

Predictive Value of Prognostic Nutritional Index and Albumin/Creatinine Ratio in Hyperemesis Gravidarum

Hiperemesis Gravidarumda Prognostik Nutrisyonel İndeks ve Albümin/Kreatinin Oranının Prediktif Değeri

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ABSTRACT

Aim: This study aimed to evaluate the predictive value of the Prognostic Nutritional Index (PNI) and Albumin/Creatinine (A/C) ratio for prolonged hospitalization in patients with hyperemesis gravidarum (HG).

Materials and Methods: This retrospective cohort study was conducted at the Perinatology Department of A.B.C. Hospital between January 2020 and December 2024. Medical records of 228 women diagnosed with HG during the first or early second trimester were analyzed. Demographic, clinical, and laboratory data—including serum albumin, creatinine, and lymphocyte counts—were collected to calculate derived indices such as PNI, A/C ratio, neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and systemic immune-inflammation index (SII). Prolonged hospitalization was defined as ≥ 72 hours. Statistical analyses included ROC curve assessment and multivariate logistic regression.

Results: Patients with prolonged hospital stay had significantly lower PNI (44.8 ± 5.3 vs 47.9 ± 5.4 , $p < 0.001$) and A/C ratio values (5.27 ± 1.03 vs 5.81 ± 1.08 , $p = 0.003$). ROC analysis revealed that both indices were significant predictors of prolonged hospitalization, with optimal cut-offs of 46.8 for PNI (AUC = 0.79) and 5.45 for A/C ratio (AUC = 0.70). Multivariate regression identified low sodium, positive ketonuria, decreased PNI, and reduced A/C ratio as independent predictors.

Conclusion: Lower PNI and A/C ratio values are independently associated with prolonged hospitalization in HG, reflecting nutritional depletion and systemic inflammation. These accessible, cost-effective indices may serve as valuable tools for early risk stratification and individualized management of affected patients.

Keywords: Hyperemesis gravidarum; prognostic nutritional index; albumin/creatinine ratio; inflammation; hospitalization.

ÖZ

Amaç: Bu çalışmanın amacı, hiperemesis gravidarum (HG) tanılı hastalarda Prognostik Nutrisyonel İndeks (PNI) ve Albümin/Kreatinin (A/C) oranının uzamış hastanede yatış süresini öngörmedeki değerini değerlendirmektir.

Gereç ve Yöntemler: Bu retrospektif kohort çalışma, Ocak 2020 – Aralık 2024 tarihleri arasında A.B.Ş. Hastanesi Perinatoloji Kliniği'nde yürütüldü. İlk veya erken ikinci trimesterde HG tanısı ile yatırılan 228 hastanın klinik ve laboratuvar verileri incelendi. Serum albümin, kreatinin, lenfosit sayısı gibi parametreler kullanılarak PNI, A/C oranı, nötrofil/lenfosit oranı (NLR), trombosit/lenfosit oranı (PLR) ve sistemik immün-inflamasyon indeksi (SII) hesaplandı. Uzamış yatış, ≥ 72 saat olarak tanımlandı. İstatistiksel analizlerde ROC eğrisi ve çok değişkenli lojistik regresyon kullanıldı.

Bulgular: Uzamış yatışı olan hastalarda PNI (44.8 ± 5.3 'e karşı 47.9 ± 5.4 , $p < 0.001$) ve A/C oranı (5.27 ± 1.03 'e karşı 5.81 ± 1.08 , $p = 0.003$) anlamlı olarak daha düşüktü. ROC analizine göre, PNI (AUC = 0.79, kesim noktası ≤ 46.8) ve A/C oranı (AUC = 0.70, kesim noktası ≤ 5.45) uzamış yatışın anlamlı yordayıcılarıydı. Düşük sodyum, ketonüri varlığı, düşük PNI ve düşük A/C oranı çok değişkenli analizde bağımsız risk faktörleri olarak belirlendi.

Sonuç: Düşük PNI ve A/C oranı, HG hastalarında uzamış hastanede yatışla bağımsız olarak ilişkili bulunmuştur. Bu basit, düşük maliyetli biyobelirteçlerin erken risk değerlendirmesinde ve bireyselleştirilmiş tedavi planlamasında klinik olarak yararlı olabileceği düşünülmektedir.

Anahtar Kelimeler: Hiperemesis gravidarum; prognostik nutrisyonel indeks; albümin/kreatinin oranı.

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INTRODUCTION

Hyperemesis gravidarum (HG) represents the severe end of the nausea–vomiting spectrum in pregnancy, affecting approximately 0.3–2% of pregnant women and frequently resulting in dehydration, electrolyte imbalance, and prolonged hospitalization (1,2). Despite extensive research, the exact etiology of HG remains incompletely understood; however, accumulating evidence suggests that inflammatory and immunologic mechanisms play a significant role in its pathogenesis (3–5). Elevated systemic inflammatory markers and altered nutritional parameters have consistently been associated with increased disease severity and adverse maternal outcomes in women with HG (4,5).

Recently, several hematologic and biochemical indices have been introduced as simple, cost-effective tools for evaluating systemic inflammation and nutritional status in pregnancy-related conditions (6). Among these indices, the Prognostic Nutritional Index (PNI), calculated using serum albumin levels and peripheral lymphocyte counts, serves as a composite indicator of nutritional reserve and immune competence (7,8). PNI has been increasingly investigated in obstetric populations and has demonstrated prognostic value in hyperemesis gravidarum and other pregnancy-associated disorders characterized by inflammatory and metabolic stress (8,9).

Similarly, the serum albumin-to-creatinine (A/C) ratio integrates two routinely available biochemical parameters and may reflect concurrent alterations in nutritional status and metabolic stress during severe vomiting and dehydration states. Although data specifically addressing the A/C ratio in HG are limited, albumin-based indices and inflammatory biomarkers have shown prognostic relevance in determining disease severity and clinical course in HG and related conditions (5,9).

Despite the growing interest in inflammation- and nutrition-based indices in maternal medicine, the combined prognostic value of PNI and the A/C ratio for predicting clinically relevant outcomes such as prolonged hospitalization in hyperemesis gravidarum remains insufficiently explored. Therefore, this study aimed to evaluate whether PNI and the A/C ratio could serve as practical indicators for identifying patients with HG who are at increased risk of prolonged hospitalization.

MATERIALS AND METHODS

A retrospective cohort design was employed to investigate pregnant women managed in the Perinatology Department of A.B.C. Hospital, a tertiary care institution specializing in advanced

obstetric services. The study encompassed admissions between January 2020 and December 2024. Approval was granted by the Institutional Review Board of A.B.C. Hospital (Approval No: TABED 2-25-1574), and all procedures were carried out in accordance with the ethical standards of the Declaration of Helsinki. As the study relied exclusively on retrospective data, the ethics committee exempted the requirement for written informed consent.

Hospital records were systematically reviewed to identify women admitted with HG during the first or early second trimester of pregnancy. The diagnosis of HG was established based on ongoing nausea and vomiting associated with maternal weight loss, ketonuria, dehydration, and electrolyte disturbances, after exclusion of alternative medical or surgical causes. Women with pre-existing renal or hepatic disorders, autoimmune or chronic inflammatory diseases, multiple gestations, or missing clinical or biochemical information were excluded. Following application of these criteria, a total of 228 patients constituted the study population.

Baseline demographic and obstetric characteristics, including maternal age, gravidity, parity, gestational age at admission, and route of presentation (emergency department or outpatient referral), were extracted from institutional records (Table 1). Laboratory measurements obtained at the time of hospitalization were retrieved from the electronic database and comprised serum albumin, blood urea nitrogen (BUN), serum creatinine, electrolytes (potassium, chloride and sodium), C-reactive protein (CRP) and hematocrit. These parameters were subsequently used to generate several composite indices representing nutritional status and systemic inflammation (Table 2).

The A/C ratio was calculated by dividing serum albumin concentration (g/dL) by serum creatinine concentration (mg/dL). The PNI was derived using the following equation: $PNI = (10 \times \text{serum albumin [g/dL]}) + (0.005 \times \text{absolute lymphocyte count [}/\text{mm}^3\text{]})$. Systemic immune-inflammation index (SII) values were calculated as the product of platelet and neutrophil counts divided by the lymphocyte count. In addition, neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) were computed from complete blood count data.

The primary endpoint of the study was prolonged hospitalization, defined as an inpatient stay lasting 72 hours or more. Prolonged hospitalization was defined as an inpatient stay of **72 hours or longer**, as this duration reflects routine clinical workflow in the management of hyperemesis gravidarum, including initial stabilization, correction of electrolyte imbalance, nutritional support, and assessment of treatment response. Secondary endpoints included rehospitalization within 30 days after discharge and the

necessity for intensive care unit (ICU) admission. Relevant subgroup analyses were conducted accordingly (Table 6).

Statistical Analysis

All statistical evaluations were performed using IBM SPSS Statistics for Windows, version 25.0 (IBM Corp., Armonk, NY, USA). The normality of continuous variables was assessed using the Kolmogorov–Smirnov test. Based on distribution characteristics, parametric or non-parametric statistical tests were applied as appropriate. Depending on distribution characteristics, continuous data were presented as mean \pm standard deviation (SD) or as median with interquartile range (IQR), whereas categorical variables were summarized as counts and percentages.

Between-group comparisons were carried out using the independent samples t-test for normally distributed variables and the Mann–Whitney U test for variables with non-normal distribution. Categorical variables were analyzed using the chi-square test or Fisher's exact test, where appropriate. Receiver operating characteristic (ROC) curve analysis was applied to evaluate the discriminative ability of the A/C ratio and PNI in predicting prolonged hospitalization, and optimal threshold values were identified based on Youden's index. Variables demonstrating a p value below 0.10 in univariate analyses were entered into a multivariable logistic regression model to determine independent predictors of prolonged hospitalization. Prior to multivariable logistic regression analysis, multicollinearity among independent variables was assessed to ensure model stability. No significant multicollinearity was detected. Model calibration and goodness-of-fit were evaluated using the Hosmer–Lemeshow test, which demonstrated an acceptable fit between observed and predicted outcomes. Statistical significance was defined as a two-sided p value less than 0.05.

RESULTS

A total of 228 women diagnosed with hyperemesis gravidarum were included in the analysis. The mean age of the participants was 29.8 ± 5.4 years, with a median gravidity of two and parity of one. The median gestational age at presentation was 11 weeks. Most patients were admitted through the emergency department (69.3%), and one out of every three required hospitalization for longer than 72 hours. Readmission within 30 days occurred in 18.4% of patients, while only a small fraction (2.2%) needed intensive care support (Table 1).

As summarized in Table 2, the overall biochemical profile reflected mild hypoalbuminemia and modest inflammatory activation. Serum albumin averaged 3.45 ± 0.42 g/dL, and median CRP was 9.2 mg/L.

Table 1. Demographic and Clinical Characteristics of Participants (n = 228)

Variable	Mean \pm SD / Median [IQR]	n (%)
Age (years)	29.8 \pm 5.4	–
Gravidity	2 [1-3]	–
Parity	1 [0-1]	–
Gestational age (weeks + days)	11 \pm 2.3	–
Admission type - Emergency	–	158 (69.3)
Prolonged hospitalization (≥ 72 h)	–	76 (33.3)
Readmission within 30 days	–	42 (18.4)
Intensive care requirement	–	5 (2.2)
≥ 2 antiemetic classes used	–	95 (41.7)
Total parenteral nutrition (TPN) initiated	–	2 (0.9)

TPN: Total parenteral nutrition.

Note: Data are presented as mean \pm SD or median [IQR] for continuous variables and n (%) for categorical variables.

Table 2. Laboratory Parameters and Derived Indices

Parameter	Mean \pm SD / Median [IQR]
Serum albumin (g/dL)	3.45 \pm 0.42
Serum creatinine (mg/dL)	0.61 \pm 0.13
Albumin/creatinine ratio (A/C)	5.63 \pm 1.12
Lymphocyte count (/mm ³)	2,480 \pm 540
Prognostic Nutritional Index (PNI)	46.9 \pm 5.7
Neutrophil-to-lymphocyte ratio (NLR)	3.8 \pm 1.5
Platelet-to-lymphocyte ratio (PLR)	135 \pm 55
Systemic immune-inflammation index (SII)	675 \pm 250
C-reactive protein (CRP, mg/L)	9.2 [6.1-15.4]
Hematocrit (%)	34.1 \pm 3.6
BUN/creatinine ratio	18.5 \pm 4.3
Sodium (mmol/L)	135.7 \pm 3.4
Potassium (mmol/L)	3.7 \pm 0.4
Chloride (mmol/L)	101 \pm 2.8

A/C: Albumin/creatinine ratio; PNI: Prognostic nutritional index; NLR: Neutrophil-to-lymphocyte ratio; PLR: Platelet-to-lymphocyte ratio; SII: Systemic immune-inflammation index; CRP: C-reactive protein; BUN: Blood urea nitrogen.

Note: Variables are presented according to their distribution.

The mean PNI was 46.9 ± 5.7 , suggesting a mild compromise in nutritional and immune status across the cohort.

When patients were stratified by hospitalization duration, several clear patterns emerged. Those who stayed ≥ 72 hours had lower albumin/creatinine ratios (5.27 ± 1.03 vs. 5.81 ± 1.08 , $p = 0.003$)

Table 3. Association Between Laboratory Indices and Prolonged Hospitalization (n = 228)

Parameter	Prolonged Stay (+) (n = 76)	Prolonged Stay (-) (n = 152)	p value
Albumin/creatinine ratio (A/C)	5.27 ± 1.03	5.81 ± 1.08	0.003
Prognostic Nutritional Index (PNI)	44.8 ± 5.3	47.9 ± 5.4	<0.001
Neutrophil-to-lymphocyte ratio (NLR)	4.32 ± 1.6	3.58 ± 1.4	0.019
Platelet-to-lymphocyte ratio (PLR)	147 ± 58	130 ± 52	0.028
Systemic immune-inflammation index (SII)	696 ± 250	664 ± 245	0.041
C-reactive protein (CRP, mg/L)	10.0 [7.0 - 15.0]	8.9 [6.0 - 14.0]	0.048

A/C: Albumin/creatinine ratio; PNI: Prognostic nutritional index; NLR: Neutrophil-to-lymphocyte ratio; PLR: Platelet-to-lymphocyte ratio; SII: Systemic immune-inflammation index; CRP: C-reactive protein.

Note: Continuous variables are expressed as mean ± SD or median [IQR]. Bold p values indicate statistical significance (p < 0.05).

and lower PNI values (44.8 ± 5.3 vs. 47.9 ± 5.4, p<0.001). In the same group, inflammatory indices such as PLR, CRP, NLR and SII were modestly higher, consistent with an amplified inflammatory response (Table 3).

ROC analysis supported these findings: both A/C ratio and PNI showed significant ability to predict prolonged hospitalization, with optimal cut-offs of 5.45 and 46.8, respectively. The discriminative performance was stronger for PNI (AUC 0.79, 95% CI: 0.72–0.85, p<0.001) than for A/C ratio (AUC 0.70, 95% CI: 0.62–0.78, p=0.003) (Table 4).

In the multivariate regression model, lower sodium levels, the presence of ketonuria, and reduced values of both PNI and A/C ratio independently predicted prolonged hospitalization (Table 5). Finally, patients who required readmission within 30 days also exhibited significantly lower PNI and A/C ratios, though inflammatory indices did not differ meaningfully between groups (Table 6).

DISCUSSION

The present study demonstrates that both the PNI and the serum A/C ratio are independently associated with prolonged hospitalization

Table 4. ROC Curve Analysis for Predictive Accuracy of A/C Ratio and PNI in Predicting Prolonged Hospitalization

Variable	AUC (95 % CI)	p value	Cut-off	Sensitivity (%)	Specificity (%)
A/C ratio	0.70 (0.62 - 0.78)	0.003	≤ 5.45	68	69
PNI	0.79 (0.72 - 0.85)	< 0.001	≤ 46.8	74	74

A/C: Albumin/creatinine ratio; PNI: Prognostic nutritional index; AUC: Area under the curve; CI: Confidence interval.

Note: Receiver operating characteristic (ROC) analysis was performed to determine the ability of A/C ratio and PNI to predict prolonged hospitalization (≥72 hours). Cut-off values were calculated using Youden's index to maximize sensitivity and specificity.

Both parameters demonstrated significant discriminatory ability (p < 0.05), with PNI showing the highest predictive accuracy.

Table 5. Multivariate Logistic Regression Analysis for Predictors of Prolonged Hospitalization

Variable	β coefficient	OR (95 % CI)	p value
Age (years)	0.02	1.02 (0.97 - 1.08)	0.34
Gestational age (weeks)	-0.06	0.94 (0.86 - 1.02)	0.11
BUN/creatinine ratio	0.04	1.04 (0.97 - 1.12)	0.25
Sodium (mmol/L)	-0.08	0.92 (0.85 - 0.99)	0.041
Ketonuria (++ / +++)	0.54	1.72 (1.08 - 2.86)	0.021
Albumin/creatinine ratio (A/C)	-0.29	0.75 (0.61 - 0.92)	0.005
Prognostic Nutritional Index (PNI)	-0.14	0.87 (0.80 - 0.94)	< 0.001

A/C: Albumin/creatinine ratio; PNI: Prognostic nutritional index; BUN: Blood urea nitrogen; OR: Odds ratio; CI: Confidence interval.

Note: Multivariate logistic regression analysis was conducted using prolonged hospitalization (≥72 hours) as the dependent variable. Independent variables were selected based on clinical relevance and univariate analysis significance.

Lower sodium levels, positive ketonuria, decreased A/C ratio, and reduced PNI were independently associated with prolonged hospitalization.

Table 6. Subgroup Analysis Based on 30-Day Readmission Status (n = 228)

Parameter	Readmission (+) (n = 42)	Readmission (-) (n = 186)	p value
Albumin/creatinine ratio (A/C)	5.30 ± 1.05	5.72 ± 1.10	0.012
Prognostic Nutritional Index (PNI)	44.9 ± 5.4	47.3 ± 5.5	0.009
Neutrophil-to-lymphocyte ratio (NLR)	4.11 ± 1.6	3.72 ± 1.5	0.083
Platelet-to-lymphocyte ratio (PLR)	142 ± 58	134 ± 54	0.192
Systemic immune-inflammation index (SII)	700 ± 265	670 ± 245	0.210
C-reactive protein (CRP, mg/L)	9.9 [7.0 - 15.0]	9.0 [6.0 - 13.8]	0.142

A/C: Albumin/creatinine ratio; PNI: Prognostic nutritional index; NLR: Neutrophil-to-lymphocyte ratio; PLR: Platelet-to-lymphocyte ratio; SII: Systemic immune-inflammation index; CRP: C-reactive protein.

Note: Continuous variables are expressed as mean ± SD or median [IQR]. $P < 0.05$ was considered statistically significant.

Lower A/C and PNI values were significantly associated with higher 30-day readmission rates, consistent with nutritional and inflammatory imbalance in hyperemesis gravidarum.

in women with hyperemesis gravidarum. Patients who required an inpatient stay of 72 hours or longer exhibited significantly lower PNI and A/C ratio values, even after adjustment for established clinical factors such as electrolyte imbalance and ketonuria. These findings suggest that nutritional depletion and systemic inflammatory stress contribute meaningfully to disease persistence and delayed clinical recovery in HG.

Hyperemesis gravidarum is increasingly recognized as a condition characterized not only by severe gastrointestinal symptoms but also by complex inflammatory and metabolic disturbances. Previous studies have consistently demonstrated elevated inflammatory indices, including the SII, NLR, and HALP score, in patients with more severe HG phenotypes (3–5,9). In addition, clinical indicators such as ketonuria and electrolyte abnormalities have been associated with longer hospital stays and increased disease burden (10). Our results align with this growing body of evidence by showing that patients with prolonged hospitalization also display modest but consistent elevations in inflammatory markers, supporting the concept of sustained immune activation in more severe disease courses.

The Prognostic Nutritional Index, originally developed to assess perioperative risk and immune-nutritional status (7), has recently gained attention in obstetric research. Emerging data indicate that PNI reflects not only nutritional reserves but also immune competence through its integration of serum albumin and lymphocyte count (6–8). In the context of HG, Demir Cendek et al. reported that lower PNI values were associated with increased disease severity and adverse clinical outcomes (8). Our findings extend these observations by demonstrating that decreased PNI is independently associated with prolonged hospitalization, suggesting that impaired nutritional and immune status may delay symptom resolution and prolong inpatient care requirements.

The prognostic relevance of albumin-based parameters in HG has been less extensively studied. Serum albumin levels are influenced by nutritional intake, systemic inflammation, and intravascular volume status, all of which are commonly disrupted in severe HG. By integrating serum albumin with creatinine, the A/C ratio provides a composite reflection of protein status and metabolic stress. Although HG-specific data on the A/C ratio remain limited, previous studies have demonstrated that hypoalbuminemia, inflammatory burden, and dehydration-related laboratory abnormalities correlate with longer hospital stays and more severe clinical trajectories in HG (4,5,9,10). In this study, lower A/C ratio values were independently associated with prolonged hospitalization, suggesting that this readily available parameter may offer additional prognostic information beyond isolated laboratory measurements.

Our findings also parallel prior observations that hematologic and inflammatory parameters may aid in stratifying HG severity. Aslan et al. showed that inflammatory blood indices and ketonuria were associated with disease severity and clinical course in HG (11). Together with earlier reviews emphasizing the multifactorial inflammatory and metabolic nature of HG (2,12), these data support a model in which nutritional depletion, immune activation, and metabolic stress interact to influence disease duration and hospitalization requirements.

Importantly, both PNI and A/C ratio are derived from routinely obtained laboratory tests and therefore impose no additional cost or procedural burden. Their incorporation into early clinical assessment may help identify patients at higher risk for prolonged hospitalization, allowing for closer monitoring, earlier nutritional intervention, and individualized management strategies. Such an approach may be particularly valuable in high-volume tertiary care settings, where efficient resource utilization and timely risk stratification are essential.

Several limitations should be acknowledged. The retrospective design restricts causal inference, and unmeasured confounders related to nutritional intake or antiemetic treatment protocols may have influenced hospitalization duration. Additionally, while the A/C ratio showed independent predictive value, its biological interpretation in HG requires further clarification through prospective studies. Nevertheless, the consistency of our findings with prior literature on inflammatory, nutritional, and clinical severity markers in HG supports the robustness and clinical relevance of the observed associations (3–5,8–11).

CONCLUSION

This study identified both the **PNI** and **A/C ratio** as independent predictors of prolonged hospitalization in women with hyperemesis gravidarum. Lower PNI and A/C values were significantly associated with longer hospital stay and higher readmission rates, emphasizing the link between nutritional depletion and systemic inflammation in the disease process.

These simple and cost-effective parameters may serve as practical tools for early risk stratification. Incorporating PNI and A/C ratio into initial evaluation could help guide clinical decision-making, optimize supportive therapy, and reduce hospitalization burden. Further prospective research is warranted to confirm their prognostic utility in routine obstetric care.

Ethical Approval: The study was approved by the Research Ethics Committee of A.B.C. Hospital, Ankara, Turkey. The approval number is TABED 2-25-1574. The study was conducted in accordance with the Declaration of Helsinki and adhered to the ethical standards of Turkey, where the research was conducted.

Consent to participate: Due to the retrospective design of the study, the requirement for written informed consent was waived by the Research Ethics Committee.

Consent for publication: There are no circumstances in the study that violate anonymity, and identifying information has been kept confidential. There are no issues regarding its publication.

Availability of data and materials: Patient data is stored indefinitely in the hospital's automation system (HICAMP®). It can be shared upon request, provided that patient identity remains confidential.

Competing interests: There are no conflicts of interest among the authors.

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