Jinekoloji - Obstetrik ve Neonatoloji Tıp Dergisi
The Journal of Gynecology-Obstetrics and Neonatology

ÖZGÜN ARAŞTIRMA / ORIGINAL ARTICLE

DOI: 10.38136/jgon.1820089

Evaluation of the Neutrophil Percentage Albumin Ratio (NPAR) Index in Predicting the Severity of Hyperemesis Gravidarum

Hiperemezis Gravidarumun Şiddetini Tahmin Etmede Nötrofil Yüzdesi Albümin Oranı (NPAR) Endeksinin Değerlendirilmesi

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ABSTRACT

Aim: The aim of this study is to investigate the effect of the neutrophil percentage to albumin ratio (NPAR) index in determining the severity of hyperemesis gravidarum in patients diagnosed with this condition.

Material and Methods: In a retrospective, single-center study, pregnant women diagnosed with HEG between January 2024 and November 2025 at the Perinatology Department of Ankara City Hospital were included. NPAR was calculated by dividing the neutrophil percentage by the albumin value. HEG severity was classified as mild, moderate, or severe using the modified PUQE-24 scoring system. The Kolmogorov-Smirnov and Shapiro-Wilk tests were used to assess the normality of data distribution. Group comparisons were performed using the Kruskal-Wallis test. ROC analysis was performed for NPAR to predict HEG severity; $p<0.05$ was considered significant.

Results: A total of 160 HEG patients were included in the study: mild n=80, moderate n=40, severe n=40. No differences were found between groups in BMI, gestational age, and other parameters; however, hospital stay, and PUQE-24 scores were significantly higher in the severe HEG group. Both the neutrophil percentage and NPAR were significantly higher in the severe HEG group ($p=0.01$ and $p=0.009$). In the ROC analysis, the best cutoff value for NPAR was found to be 1.77; sensitivity was 70%, specificity was 68%, and AUC was 0.675 ($p=0.005$).

Conclusion: NPAR showed a statistically significant correlation in predicting HEG severity and partially distinguished between mild and severe HEG; however, its limited performance, with an AUC of 0.675, indicates that NPAR alone is not sufficient for clinical decision-making. These findings suggest that NPAR may provide additional information when used with PUQE-24 and necessitate validation through prospective/multicenter studies.

Keywords: Hyperemesis gravidarum, neutrophil percentage albumin ratio, severity

ÖZ

Amaç: Bu çalışmadaki amacımız hiperemezis gravidarum tanılı hastalarda nötrofil yüzdesinin albümine oranı(NPAR) indeksinin hastalığın şiddetini belirlemede etkisini araştırmak.

Gereç ve Yöntemler: Retrospektif, tek merkezli bir çalışmada, Ankara Şehir Hastanesi Perinatoloji Bölümü'nde Ocak 2024 – Kasım 2025 döneminde HEG tanısı konulan gebeler dahil edildi. NPAR hesaplanırken neutrofil yüzdesi, albumin değerine bölünerek elde edildi. HEG şiddeti, modifiye PUQE-24 skorlama sistemiyle mild, moderate ve severe olarak sınıflandırıldı. Veri dağılımı normalliği için Kolmogorov-Smirnov ve Shapiro-Wilk testleri kullanıldı. Grup karşılaştırmaları Kruskal-Wallis testiyle yapıldı. HEG'nin şiddetini tahmin etmek için NPAR için ROC analizi yapıldı; $p<0,05$ anlamlı kabul edildi.

Bulgular: Toplam 160 HEG hastası çalışmaya alındı: hafif n=80, orta n=40, ağır n=40. BMI, gebelik süresi ve diğer bazı parametrelerde gruplar arasında fark saptanmadı; ancak ağır HEG grubunda hastanede kalış süresi ve PUQE-24 skorları anlamlı derecede yüksek bulundu. Hem neutrofil yüzdesi hem de NPAR, ağır HEG grubunda anlamlı olarak yüksekti ($p=0,01$ ve $p=0,009$). ROC analizinde NPAR için en iyi kesim değeri 1.77 olarak bulundu; sensivite %70, spesifiklik %68, AUC 0,675 ($p=0,005$).

Sonuç: NPAR, HEG şiddetinin tahmininde istatistiksel olarak anlamlı bir ilişki gösterdi ve hafif ile ciddi HEG arasındaki ayırımı kısmen sağladı; ancak AUC 0,675 gibi sınırlı bir performans olması NPAR'ın tek başına klinik karar için yeterli olmadığını göstermektedir. Bu bulgular, NPAR'ın PUQE-24 ile kullanıldığında ek bilgi sağlayabileceğini ve prospective/çok merkezli çalışmalarla doğrulamanın gerekliliğini düşündürmektedir.

Anahtar Kelimeler: Hiperemezis gravidarum, nötrofil yüzdesinin albümine oranı, şiddet

Cite as: Bozkurt Ozdal B, Sahin D. Evaluation of the Neutrophil Percentage Albumin Ratio (NPAR) index in predicting the severity of hyperemesis gravidarum. Jinekoloji-Obstetrik ve Neonatoloji Tıp Dergisi 2025;22(4):449–454.

Geliş/Received: 14.11.2025 • **Kabul/Accepted:** 27.11.2025

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Çevrimiçi Erişim/Available online at: https://dergipark.org.tr/tr/pub/jgon

INTRODUCTION

Nausea is a common condition in early pregnancy, and mild nausea can be considered a normal part of pregnancy physiology in the first and early second trimesters. However, these symptoms significantly affect the quality of life of both the pregnant person and their family, especially when they are persistent and/or severe.Severe symptoms can negatively affect daily functioning, lead to anxiety and depression, and in some patients, cause thoughts of terminating the pregnancy or avoiding future pregnancies (1-3).

The etiology of nausea and vomiting is not fully understood. Factors such as genetics, hormonal changes, abnormal gastrointestinal motility, and H. pylori are considered in the etiology (4).

Patients with severe nausea and vomiting (hyperemesis gravidarum) may present with orthostatic hypotension, laboratory abnormalities (e.g., electrolyte, thyroid, and liver abnormalities), and signs of hypovolemia. They usually require hospitalization for stabilization and initiation of pharmacotherapy (5).

Albumin has gained prominence in obstetric research due to its easy accessibility and potential prognostic value in pregnancy-related complications(5, 6) . These indices, which include albumin as an important component, provide insight into both the inflammatory and nutritional status of patients. While white blood cells provide additional information about the inflammatory process, albumin levels are an indicator of nutritional status (7).

It was hypothesized that an index created using albumin and white blood cells would be effective in determining the severity of hyperemesis gravidarum (HEG), given the deterioration of the mother's nutritional status and the immune-related nature of pregnancy associated with HEG. This formed the basis of our study.

The aim of this study is to evaluate the neutrophil percentage to albumin ratio (NPAR) index in determining the severity of HEG.

MATERIALS AND METHODS

Study Population

This study was retrospective, single-center, and conducted at a tertiary care hospital. Patients diagnosed with HEG and treated at the Perinatology Department of Ankara City Hospital between January 2024 and November 2025 were included in this study. Informed consent forms were obtained from all patients included in the study. Approval was obtained from the Ankara City Hospital Ethics Committee for this study (TABED-2-25-1629). The Helsinki Declaration guidelines were followed at every stage of the study.

For each patient included in the study, the following clinical and obstetric data were retrospectively recorded from the hospital database: age, gravida, parity, body mass index, gestational age at the onset of HEG, length of hospital stay, results of routine liver function tests performed at diagnosis, electrolyte levels, ketone levels in spot urine, thyroid function test results, hemoglobin, neutrophil percentage, and albumin, NPAR values, were retrospectively recorded from the hospital database.

NPAR was calculated by dividing the neutrophil percentage by the albumin value.

The diagnosis of HEG was made when severe vomiting, weight loss of more than 5%, and urinary ketonuria or maternal serum electrolyte imbalance were observed in the first weeks of pregnancy after other causes were excluded (8). The severity of HEG was assessed using the modified PUQE-24 system (9) based on anamnesis information (Table 1). Using the PUQE-24 scoring system, patients with HEG were divided into three groups: mild, moderate, and severe.

The study excluded patients with multiple pregnancies, hypertensive patients, diabetic patients, psychiatric patients, patients with a history of molar pregnancy, and those with missing or inaccessible data.

Statistical Analysis

In this study, the sample size was analyzed using G Power software (version 3.1; Franz Foul, Universitat Kiel, Kiel, Germany). A 0.05

Table 1. Pregnancy-Unique Quantification of Emesis Scoring System

In the last 24 hours, for how long have you felt nauseated or sick to your stomach?	Not at all (1)	1 hour or less (2)	2-3 hours (3)	4–6 hours (4)	More than 6 hours (5)
In the last 24 hours, have you vomited or thrown up?	I did not throw up (1)	1–2 times (2)	3–4 times (3)	5–6 times (4)	7 or more times (5)
in the last 24 hours, how many times have you had retching or dry heaves without bringing anything up?	No time (1)	1–2 times (2)	3–4 times (3)	5–6 times (4)	7 or more times (5)

Mild = ≤6; Moderate = 7–12; Severe = 13–15.

Table 2. Clinicodemographic and obstetric data, length of hospital stay, and PUQE-24 scores of the patients with HEG

Variables	Mild HG N:80	Moderate HG N:40	Severe HG N:40	P-value
Age (year)	28(19-41)	27(20-43)	28(23-38)	0.413
Gravida	2.0(1.0-5.0)	2.0(1.0-8.0)	2.0(1.0-4.0)	0.983
Parity	0.0(0.0-4.0)	0.0(0.0-5.0)	0.0(0.0-2.0)	0.643
BMI (kg/m^2)	24(18-32)	23(20-30)	24(21-35)	0.756
Miscarriage	0.0(0.0-4.0)	0.0(0.0-2.0)	0.0(0.0-3.0)	0.212
Gestational week	11.0(6.0-20.0)	10.0(6.0-19.0)	9.0(4.0-15.0)	0.302
Length of hospital stay	2.0(1.0-3.0)	5.0(1.0-.5.0)	9.0(7.0-29)	**<0.001**
PUQE-24 score	3.0(1.0-5.0)	7.0(6.0-12.0)	15(12.0-15.0)	**<0.001**

HEG: hyperemesis gravidarum, PUQE: Pregnancy-Unique Quantification of Emesis
Descriptive analyses used median min-max for non-normally distributed variables. Statistically significant at p < 0.05

(two-tailed) p-value and 95% power with an 0.80 (large) effect size were determined for the sample size. The sample size was calculated as 100 patients in each group.The SPSS 22.0 statistical program (SPSS Inc., Chicago, IL, USA) was used for data analysis. The Kolmogorov–Smirnov test and Shapiro–Wilk test were used to analyze the normality of the data distribution. The Kruskal-Wallis test was used to compare variables that did not follow a normal distribution. Descriptive analyses used median min-max for non-normally distributed variables. The "ROC" curve was used to determine the cut-off point of NPAR in predicting HEG severity. A P value of less than 0.05 was considered statistically significant.

RESULTS

A total of 160 HEG patients were included in the study. Patients were divided into three groups based on the severity of HEG. There were 80 patients in the mild HG group, 40 in the moderate HG group, and 40 in the severe HEG group. Table 2 presents the patients clinical demographic and obstetric data, body mass index (BMI), gestational age at diagnosis, length of stay and PUQE-24 scores.

There was no significant difference in body mass index among the three groups in terms of gestational age at diagnosis of gravida, parity, miscarriage, and HEG (p>0.05) (Table 2). Hospitalization durations and PUQE-24 scores were statistically significantly higher in the severe HEG group (p<0.001, respectively).

Table 3 shows the comparison of laboratory blood results and NPAR values between mild, moderate, and severe HEG groups. In terms of laboratory values, ALT and AST values were found to be higher in the severe HEG group among the three groups (p=0.008; p<0.001, respectively). Neutrophil percentages and NPAR values were also found to be higher in severe HEG (P=0.01; 0.009, respectively). No difference was observed between the three groups in terms of glucose, creatinine, calcium, sodium, potassium, (Thyroxine) T4, TSH (Thyroid Stimulating Hormone), total albumin, and albumin levels (p>0.05). Urea levels were lower in the severe HEG group (p=0.021).

Spot urine ketone levels for the HEG groups are presented in Table 3. There was no significant difference between the three groups in terms of ketone levels measured in spot urine (p>0.05).

In the ROC analysis, the optimal cutoff value of NPAR for predicting severe HEG was determined to be 1.77 with 70% sensitivity and 68% specificity (area under the curve = 0.675; p=0.005) (Figure 1).

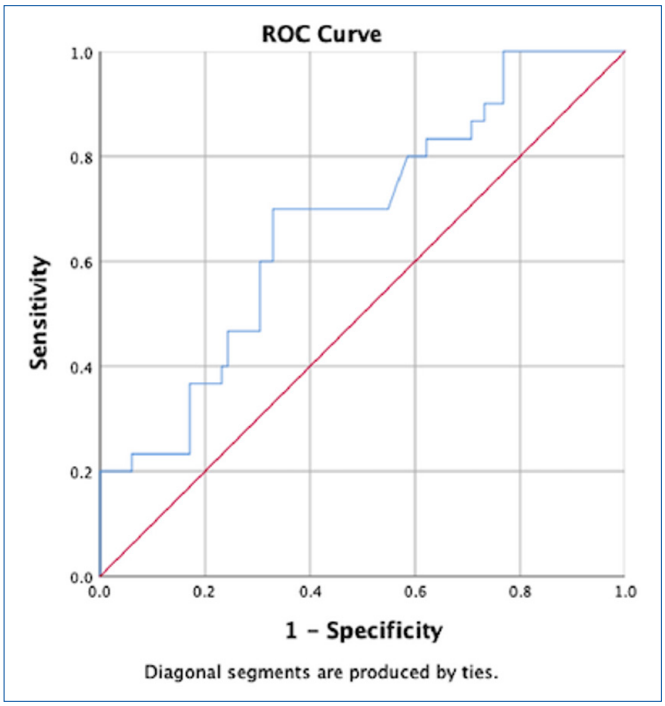

Figure 1. The ROC curve for the Neutrophil Percentage Albumin Ratio ratio to predict severe hyperemesis gravidarum

Table 3. Laboratory parameters and NPAR values of the patients with HEG

Variables	Mild HG N:80	Moderate HG N:40	Severe HG N:40	P-value
Glucose(mg/dl)	82(56-149)	86(68-116)	83(68-109)	0.772
ALT (IU/L)	20(8-186)	35(10-135)	40(9-68)	**0.008**
AST (IU/L)	15(4-71)	16(6-64)	22(10-81)	**<0.001**
Creatinine (mg/dL)	0.50(0.34-0.75)	0.53(0.15-0.71)	0.51(0.38-0.64)	0.331
Calsium(mEq/L)	9.4(8.4-10.1)	9.1(8.9-9.3)	9.2(8.8-9.7)	0.298
Urea(mg/dl)	17(10-34)	16(9-21)	15(9-21)	**0.021**
Sodium (mEq/L)				0.357
Chlorine(mEq/L)	105(102-110)	103(103-107)	103(101-105)	0.181
Potassium (mEq/L)	3.8(3.4-4.1)	3.75(3.4-4.1)	4.1(4.0-4.2)	0.703
T4 (ng/dl)	1.19(0.88-3.0)	1.64(1.29-3.35)	1.24(0.95-3.19)	0.105
TSH (mU/ml)	0.7(0.00-2.51)	0.02(0.00-0.21)	0.65(0.00-1.72)	0.752
Hemoglobin	12.9(10.3-14.8)	12.5(11.2-15.5)	13.4(10.5-15.5)	**0.028**
WBC	8.97(3.14-14.9)	9.73(6.53-15.9)	8.19(6.41-17.0)	0.764
Neutrophil persentage	71.8(56.5-92.8)	76.4(65.3-88.2)	80.0(68.7-81.6)	**0.001**
Total protein	67(54-81)	66(59-73)	66(55-82)	0.452
Albumin (g/dL)	43(32-51)	38(36-45)	43(32-53)	0.666
NPAR	1.72(1.37-2.29)	1.78(1.56-2.48)	1.81(1.46-2.27)	**0.009**
Ketone	3(0-4)	3(0-4)	4(4-4)	**0.018**

NPAR:Neutrophil persentage albümin ratio,HG: hyperemesis gravidarum, ALT: alanine aminotransferase, AST: aspartate aminotransferase, TSH: thyroid-stimulating hormone
Descriptive analyses used median min-max for non-normally distributed variables. Statistically significant at $p < 0.05$

DISCUSSION

In this study, we evaluated the effect of NPAR in predicting disease severity in HEG patients. We found that NPAR had 70% sensitivity and 67% specificity in predicting the severity of HG.

Nausea, with or without vomiting, occurs in up to 90% of pregnancies (9).

Nausea begins in the 5th to 6th week of pregnancy, peaks around the 9th week, and usually subsides between the 16th and 20th weeks. Sixty percent of patients are asymptomatic six weeks after the onset of nausea (10). However, symptoms persist into the third trimester in 15 to 20 percent of patients and until delivery in 5 percent (11). Although mild pregnancy-related nausea and vomiting are often referred to as “morning sickness,” symptoms can occur at any time of day, may only occur in the evenings, and typically persist throughout the day (80%) (12).

Hyperemesis gravidarum is a term used to describe the severe end of the symptom spectrum (13). Severe symptoms can negatively impact daily functioning, leading to anxiety and depression. In some cases, it may even cause patients to consider terminating the pregnancy or avoiding future pregnancies (14).

The indices used to determine the severity of hyperemesis in hyperemesis gravidarum are the Motherisk-PUQE Scoring Index and the Rhodes Index. The Motherisk-PUQE Scoring Index is specifically designed for pregnant individuals to assess symptoms within the 12 hours prior to clinical evaluation and has been used primarily in research studies (15). The modified PUQE score is designed to assess symptoms throughout the entire first trimester (16). We also used the modified PUQE scoring index in our study. The scoring system includes the number of hours the individual felt nauseous, the number of times they vomited, and the number of times they experienced dry retching in a day. A high score should prompt immediate evaluation for hypovolemia and serum electrolyte abnormalities. As the severity of HEG increases, maternal and perinatal outcomes become more complicated(8) . Therefore, predicting the severity of the disease and implementing personalized treatment approaches for patients is crucial for improving maternal and perinatal outcomes.

In a meta-analysis compiling studies predicting HEG severity, inconsistent relationships with HEG were found in studies on human chorionic gonadotropin, thyroid hormones, leptin, estradiol, progesterone, and white blood cell count; lymphocytes were found to be higher in women with HEG.In our study, although the white blood cell count was the same in all three groups, the neutrophil percentage was found to be higher in the HEG group (17). Another study found that the neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) were higher in the HEG group (18). The usefulness of these methods remains controversial, and their relative superiority is unclear.

Albumin constitutes more than half of total serum proteins. It plays a role in various functions, including osmotic regulation, antioxidant

and anti-inflammatory effects, nutrient and drug transport, and acid-base balance regulation (19). Neutrophils are also mediators involved in the inflammatory process. The combination of these two components may be used to predict HEG severity, given that vomiting leads to maternal malnutrition and pregnancy is associated with an immune response.

As this study was retrospective, single-center, and conducted in a tertiary hospital, the generalizability of the findings is limited. Due to tertiary capacity, the focus was on a patient group with complex cases, and it may reflect the performance of NPAR at a different level in different healthcare system settings. Due to the limited sample size, the predictive power may be limited and may not fully reflect the effect of rare subgroups. The true clinical diversity may not be fully represented due to cases excluded from the study (multiple pregnancies, molar pregnancies, hypertension, diabetes mellitus, psychiatric disorders, those with major fetal anomalies, and those with missing/lost data).

There are some limitations in terms of diagnosis and classification. HEG severity was classified using a modified scoring system based on PUQE-24; this approach is subject to clinically subjective biases and may lead to inconsistencies when applied by different clinicians. Furthermore, neutrophil percentage and albumin values in NPAR calculation were obtained at a single time point; dynamic changes (course, treatment effects) could not be considered.

On the other hand, examining the potential role of NPAR, which reflects inflammation and nutritional status, for early prediction of HEG severity offers a valuable perspective for clinical practice. Modifying PUQE-24 to classify HEG severity and integrating biochemical and hematological parameters could provide a broad knowledge base for clinical decisions.

The fact that the NPAR value consists of simple and widely accessible laboratory parameters, and that NPAR can rapidly reflect inflammation and nutritional status, makes it a potential decision support tool.In the severe HG group, the significant elevation of the neutrophil percentage and certain biochemical differences with NPAR are noteworthy, supporting the notion of a strengthened relationship between inflammation and nutritional status.

This study has demonstrated that NPAR shows high sensitivity in predicting disease severity in HEG patients. When evaluated together with the PUQE-24 score, NPAR may be useful as a clinical decision support tool; however, it is not sufficient for decision-making on its own.

Future studies should be conducted with prospective, multicenter designs and the development of multivariate models: The integration of inflammation and nutrition indicators such as NLR, PLR, CRP, IL-6, and total protein/albumin ratios in addition to NPAR will more clearly demonstrate the prognostic value and clinical benefit of NPAR.

Ethics Committee Approval: The study received ethical approval from the Ethics Committee of Ankara City Hospital (TABED-2-25-1629). All procedures were performed according to the Declaration of Helsinki.

Availability of Data and Materials: The data supporting this study is available through the corresponding author upon reasonable request.

Competing Interests: The authors have no relevant financial or non-financial interests to disclose.

Funding Score: The authors declare that no funds, grants, or other support were received during the preparation of this manuscript, and this research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Author Contribution: BBÖ: Design the method to achieve results, Data collecting and processing, Literature scan, Article writing; DS: Article writing, Critical examination, Critical examination

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