2 (0.761) further suggests that the model explains a substantial proportion of variance. However, internal validation through bootstrapping was not performed, which is an acknowledged limitation. Future studies should model NPS as a continuous variable and employ resampling-based validation to yield more stable effect size estimates.

In the oncology literature, NPS has been defined as an immunonutritional index used to stratify long-term survival and treatment response [19]. The reported AUC for NPS in predicting five-year overall survival in resectable gastric cancer is 0.708 [49]. Following neoadjuvant therapy, the AUC values for NPS in esophageal squamous cell carcinoma for overall survival and progression-free survival were reported as 0.63 and 0.67, respectively [50]. In our study, the AUC of 0.939 for discriminating ketonuria severity suggests that NPS may more accurately reflect acute physiological stress load in a non-malignant clinical context in which HG is considered a benign immunonutritional crisis. In oncology, AUC values are influenced by the

long-term and multifactorial nature of cancer outcomes. In HG, by contrast, inflammatory and nutritional deterioration occur acutely and correlate more closely with immediate severity markers such as ketonuria. These differences likely explain the higher AUC observed in our study; however, direct comparisons across disease contexts should be interpreted with caution. Pregnancy-specific cutoff values should be prospectively validated and tested in external cohorts, and such validation is essential for clinical triage, especially in emergency settings.

Limitations

This study has several limitations that should be considered. As a retrospective single-center study, it is vulnerable to selection bias, and the results may not be generalizable to other settings. In addition, the absence of a healthy control group limited the analysis to within-group comparisons among HG patients, and therefore, the ability of NPS to distinguish HG from normal pregnancy could not be addressed. Urine dipstick for ketonuria is also imperfect; it is semi-quantitative and may be unreliable around clinically relevant threshold values. The absence of more sensitive biochemical measures, such as serum beta-hydroxybutyrate, should also be acknowledged as a limitation. The fact that the cutoff values used for NPS were largely derived from oncology cohorts further complicates interpretation. The lack of established pregnancy-specific threshold values, in the context of physiological hemodilution and immune adaptation during pregnancy, adds another layer of uncertainty to the interpretation of our findings. The original Galizia thresholds were deliberately retained to preserve comparability with the broader NPS literature, while acknowledging that pregnancy-specific recalibration is a necessary next step prior to clinical adoption. Furthermore, clinical prognostic inference is limited because treatment response and pregnancy outcomes, such as preterm birth and low birth weight, were not evaluated. An important conceptual limitation should be acknowledged. Since the NPS components (NLR, LMR, albumin, and total cholesterol) directly reflect inflammatory and nutritional status, both of which deteriorate in parallel with ketonuria severity, the strong association observed may partly reflect this shared pathophysiological basis rather than true independent predictive value. This does not negate the clinical utility of NPS as a composite bedside marker; however, prospective validation against more objective endpoints, such as serum beta-hydroxybutyrate, is required before routine recommendation for triage in HG. Nevertheless, the adequate sample size and consistently strong statistical signal support the hypothesis-generating nature of these findings and their potential to inform future validation studies.

5. Conclusions

In this retrospective cross-sectional study, NPS demonstrated a strong cross-sectional association with ketonuria severity and excellent discriminatory performance for severe ketonuria in pregnant women hospitalized for HG. By combining inflammatory markers (NLR, LMR) and nutritional markers (serum albumin, total cholesterol) into a single scale, NPS reliably distinguished severe from mild-to-moderate ketonuria, and an NPS $\geq$3 was independently associated with severe ketonuria. However, because the comparator (ketonuria) is itself an imperfect surrogate for overall HG severity, and because both NPS and ketonuria represent concurrent markers of inflammatory–nutritional stress measured at the same time point, the apparent discriminatory performance partially reflects shared pathophysiology and should not be interpreted as evidence of prospective predictive validity. The present findings therefore establish biological coherence between NPS and acute metabolic stress at admission but do not, by themselves, justify the use of NPS as a standalone clinical triage tool. Prospective, multicenter validation studies linking NPS to validated clinical severity measures (PUQE score, weight loss, electrolyte disturbances, and length of hospital stay) and pregnancy outcomes, together with the determination of pregnancy-specific threshold, are required before NPS can be recommended for routine clinical use.

Availability of Data and Materials

The datasets generated and analyzed during the current study are not publicly available due to institutional and patient confidentiality policies, but are available from the corresponding author upon reasonable request.

Author Contributions

MFO: conceptualization, methodology, formal analysis, investigation, writing—original draft, and visualization. GS: conceptualization, methodology, writing—review and editing, and supervision. MO: formal analysis, visualization, and writing—review and editing. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

The study protocol was approved by the Institutional Clinical Research Ethics Committee of Karamanoğlu Mehmetbey University (Approval date: 24.12.2025, decision no: 28) and carried out in accordance with the ethical principles of the Declaration of Helsinki. Due to the retrospective nature of the study, it was exempt from the informed consent requirement.

Acknowledgment

Not applicable.

Funding

This research received no external funding.

Conflicts of Interest

The authors declare no conflicts of interest.

References

[1] Martinez de Tejada B, Vonzun L, Von Mandach DU, Burch A, Yaron M, Hodel M, et al. Nausea and vomiting of pregnancy, hyperemesis gravidarum. European Journal of Obstetrics & Gynecology, and Reproductive Biology. 2025; 304: 115–120. https://doi.org/10.1016/j.ejogrb.2024.11.006

[2] Vadakekut ES, Mahdy H. Hyperemesis gravidarum. StatPearls Publishing: Treasure Island (FL). 2025.

[3] Nana M, Morgan H, Ahmed H, Williamson C. Hyperemesis gravidarum in the primary care setting: cross-sectional study of GPs. BJGP Open. 2022; 6: BJGPO.2021.0119. https://doi.org/10.3399/BJGPO.2021.0119

[4] Nana M, Painter R, Williamson C, Nelson-Piercy C. Hyperemesis gravidarum. Lancet. 2026; 407: 78–89. https://doi.org/10.1016/S0140-6736(25)01454-0

[5] McCarthy FP, Lutomski JE, Greene RA. Hyperemesis gravidarum: current perspectives. International Journal of Women's Health. 2014; 6: 719–725. https://doi.org/10.2147/IJWH.S37685

[6] Jansen LAW, Nijsten K, Limpens J, van Eekelen R, Koot MH, Grooten IJ, et al. Perinatal outcomes of infants born to mothers with hyperemesis gravidarum: A systematic review and meta-analysis. European Journal of Obstetrics, Gynecology, and Reproductive Biology. 2023; 284: 30–51. https://doi.org/10.1016/j.ejogrb.2023.03.004

[7] Committee on Practice Bulletins-Obstetrics. ACOG Practice Bulletin No. 189: Nausea And Vomiting Of Pregnancy. Obstetrics and Gynecology. 2018; 131: e15–e30. https://doi.org/10.1097/AOG.0000000000002456

[8] Yilmaz S, Ozgu-Erdinc AS, Demirtas C, Ozturk G, Erkaya S, Uygur D. The oxidative stress index increases among patients with hyperemesis gravidarum but not in normal pregnancies. Redox Report. 2015; 20: 97–102. https://doi.org/10.1179/1351000214Y.0000000110

[9] Fait V, Sela S, Ophir E, Khoury S, Nissimov J, Tkach M, et al. Hyperemesis gravidarum is associated with oxidative stress. American Journal of Perinatology. 2002; 19: 93–98. https://doi.org/10.1055/s-2002-23554

[10] Cabanillas-Lazo M, Castro-Suárez P, Uriol-Alvino S, Fernandez-Navarro M, Mayta-Tovalino F. Laboratory and Clinical Values of the Neutrophil-to-Lymphocyte Ratio in Women With Hyperemesis Gravidarum: A Systematic Review and Meta-Analysis. Journal of Pregnancy. 2025; 2025: 4872025. https://doi.org/10.1155/jp/4872025

[11] Caltekin M, Caltekin I, Onat T, Kirmizi D, Başer E, Yalcin S, et al. Can Subclinical Inflammatory Markers Predict Birth Time and Birth Weight in Hyperemesis Gravidarum?: A Comparative Study and Comprehensive Current Literature Review. The Medical Bulletin of Haseki. 2021; 59: 139–144. https://doi.org/10.4274/haseki.galenos.2021.6799

[12] van Stuijvenberg ME, Schabort I, Labadarios D, Nel JT. The nutritional status and treatment of patients with hyperemesis gravidarum. American Journal of Obstetrics and Gynecology. 1995; 172: 1585–1591. https://doi.org/10.1016/0002-9378(95)90501-4

[13] Zybkina O, Monsen AL, Dierkes J, Trovik J. Prealbumin is a marker of nutritional risk in hyperemesis gravidarum. European Journal of Obstetrics and Gynecology and Reproductive Biology. 2016; 206: e193. https://doi.org/10.1016/j.ejogrb.2016.07.473

[14] Soysal C, Bilir C, Zambak AB, İnce O, Taşçı Y. Association of hyperemesis gravidarum severity with HALP score and hematologic inflammatory markers. Scientific Reports. 2025; 15: 36376. https://doi.org/10.1038/s41598-025-20486-9

[15] Ustün Y, Engin-Ustün Y, Dökmeci F, Söylemez F. Serum concentrations of lipids and apolipoproteins in normal and hyperemetic pregnancies. The Journal of Maternal-Fetal & Neonatal Medicine. 2004; 15: 287–290. https://doi.org/10.1080/14767050410001680028

[16] Birkeland E, Stokke G, Tangvik RJ, Torkildsen EA, Boateng J, Wollen AL, et al. Norwegian PUQE (Pregnancy-Unique Quantification of Emesis and nausea) identifies patients with hyperemesis gravidarum and poor nutritional intake: a prospective cohort validation study. PLoS ONE. 2015; 10: e0119962. https://doi.org/10.1371/journal.pone.0119962

[17] Koot MH, Grooten IJ, Post JAMV, Bais JMJ, Ris-Stalpers C, Naaktgeboren CA, et al. Ketonuria is not associated with hyperemesis gravidarum disease severity. European Journal of Obstetrics, Gynecology, and Reproductive Biology. 2020; 254: 315–320. https://doi.org/10.1016/j.ejogrb.2020.08.014

[18] Grooten IJ, Roseboom TJ, Painter RC. Barriers and Challenges in Hyperemesis Gravidarum Research. Nutrition and Metabolic Insights. 2015; 8: 33–39. https://doi.org/10.4137/NMI.S29523

[19] Galizia G, Lieto E, Auricchio A, Cardella F, Mabilia A, Podzemny V, et al. Naples Prognostic Score, Based on Nutritional and Inflammatory Status, is an Independent Predictor of Long-term Outcome in Patients Undergoing Surgery for Colorectal Cancer. Diseases of the Colon and Rectum. 2017; 60: 1273–1284. https://doi.org/10.1097/DCR.0000000000000961

[20] Peng SM, Ren JJ, Yu N, Xu JY, Chen GC, Li X, et al. The prognostic value of the Naples prognostic score for patients with non-small-cell lung cancer. Scientific Reports. 2022; 12: 5782. https://doi.org/10.1038/s41598-022-09888-1

[21] Jiang Y, Chen Y, Lu W, Peng Y, Chen L, Lin Y. The Prognostic Role of Naples Prognostic Score in Patients with Coronary Artery Disease. Journal of Inflammation Research. 2025; 18: 6999–7012. https://doi.org/10.2147/JIR.S527868

[22] Uçkan K, Demir H, Demir C. Maternal serum ischemia-modified albumin (IMA), total-sulphydryl concentrations, and some subclinic inflammatory markers in hyperemesis gravidarum (HG). Taiwanese Journal of Obstetrics & Gynecology. 2023; 62: 101–106. https://doi.org/10.1016/j.tjog.2022.10.006

[23] Kaplan PB, Gücer F, Sayin NC, Yüksel M, Yüce MA, Yardim T. Maternal serum cytokine levels in women with hyperemesis gravidarum in the first trimester of pregnancy. Fertility and Sterility. 2003; 79: 498–502. https://doi.org/10.1016/s0015-0282(02)04699-x

[24] Jansen LAW, Shaw V, Grooten IJ, Koot MH, Dean CR, Painter RC. Diagnosis and treatment of hyperemesis gravidarum. CMAJ: Canadian Medical Association Journal. 2024; 196: E477–E485. https://doi.org/10.1503/cmaj.221502

[25] Kurt RK, Güler A, Silfeler DB, Ozçil MD, Karateke A, Hakverdi AU. Relation of inflammatory markers with both presence and severity of hyperemesis gravidarum. Ginekologia Polska. 2014; 85: 589–593. https://doi.org/10.17772/gp/1776

[26] Beyazit F, Öztürk FH, Pek E, Ünsal MA. Evaluation of the hematologic system as a marker of subclinical inflammation in hyperemesis gravidarum: a case control study. Ginekologia Polska. 2017; 88: 315–319. https://doi.org/10.5603/GP.a2017.0059

[27] Tayfur C, Burcu DC, Gulten O, Betul D, Tugberk G, Onur O, et al. Association between platelet to lymphocyte ratio, plateletcrit and the presence and severity of hyperemesis gravidarum. The Journal of Obstetrics and Gynaecology Research. 2017; 43: 498–504. https://doi.org/10.1111/jog.13228

[28] Abu-Raya B, Michalski C, Sadarangani M, Lavoie PM. Maternal Immunological Adaptation During Normal Pregnancy. Frontiers in Immunology. 2020; 11: 575197. https://doi.org/10.3389/fimmu.2020.575197

[29] Bert S, Ward EJ, Nadkarni S. Neutrophils in pregnancy: New insights into innate and adaptive immune regulation. Immunology. 2021; 164: 665–676. https://doi.org/10.1111/imm.13392
[30] Hershko Klement A, Hadi E, Asali A, Shavit T, Wiser A, Haikin E, et al. Neutrophils to lymphocytes ratio and platelets to lymphocytes ratio in pregnancy: A population study. PLoS ONE. 2018; 13: e0196706. https://doi.org/10.1371/journal.pone.0196706
[31] Kan E, Emektar E, Corbacioglu K, Safak T, Sariaydin T, Cevik Y. Evaluation of relationship between inflammatory markers and hyperemesis gravidarum in patients admitted to emergency department. The American Journal of Emergency Medicine. 2020; 38: 292–295. https://doi.org/10.1016/j.ajem.2019.05.007
[32] Özay ÖE, Özay AC. Inflammatory Markers in Hyperemesis Gravidarum. European Archives of Medical Research. 2021; 37: 27–31. https://doi.org/10.4274/eamr.galenos.2020.32448
[33] Cicek S, Coskun EI, Abdurahmanova N, Yilmaz E. Inflammation-driven pathogenesis of hyperemesis gravidarum: assessing the role of pan-immune-inflammation value and hematologic parameters. Archives of Gynecology and Obstetrics. 2025; 312: 2001–2010. https://doi.org/10.1007/s00404-025-08163-8
[34] Niemeijer MN, Grooten IJ, Vos N, Bais JMJ, van der Post JA, Mol BW, et al. Diagnostic markers for hyperemesis gravidarum: a systematic review and metaanalysis. American Journal of Obstetrics and Gynecology. 2014; 211: 150.e1–150.e15. https://doi.org/10.1016/j.ajog.2014.02.012
[35] Beser DM, Oluklu D, Hendem DU, Ayhan SG, Sahin D. The role of systemic immune-inflammation index in the severity of hyperemesis gravidarum. Journal of Gynecology Obstetrics and Human Reproduction. 2023; 52: 102583. https://doi.org/10.1016/j.jogoh.2023.102583
[36] Maslin K, Dean C. Nutritional consequences and management of hyperemesis gravidarum: a narrative review. Nutrition Research Reviews. 2022; 35: 308–318. https://doi.org/10.1017/S0954422421000305
[37] Aksoy H, Aksoy AN, Ozkan A, Polat H. Serum lipid profile, oxidative status, and paraoxonase 1 activity in hyperemesis gravidarum. Journal of Clinical Laboratory Analysis. 2009; 23: 105–109. https://doi.org/10.1002/jcla.20298
[38] Bartels Ä, O'Donoghue K. Cholesterol in pregnancy: a review of knowns and unknowns. Obstetric Medicine. 2011; 4: 147–151. https://doi.org/10.1258/om.2011.110003
[39] Henson MC. Pregnancy maintenance and the regulation of placental progesterone biosynthesis in the baboon. Human Reproduction Update. 1998; 4: 389–405. https://doi.org/10.1093/humupd/4.4.389
[40] Edison RJ, Berg K, Remaley A, Kelley R, Rotimi C, Stevenson RE, et al. Adverse birth outcome among mothers with low serum cholesterol. Pediatrics. 2007; 120: 723–733. https://doi.org/10.1542/peds.2006-1939
[41] Oluwole AA, Adegbesan-Omilabu MA, Okunade KS. Preterm delivery and low maternal serum cholesterol level: Any correlation? Nigerian Medical Journal. 2014; 55: 406–410. https://doi.org/10.4103/0300-1652.140381
[42] Klajnbard A, Szecsi PB, Colov NP, Andersen MR, Jørgensen M, Bjørngaard B, et al. Laboratory reference intervals during pregnancy, delivery and the early postpartum period. Clinical Chemistry and Laboratory Medicine. 2010; 48: 237–248. https://doi.org/10.1515/CCLM.2010.033
[43] Kim S, McClave SA, Martindale RG, Miller KR, Hurt RT. Hypoalbuminemia and Clinical Outcomes: What is the Mechanism behind the Relationship? The American Surgeon. 2017; 83: 1220–1227. https://doi.org/10.1177/000313481708301123
[44] Sugimoto A, Fukuoka T, Shibutani M, Kasashima H, Kitayama K, Ohira M, et al. Prognostic significance of the Naples prognostic score in colorectal cancer patients undergoing curative resection: a propensity score matching analysis. BMC Gastroenterology. 2023; 23: 88. https://doi.org/10.1186/s12876-023-02722-6
[45] Aoyama T, Kato A, Hashimoto I, Maezawa Y, Hara K, Kazama K, et al. The Naples Prognostic Score Is an Independent Prognostic Factor for Gastric Cancer Patients Who Receive Curative Treatment. In Vivo. 2024; 38: 890–896. https://doi.org/10.21873/invivo.13515
[46] Gulturk I, Yilmaz M, Tacar SY, Bakkaloglu OK, Sonmezoz GB, Erdal GS, et al. Naples prognostic score may predict overall survival in metastatic pancreatic cancer. Journal of Cancer Research and Therapeutics. 2024; 20: 249–254. https://doi.org/10.4103/jcrt.jcrt_1392_22
[47] Aydın SŞ, Aydemir S, Özmen M, Aksakal E, Saraç İ, Aydınyılmaz F, et al. The importance of Naples prognostic score in predicting long-term mortality in heart failure patients. Annals of Medicine. 2025; 57: 2442536. https://doi.org/10.1080/07853890.2024.2442536
[48] Pang H, Dai F, Chen L, Yan M, Zhao Z, Sun H. Prognostic value of the pretreatment Naples prognostic score in gastrointestinal cancer patients: an updated meta-analysis with 28 studies. Systematic Reviews. 2025; 14: 191. https://doi.org/10.1186/s13643-025-02944-7
[49] Xiong J, Hu H, Kang W, Liu H, Ma F, Ma S, et al. Prognostic Impact of Preoperative Naples Prognostic Score in Gastric Cancer Patients Undergoing Surgery. Frontiers in Surgery. 2021; 8: 617744. https://doi.org/10.3389/fsurg.2021.617744
[50] Chen W, Xu G, Yan X, Wang S, Xie Q, Liu Q, et al. Naples Prognostic Score as a Novel Prognostic Prediction Tool for Resectable Locally Advanced Esophageal Squamous Cell Carcinoma After Neoadjuvant Therapy. Journal of Inflammation Research. 2025; 18: 4843–4856. https://doi.org/10.2147/JIR.S502058