

Jinekoloji - Obstetrik ve Neonatoloji Tıp Dergisi

The Journal of Gynecology-Obstetrics and Neonatology

Cilt/Vol: 23 • Sayı/No: 2 • Haziran/June 2026

E-ISSN 2667-7849

Özgün Araştırma / Original Articles

Neonatoloji

- ▶ **Impact of Maternal Anemia on Neonatal Anthropometric Parameters: Weight, Length and Head Circumference**
Maternal Aneminin Yenidoğan Antropometrik Parametreleri Üzerine Etkisi: Ağırlık, Boy ve Baş Çevresi
- ▶ **Impact of COVID-19 Measures on Neonatal Respiratory Tract Infections Across Different Pandemic Periods**
Farklı Pandemi Dönemlerinde COVID-19 Önlemlerinin Yenidoğan Solunum Yolu Enfeksiyonlarına Etkisi

Genel Obstetri/Perinatoloji

- ▶ **Predictive Value of First-Trimester Inflammatory Hematological Indices for Gestational Hypertension**
Birinci Trimesterde Ölçülen İnflamatuvar Hematolojik İndekslerin Gestasyonel Hipertansiyonu Öngörmedeki Prediktif Değeri
- ▶ **Evaluation of AST/Platelet Ratio Index, AST/Creatinine Ratio Index, and AST/ALT Ratio (De Ritis) in Type 2 Diabetes Mellitus: A Tertiary Center Case-Control Study**
Tip 2 Diabetes Mellitus Tanılı Gebe Hastaların AST/Platelet Ratio Index ve AST/Kreatinin Ratio İndeks, AST/ALT Ratio İndekslerinin Değerlendirilmesi. Bir Tersiye Merkez Vaka -Kontrol Çalışması
- ▶ **Unmasking Age or Condition? A Retrospective Analysis of Neonatal Outcomes in Advanced Maternal Age Pregnancies**
Yaş mı Etken, Eşlik Eden Durumlar mı? İleri Anne Yaşında Neonatal Sonuçların Retrospektif Değerlendirmesi
- ▶ **The Effect of Diurnal Rhythm on Fetal Biophysical Profile in Term and Postterm Pregnancies**
Diurnal Ritmin Term ve Postterm Gebeliklerde Fetal Biyofizik Profil Üzerine Etkisi
- ▶ **Comparison of Liver Function-Based Scoring Systems and Development of a Predictive Model for Intrahepatic Cholestasis of Pregnancy: A Retrospective Cohort Study**
Karaciğer Fonksiyon Testlerine Dayalı Puanlama Sistemlerinin Karşılaştırılması ve Gebelikte İntrahepatik Kolestaz için Yeni Bir Tanı Modelinin Geliştirilmesi: Retrospektif Kohort Çalışması
- ▶ **Impact of COVID-19 Vaccination on Anxiety in Pregnant Women: Insights from a Cross-Sectional Study at a Tertiary Pandemic Center**
COVID-19 Aşılmasının Gebelerde Anksiyete Üzerine Etkisi: Bir Üçüncü Basamak Pandemi Merkezinde Yapılan Kesitsel Çalışmadan Bulgular
- ▶ **Comparison of Four Cervical Ripening and Labor Induction Strategies in Term Singleton Pregnancies with an Unfavorable Cervix: A Retrospective Cohort Study**
Elverişsiz Serviksi Olan Term Tekil Gebeliklerde Dört Servikal Olgunlaştırma ve Doğum İndüksiyonu Stratejisinin Karşılaştırılması: Retrospektif Kohort Çalışma

- ▶ **Association of Antenatal Education Attendance with Early Postpartum Edinburgh Postnatal Depression Scale (EPDS) Scores: A Retrospective Observational Study**
Doğum Öncesi Eğitime Katılımın Erken Edinburgh Doğum Sonrası Depresyon Ölçeği Puanlarıyla İlişkisi: Retrospektif Gözlemsel Bir Çalışma

Genel Jinekoloji

- ▶ **Expression of Endothelial and Inducible Nitric Oxide Synthases in Tubal Ectopic Pregnancy: An Immunohistochemical Evaluation**
Tubal Ektopik Gebelikte Endotelial ve İndüklenebilir Nitrik Oksit Sentazların İfadesi: Immunohistokimyasal Bir Değerlendirme
- ▶ **Menstrual Hassasiyet İndeksi: Türkçe Geçerlik ve Güvenilirlik Çalışması**
Menstrual Sensitivity Index: Turkish Validity and Reliability Study
- ▶ **Comparative Clinical Outcomes of V-NOTES and Total Laparoscopic Hysterectomy: A One-Year Retrospective Cohort Study at a Tertiary Center**
V-NOTES ve Total Laparoskopik Histerektominin Klinik Sonuçları: Üçüncü Basamak Bir Merkezde Bir Yıllık Retrospektif Kohort Çalışması
- ▶ **Anormal Uterin Kanaması Olan Ergenlerde ABO Kan Gruplarının Kanama Şiddeti ve Seyri ile İlişkisi**
The Relationship Between ABO Blood Groups and the Severity and Clinical Course of Abnormal Uterine Bleeding in Adolescents
- ▶ **The Effect of Sexual Health Education and Pelvic Floor Exercises on Body Image and Anxiety Levels in Women Diagnosed with Vaginismus**
Vajinismus Tanısı Konmuş Kadınlarda Cinsel Sağlık Eğitimi ve Pelvik Taban Egzersizlerinin Vücut Algısı ve Kaygı Düzeyleri Üzerindeki Etkisi

Jinekolojik Onkoloji

- ▶ **Change in Liver Function Tests After Liver Mobilization for Gynecologic Cancers; Does Metastasectomy Affect the Course?**
Jinekolojik Kanserlerde Karaciğer Mobilizasyonu Sonrası Karaciğer Fonksiyon Testlerindeki Değişim; Metastektomi Seyri Etkiler mi?
- ▶ **Laparoscopic Surgical Staging in Gynecologic Cancers: Nodal Adequacy and Perioperative Outcomes in 105 Patients**
Jinekolojik Kanserlerde Laparoskopik Cerrahi Evreleme: 105 Hastada Nodal Yeterlilik ve Perioperatif Sonuçlar

Olgu Sunumu / Case Report

- ▶ **Konjenital Kalp Hastalığı Nedeniyle İki Kez Fontan Ameliyatı Olan Hastada Gebelik ve Doğum: Olgu Sunumu**
Pregnancy and Childbirth in a Patient Who Underwent Two Fontan Surgeries Due To Congenital Heart Disease: Case Report

Editörden Size/ Editorial

Değerli Bilim İnsanları,

Yaz mevsiminin enerjisini hissettiğimiz bu günlerde, dergimizin 2026 yılı Haziran sayısını her zamanki enerjimiz ve heyecanımızla sizlerle buluşturmanın mutluluğunu yaşıyoruz.

Hepsi birbirinden değerli 16 özgün makale ve 1 adet olgu sunumu bu sayımızda bulunmaktadır. Neonatoloji alanında 2, obstetri-perinatoloji alanında 7 ve genel jinekoloji alanında 5 özgün makaleyi sizlerin beğenisine sunduk. Jinekolojik onkoloji alanına ait 2 araştırma makalesini de bu güzel sayımıza ekledik.

Bu sayımızda yer alan makaleler için emek veren tüm yazar ve hakemlerimize teşekkür eder, bilimin aydınlatıcı ışığında keyifli ve huzurlu bir yaz geçirmenizi dileriz...

Prof. Dr. Levent ÖZTÜRK

*Jinekoloji - Obstetrik ve Neonatoloji
Tıp Dergisi İmtiyaz Sahibi*

Prof. Dr. Özlem MORALOĞLU TEKİN

*Jinekoloji - Obstetrik ve Neonatoloji
Tıp Dergisi Baş Editörü*

İçindekiler / Contents

Özgün Araştırma / Original Articles

Neonatoloji

111 Impact of Maternal Anemia on Neonatal Anthropometric Parameters: Weight, Length and Head Circumference

Maternal Aneminin Yenidoğan Antropometrik Parametreleri Üzerine Etkisi: Ağırlık, Boy ve Baş Çevresi

Adile Nur ŞAHİN, Egemen TURAL, Akın DAYAN

118 Impact of COVID-19 Measures on Neonatal Respiratory Tract Infections Across Different Pandemic Periods

Farklı Pandemi Dönemlerinde COVID-19 Önlemlerinin Yenidoğan Solunum Yolu Enfeksiyonlarına Etkisi

Gökçe ÇIPLAK, Evrim ALYAMAC DİZDAR, Cem BECERİR, Halise MERCAN, Isil ALTAN, Aslinur OZKAYA PARLAKAY, Fatma Nur SARI

Genel Obstetri/Perinatoloji

124 Predictive Value of First-Trimester Inflammatory Hematological Indices for Gestational Hypertension

Birinci Trimesterde Ölçülen İnflamatuvar Hematolojik İndekslerin Gestasyonel Hipertansiyonu Öngörmedeki Prediktif Değeri

Aykut KINDAN, Ahmet KURT, Özgür Volkan AKBULUT, Sait ERBEY, Alican SAPMAZ, Murat POLAT

132 Evaluation of AST/Platelet Ratio Index, AST/Creatinine Ratio Index, and AST/ALT Ratio (De Ritis) in Type 2 Diabetes Mellitus: A Tertiary Center Case-Control Study

Tip 2 Diabetes Mellitus Tanılı Gebe Hastaların AST/Platelet Ratio Index ve AST/Kreatinin Ratio İndeks, AST/ALT Ratio İndekslerinin Değerlendirilmesi. Bir Tersiyeer Merkez Vaka -Kontrol Çalışması

Hüseyin KAYAAALP, Sertaç AYÇİÇEK

139 Unmasking Age or Condition? A Retrospective Analysis of Neonatal Outcomes in Advanced Maternal Age Pregnancies

Yaş mı Etken, Eşlik Eden Durumlar mı? İleri Anne Yaşında Neonatal Sonuçların Retrospektif Değerlendirmesi

Halil DEĞİRMENCİOĞLU, Enes KARAMAN

147 The Effect of Diurnal Rhythm on Fetal Biophysical Profile in Term and Postterm Pregnancies

Diurnal Ritmin Term ve Postterm Gebeliklerde Fetal Biyofizik Profil Üzerine Etkisi

Muhammed Alperen ALAYBEYOĞLU, Mehmet ÇINAR, İbrahim TAŞKUM, Cennet Meltem ALAYBEYOĞLU, Selcan SINACI

154 Comparison of Liver Function-Based Scoring Systems and Development of a Predictive Model for Intrahepatic Cholestasis of Pregnancy: A Retrospective Cohort Study

Karaciğer Fonksiyon Testlerine Dayalı Puanlama Sistemlerinin Karşılaştırılması ve Gebelikte İntrahepatik Kolestaz için Yeni Bir Tanı Modelinin Geliştirilmesi: Retrospektif Kohort Çalışması

İsmail BAGLAR, Esra KELES, Fatih ŞANLIKAN, Uğur Kemal ÖZTÜRK, Metin AYĞAR, Sahra Sultan KARA, Esra Buse ERGÜN

160 Impact of COVID-19 Vaccination on Anxiety in Pregnant Women: Insights from a Cross-Sectional Study at a Tertiary Pandemic Center

COVID-19 Aşılmasının Gebelerde Anksiyete Üzerine Etkisi: Bir Üçüncü Basamak Pandemi Merkezinde Yapılan Kesitsel Çalışmadan Bulgular

Rahime Begüm KARACUHA, Mervenur KEMENT, Orhan Seyfi AKSAKAL

168 Comparison of Four Cervical Ripening and Labor Induction Strategies in Term Singleton Pregnancies with an Unfavorable Cervix: A Retrospective Cohort Study

Elverişsiz Serviksi Olan Term Tekil Gebeliklerde Dört Servikal Olgunlaştırma ve Doğum İndüksiyonu Stratejisinin Karşılaştırılması: Retrospektif Kohort Çalışma

Cemal ÜNLÜ, Gonca TÜRKER ERGÜN, Özlem MORALOĞLU TEKİN

174 Association of Antenatal Education Attendance with Early Postpartum Edinburgh Postnatal Depression Scale (EPDS) Scores: A Retrospective Observational Study

Doğum Öncesi Eğitime Katılımın Erken Edinburgh Doğum Sonrası Depresyon Ölçeği Puanlarıyla İlişkisi: Retrospektif Gözlemsel Bir Çalışma

Berna SEYHAN, Hasan Mert BAŞBUĞA, Hamza Arda AÇIKGÖZ, Emel ÖZALP, Çağanay SOYSAL

Genel Jinekoloji

182 Expression of Endothelial and Inducible Nitric Oxide Synthases in Tubal Ectopic Pregnancy: An Immunohistochemical Evaluation

Tubal Ektopik Gebelikte Endotelial ve İndüklenebilir Nitrik Oksit Sentazların İfadesi: Immunohistokimyasal Bir Değerlendirme

Fatma ESKİCİOĞLU, Tuna ONAL, Melis Aylin UNER AKMAN, Semih TASKENT, Tulay GOKMEN, Kemal OZBİLGİN

190 Menstrual Hassasiyet İndeksi: Türkçe Geçerlik ve Güvenirlik Çalışması

Menstrual Sensitivity Index: Turkish Validity and Reliability Study

Ebru İNAN KIRMIZIGÜL, Didem ŞİMŞEK KÜÇÜKKELEPÇE

Jinekoloji - Obstetrik ve Neonatoloji Tıp Dergisi

The Journal of Gynecology-Obstetrics and Neonatology

Cilt/Vol: 23 • Sayı/No: 2 • Haziran/June 2026

198 Comparative Clinical Outcomes of V-NOTES and Total Laparoscopic Hysterectomy: A One-Year Retrospective Cohort Study at a Tertiary Center

V-NOTES ve Total Laparoskopik Histerektominin Klinik Sonuçları: Üçüncü Basamak Bir Merkezde Bir Yıllık Retrospektif Kohort Çalışması
Alaattin KARABULUT, Sercan KANTARCI, Uğurcan DAĞLI, Fatih YILDIRIM, Serhat SARIKAYA, Abdurrahman Hamdi İNAN, Adnan BUDAK, Alper İLERİ

203 Anormal Uterin Kanaması Olan Ergenlerde ABO Kan Gruplarının Kanama Şiddeti ve Seyri ile İlişkisi

The Relationship Between ABO Blood Groups and the Severity and Clinical Course of Abnormal Uterine Bleeding in Adolescents
Demet AYGÜN ARI, Gürses ŞAHİN, Semra ÇETİNKAYA

209 The Effect of Sexual Health Education and Pelvic Floor Exercises on Body Image and Anxiety Levels in Women Diagnosed with Vaginismus

Vajinismus Tanısı Konmuş Kadınlarda Cinsel Sağlık Eğitimi ve Pelvik Taban Egzersizlerinin Vücut Algısı ve Kaygı Düzeyleri Üzerindeki Etkisi
Gonca TURKER ERGUN, Ayşe KUYULU AKMAN

Jinekolojik Onkoloji

215 Change in Liver Function Tests After Liver Mobilization for Gynecologic Cancers; Does Metastasectomy Affect the Course?

Jinekolojik Kanserlerde Karaciğer Mobilizasyonu Sonrası Karaciğer Fonksiyon Testlerindeki Değişim; Metastazektomi Seyri Etkiler mi?
Halise Meltem BATUR, Burak ERSK, Mehmet UNSAL, Günsu Kimyon COMERT, Mert İshak KAYA, Melih Emre TORUN,
Gonca TÜRKER ERGÜN, Aziz Ahmet SUREL, Taner TURAN

221 Laparoscopic Surgical Staging in Gynecologic Cancers: Nodal Adequacy and Perioperative Outcomes in 105 Patients

Jinekolojik Kanserlerde Laparoskopik Cerrahi Evreleme: 105 Hastada Nodal Yeterlilik ve Perioperatif Sonuçlar
Özgün CEYLAN, Tuba ZENGİN AKSEL, Mustafa ŞAHİN

Olgu Sunumu / Case Report

228 Konjenital Kalp Hastalığı Nedeniyle İki Kez Fontan Ameliyatı Olan Hastada Gebelik ve Doğum: Olgu Sunumu

Pregnancy and Childbirth in a Patient Who Underwent Two Fontan Surgeries Due To Congenital Heart Disease: Case Report
Vefa ŞAKAR, Kübra Dilşad SÖNMEZ ÖZGÜR, Özhan ÖZDEMİR

Impact of Maternal Anemia on Neonatal Anthropometric Parameters: Weight, Length and Head Circumference

Maternal Aneminin Yenidoğan Antropometrik Parametreleri Üzerine Etkisi: Ağırlık, Boy ve Baş Çevresi

 Adile Nur ŞAHİN¹,  Egemen TURAL²,  Akın DAYAN³

¹Sancaktepe District Health Directorate, İstanbul, Türkiye

²Kağıthane District Health Directorate, İstanbul, Türkiye

³Department of Family Medicine, Haydarpaşa Numune Training and Research Hospital, İstanbul, Türkiye

ABSTRACT

Aim: Although many studies have investigated anemia, the evidence concerning how its severity impacts maternal and fetal health remains scarce and inconsistent. Our study aimed to evaluate the effects of maternal hemoglobin levels in the first and second trimesters on neonatal length, weight, and head circumference.

Materials and Methods: This retrospective, cross-sectional study was conducted with 146 individuals who underwent pregnancy and neonatal follow-up at a Family Health Center in İstanbul between January 1, 2019, and December 31, 2020. The demographic characteristics of the pregnant women and their hemogram values from the first and second trimesters were recorded. Neonatal length, weight, and head circumference at birth were also measured and compared. A statistical significance level of 0.05 was used.

Results: The average age of the pregnant women was 29.0±4.8 years, with hemoglobin levels recorded at 11.9±1.1 g/dL in the first trimester and 11.7±1.4 g/dL in the second trimester. Newborns of mothers with first-trimester anemia showed modest but statistically significant reductions in birth weight, head circumference, and length compared with those of non-anemic mothers (p=0.002, p=0.044, p<0.001, respectively). No significant differences were found between mothers with and without anemia in the second trimester (p>0.05). First trimester hemoglobin levels were significant negative predictors of neonatal weight (p=0.011) and length (p=0.002).

Conclusion: First trimester anemia appeared to be associated with lower birth in newborns, but this difference was not seen in the second trimester. These findings suggest a possible influence of earlier maternal anemia on fetal growth, underscoring the value of routine screening and timely management in Family Health Centers.

Keywords: Anemia, Birth Weight, Pregnancy, Hemoglobin

ÖZ

Amaç: Anemi üzerine birçok çalışma yapılmış olmasına rağmen, aneminin şiddetinin maternal ve fetal sağlık üzerindeki etkilerine ilişkin kanıtlar hâlâ sınırlı ve tutarsızdır. Bu çalışmada, gebeliğin birinci ve ikinci trimesterlerindeki maternal hemoglobin düzeylerinin yenidoğanın boyu, ağırlığı ve baş çevresi üzerine etkilerini değerlendirmek amaçlanmıştır.

Gereç ve Yöntemler: Retrospektif, kesitsel nitelikteki bu çalışma, 1 Ocak 2019-31 Aralık 2020 tarihleri arasında İstanbul'daki bir Aile Sağlığı Merkezi'nde gebelik ve yenidoğan takibi yapılmış 146 birey üzerinde gerçekleştirilmiştir. Gebelerin demografik özellikleri ve birinci ile ikinci trimesterlerdeki hemogram değerleri kaydedilmiştir. Yenidoğanların doğumdaki boy, ağırlık ve baş çevresi ölçümleri alınmış ve karşılaştırılmıştır. İstatistiksel anlamlılık düzeyi 0,05 olarak kabul edilmiştir.

Bulgular: Gebelerin ortalama yaşı 29,0±4,8 yıl olup, birinci trimester hemoglobin düzeyi 11,9±1,1 g/dL, ikinci trimester hemoglobin düzeyi ise 11,7±1,4 g/dL olarak bulunmuştur. Birinci trimesterde anemisi olan annelerin yenidoğanlarında doğum ağırlığı, baş çevresi ve boy uzunluğu açısından, anemisi olmayanlara göre hafif düzeyde ancak istatistiksel olarak anlamlı düşüşler gözlenmiştir (sırasıyla p=0.002, p=0.044, p<0.001). İkinci trimesterde anemisi olan ve olmayan annelerin yenidoğanları arasında anlamlı fark saptanmamıştır (p>0,05). Birinci trimester hemoglobin düzeyleri, yenidoğan ağırlığı (p=0,011) ve boyu (p=0,002) için anlamlı negatif yordayıcı bulunmuştur.

Sonuç: Birinci trimesterdeki aneminin yenidoğanda daha düşük doğum ölçüleriyle ilişkili olabileceği görülmüş, ancak bu ilişki ikinci trimesterde gözlenmemiştir. Bu bulgular, erken gebelik dönemindeki maternal aneminin fetal büyüme üzerinde olası bir etkisi olabileceğini düşündürmekte ve Aile Sağlığı Merkezlerinde rutin tarama ile zamanında yönetimin önemini vurgulamaktadır.

Anahtar Kelimeler: Anemi, Doğum Ağırlığı, Gebelik, Hemoglobin

Cite as: Şahin AN, Tural E, Dayan A. Impact of Maternal Anemia on Neonatal Anthropometric Parameters: Weight, Length and Head Circumference. Jinekoloji-Obstetrik ve Neonatoloji Tıp Dergisi 2026;23(2):111–117.

Geliş/Received: 31.08.2025 • **Kabul/Accepted:** 06.01.2026

Sorumlu Yazar/Corresponding Author: Egemen Tural, Kağıthane District Health Directorate, İstanbul, Türkiye

E-mail: egementural1@gmail.com

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

INTRODUCTION

Hemoglobin (Hb) is a risk factor for unfavorable pregnancy outcomes that can potentially be modified. Anemia during pregnancy is characterized by a Hb concentration of less than 110 g/L (11 g/dL) at sea level (1). During the first trimester, the demand for iron decreases due to the absence of menstruation. However, in the second trimester, the increased red cell mass and the rapid growth of the fetus lead to a continuous rise in iron requirements. If these iron needs are not met, anemia develops in the pregnant woman (2,3).

According to the most recent report from the World Health Organization, anemia prevalence among women aged 15 to 49, both pregnant and non-pregnant, has increased in most countries between 2012 and 2016 (4).

Iron deficiency anemia in pregnancy is linked to higher risks of low birth weight, early delivery, and perinatal mortality (5). Maternal anemia may negatively influence fetal growth through physiologic mechanisms such as reduced oxygen transportation to the fetus and inadequate iron reserves during early pregnancy, as highlighted in a recent systematic review and meta-analysis (6). Several studies have reported that infants born to anemic mothers tend to have slightly lower anthropometric measurements, including birth weight, length, head circumference, and mid-arm circumference (7,8).

During pregnancy, normal shifts in blood volume cause a physiological form of anemia. Nevertheless, when maternal hemoglobin levels fall below 7 g/dL, this severe anemia impairs fetal oxygen supply, leading to concerning fetal heart rate changes, reduced amniotic fluid levels, cerebral vasodilation in the fetus, and, in some cases, fetal death (9).

Despite numerous studies on anemia, the data regarding the relationship between the severity of anemia and maternal-fetal health are limited and contradictory (10-12). There is some limited evidence indicating that severe anemia could elevate the risk of low birth weight, whereas mild anemia might offer a degree of protection against it (13). Anemia is a common medical condition affecting pregnancy, particularly in low- and middle-income countries, making it crucial to understand the impact of maternal anemia levels on newborn outcomes (14).

In our study, we aimed to evaluate the effects of maternal hemoglobin levels in the first and second trimesters on neonatal length, weight, and head circumference.

MATERIALS AND METHODS

Patients and Ethical Approval

This study is a retrospective, cross-sectional research. The medical records of pregnant women and their newborns who were followed at a Family Health Center in Istanbul between January 1, 2019, and December 31, 2020, were reviewed, and 157 pregnant women were considered as the study population. A sample size calculation determined that the minimum required number of participants was 127. Considering a potential 15% loss, 146 participants were randomly selected using simple random sampling. The Clinical Research Ethics Committee of the Training and Research Hospital granted ethical approval for the study, with decision number 2022/KK/88, on May 30, 2022.

Inclusion and Exclusion Criteria

Pregnant women with singleton pregnancies whose demographic data were recorded were included in the study. Those with multiple pregnancies, pregestational or gestational chronic illnesses, acute bleeding, conditions affecting blood parameters such as thalassemia, and severe anemia (Hb <7 g/dL) were excluded from the study.

Study Design

The demographic characteristics and hemogram values of the pregnant women were recorded, along with the birth weight, head circumference and length of the newborns. Pregnant women were divided into two categories: those with anemia (hemoglobin levels less than 11 g/dL) and those without anemia (hemoglobin levels of 11 g/dL or more). Additionally, newborns delivered between 37 and 42 weeks were recorded as term, while those born before 37 weeks were categorized as preterm.

Both term and preterm infants followed in the same family health center were included in the analysis to reflect real-life primary care practice. Out of the 146 pregnant women included in the study, 39 did not have their second trimester Hb values monitored. The anemia group consisted of 146 women during the first trimester, while 107 were evaluated during the second trimester. The first and second hemoglobin values measured during pregnancy were recorded. The first measurement was taken up to the 10th week, while the second measurement was conducted between the 20th and 30th weeks. Hemoglobin levels were measured using the "Cyanide-free SLS hemoglobin" method on a Sysmex XN-1000 (Sysmex Europe GMBH, Bornbach, Germany) automated hematology analyzer.

Statistical Analysis

This study employed descriptive statistics to summarize the data. Continuous variables were expressed as mean $\pm$ standard deviation or median with their corresponding minimum and maximum

values based on distribution. Categorical variables were shown as counts and percentages, and normality of numerical variables was evaluated visually and via the Shapiro-Wilk test.

For comparing categorical variables in 2x2 contingency tables, the Pearson Chi-Square test was used for expected cell counts of 5 or more. Independent groups were analyzed with the Independent Samples T-Test for normally distributed variables and the Mann-Whitney U test for non-normally distributed ones. Relationships among non-normally distributed numerical variables were examined using the Spearman's Rho correlation coefficient. Factors affecting newborn weight, head circumference, and length were analyzed through univariate and multiple linear regression models. Statistical analyses utilized Jamovi (Version 2.2.5.0) and JASP (Version 0.16.1) software, with a significance threshold of 0.05.

RESULTS

The study included 146 pregnant women with a mean age of 29.0 ± 4.8 years. Hemoglobin levels averaged 11.9 ± 1.1 g/dL in the first trimester and 11.7 ± 1.4 g/dL in the second trimester. Among the deliveries, 140 were mature and 6 were premature, with anemia rates of 17.1% in the first trimester and 23.4% in the second trimester (Table 1).

Of the 146 newborns, 71 were boys and 75 were girls. The median birth weight was 3300 [1350.0 – 4800.0] grams, with a length of 50.0 [43.0 – 53.0] cm and a head circumference of 35.0 [31.0 – 38.0] cm (Table 2). Mothers with first trimester anemia had a higher median age (30 years) compared to those

Table 2. Demographic and Clinical Characteristics of Newborns

	Total (n=146)
Gender *	
Female	75 (51.4)
Male	71 (48.6)
Head Circumference (cm) ‡	35.0 [31.0 – 38.0]
Weight (gr) §	3300.0 [1350.0 – 4800.0]
Length (cm) §	50.0 [43.0 – 53.0]

*, n (%), ‡, median [minimum-maximum]

Abbreviations: n: number, cm: centimeter, gr: gram

without anemia (28 years; $p=0.041$). Newborn gender distribution was similar across groups ($p=0.466$). Babies of anemic mothers showed lower weight (3000.0 [2400.0–4200.0] g vs. 3320.0 [1350.0–4800.0] g), head circumference (34.0 [32.0–38.0] cm vs. 35.0 [31.0–37.0] cm), and length values (48.0 [45.0–52.0] cm vs. 50.0 [43.0–53.0] cm) ($p=0.002$, $p = 0.044$, $p<0.001$, respectively), while no significant differences were noted in the second trimester ($p>0.05$) (Table 3).

Negative correlations were found between newborn length and maternal age ($r = -0.166$, $p = 0.046$), and positive correlations with first trimester hemoglobin levels ($r = 0.167$, $p = 0.044$). Other correlations were not significant ($p>0.05$) (Table 4).

Table 5 shows regression analysis results indicating that first trimester anemia significantly predicted lower newborn weight ($p=0.011$) and length ($p = 0.002$).

DISCUSSION

Our results demonstrated that newborns of mothers with first-trimester anemia had significantly lower birth weights, shorter lengths, and smaller head circumferences compared to those of non-anemic mothers. Furthermore, first-trimester anemia emerged as statistically significant negative predictors of newborn weight and length, suggesting that maternal anemia in early pregnancy may influence fetal development. The observed differences in neonatal length and head circumference were small in magnitude, yet reached statistical significance. These findings may reflect subtle effects of reduced maternal hemoglobin levels on fetal oxygenation and linear growth, although the clinical relevance of these differences is limited.

We identified anemia in 25 out of 146 pregnant women in the first trimester (17.1%) and in 25 women in the second trimester

Table 1. Maternal Characteristics

	Total (n=146)
Maternal Age (years) *	29.0 ± 4.8
1st Trimester Hemoglobin (g/dL) #	11.9 ± 1.1
1st Trimester Anemia Group (n=146) *	
No Anemia (Hemoglobin ≥ 11 g/dL)	121 (82.9)
Anemia Present (Hemoglobin <11 g/dL)	25 (17.1)
2nd Trimester Hemoglobin (g/dL) #	11.7 ± 1.4
2nd Trimester Anemia Group (n=107) *	
No Anemia (Hemoglobin ≥ 11 g/dL)	82 (76.6)
Anemia Present (Hemoglobin <11 g/dL)	25 (23.4)

*, n (%), #: mean $\pm$ standard deviation

Abbreviations: n: number, g:gram, dL: decilitre

Table 3. Comparison of Maternal and Newborn Characteristics Among Pregnant Women with and without Anemia in the First and Second Trimester

	First Trimester Anemia Status			Second Trimester Anemia Status		
	No Anemia (n=121)	Anemia Present (n=25)	p	No Anemia (n=82)	Anemia Present (n=25)	p
Mother's Age (years) [§]	28.0 [19.0 – 40.0]	30.0 [23.0 – 40.0]	0.041*	29.0 [19.0 – 39.0]	30.0 [19.0 – 39.0]	0.682*
Newborn						
Gender [†]						
Female	60 (49.6)	15 (60.0)	0,466***	43 (52.4)	15 (60.0)	0.664***
Male	61 (50.4)	10 (40.0)		39 (47.6)	10 (40.0)	
Weight (gr) ^{§-#}	3320.0 [1350.0 – 4800.0] [§]	3000.0 [2400.0 – 4200.0] [§]	0.002*	3328.9 ± 531.8 [#]	3291.8 ± 560.3 [#]	0,71**
Length (cm) [§]	50.0 [43.0 – 53.0]	48.0 [45.0 – 52.0]	<0.001*	50.0 [45.0 – 53.0]	49.0 [45.0 – 52.0]	0.210*
Head Circumference (cm) [§]	35.0 [31.0 – 37.0]	34.0 [32.0 – 38.0]	0.044*	35.0 [32.0 – 38.0]	35.0 [32.0 – 36.0]	0.357*

†: n (%), §: median [minimum-maximum], #: mean ± standard deviation, *: Mann-Whitney U test, **: Independent Samples T-Test,***: Pearson Chi-Square, Abbreviations: n: number, cm: centimeter, gr: gram

Table 4. Correlation of Gestational Age, First and Second Trimester Hemoglobin Values with Newborns' Morphometric Characteristics at Birth

	Maternal Age		1st Trimester Hemoglobin		2nd Trimester Hemoglobin	
	Rho	p	Rho	p	Rho	p
Maternal Age	-	-	-0.144	0.084	-0.077	0.430
Newborn-Weight	-0.072	0.386	0.147	0.076	-0.023	0.814
Newborn- Length	-0.166	0.046	0.167	0.044	0.033	0.740
Newborn- Head Circumference	-0.122	0.143	0.041	0.623	-0.008	0.933

Spearman's rho correlation coefficient was used.

Table 5. Regression Analysis of Variables Affecting Newborns' Morphometric Characteristics at Birth.

Dependent Variable	B	Beta	p	%95 CI	
				Lower Bound	Upper Bound
Newborn - Weight (gr)					
Maternal Age (Years)	1.17	4.36	0.637	-13.71	22.44
First Trimester Anemia	-292.61	-299.97	0.011	-527.7	-72.25
Newborn-Length (cm)					
Maternal Age (Years)	-0.03	-0.02	0.425	-0.08	0.03
First Trimester Anemia	-1.15	-1.11	0.002	-1.81	-0.04
Newborn-Head Circumference (cm)					
Maternal Age (Years)	-0.01	-0.01	0.619	-0.04	-0.03
First Trimester Anemia	-0.3	-0.29	0.213	-0.74	0.16

Abbreviations: cm: centimeter, gr: gram CI: confidence interval.

(%23.4). Similarly, a study by Tekbaş et al. found that %17.2 of their group of 430 pregnant women had anemia. In that study, the prevalence of anemia was %10.4 in the first trimester, %21.5 in

the second trimester, and %27.7 in the third trimester (15). Another study involving over 5000 pregnant women in Turkey reported an anemia prevalence of %20 at the time of pregnancy diagnosis (16).

Comparing these findings with our results, we observed that the anemia prevalence among the pregnant women in our study aligns closely with national data.

Malhotra et al. reported that severe anemia (Hb <7 g/dL) increases the rates of low birth weight, labor induction, operative delivery, and prolonged labor. In contrast, they found that pregnant women with mild anemia (Hb 9-10.9 g/dL) had the best perinatal outcomes (13). They attributed this to the better placental perfusion in mildly anemic women, which is likely due to increased plasma volume compared to women with higher hemoglobin levels (Hb >11 g/dL). Adequate nutrient transport to the fetus during pregnancy requires an increase in plasma volume. High hemoglobin levels may lead to increased blood viscosity, reducing placental perfusion and potentially causing placental infarcts, which can result in intrauterine growth restriction (17,18). Xiong et al. conducted a meta-analysis of studies from 1966 to 1999 and found that anemia detected in the first and second trimesters slightly increases the risk of preterm birth; however, no effect was observed for anemia in the third trimester. According to their findings, anemia in the first trimester is not associated with low birth weight, while a negative relationship exists between third-trimester anemia and low birth weight (19). Severe anemia (Hb<7 g/dL) can lead to low birth weight and preterm labor due to maternal complications such as hemoglobinopathy, malnutrition, chronic infection, and inadequate prenatal care, which can also contribute to the development of anemia itself. When severe anemia is excluded, mild anemia (Hb 10-11 g/dL) may not lead to poor perinatal outcomes. Lao et al. compared pregnant women who experienced anemia throughout pregnancy with those without anemia complaints and concluded that anemia does not adversely affect perinatal outcomes (20). Haliloğlu et al. conducted a study in 2007 involving a total of 750 anemic and non-anemic women in the third trimester, finding no statistically significant difference in birth weight between the two groups (11). Similarly, Paiva Ade et al. in 2007 studied 95 pregnant women and also reported no differences in newborn birth weight between anemic and non-anemic mothers (21). In contrast, Rahmati et al. argued in their review and meta-analysis that maternal anemia in the first trimester could be a risk factor for poorer pregnancy outcomes (22). Similarly, Lone et al. studied 626 pregnant women, comparing those with and without anemia, and found that the risk of preterm birth was four times higher, the risk of low birth weight was 1.9 times higher, the likelihood of low APGAR scores was 1.8 times greater, and the rate of intrauterine death was 3.7 times higher in anemic mothers (12). The heterogeneity and occasional inconsistency observed across studies may be explained by differences in the timing of anemia assessment, variability in anemia severity, methodological disparities including sample size and adjustment for key confounders, and population-

specific factors such as nutritional status and access to prenatal care. These variations likely contribute to the differing conclusions regarding the impact of maternal anemia on neonatal outcomes. Our study identified negative outcomes, particularly lower birth weight, associated with first-trimester maternal anemia. This association may be partly explained by impaired fetal oxygenation and inadequate maternal iron stores in early pregnancy, mechanisms that have been described in previous research (6). Additionally, because physiologic hemodilution and plasma-volume expansion predominantly occur later in pregnancy, anemia detected in the first trimester may reflect inadequate early placental adaptation rather than the improved perfusion described in mild, late-gestational anemia. This could partly explain why our study observed adverse neonatal anthropometric outcomes only in early-pregnancy anemia. Although the reductions we observed were statistically significant, the median birth weight, length, and head circumference values in both groups remained within expected normal ranges for term infants. This suggests that the differences likely represent modest variations rather than clinically severe growth restriction. Nonetheless, the consistent decrease across several anthropometric parameters indicates that early-pregnancy anemia may still have a measurable impact on fetal growth.

In our study, the average age of pregnant women with anemia in the first trimester was 30 years, compared to 28 years for non-anemic women, indicating that anemic pregnant women were generally older. However, correlation analysis indicated no significant relationship between age and anemia. Similarly, a study conducted by Çıtlı et al. in our country reported no association between age groups and anemia during pregnancy (23). However, a study involving 20,000 live births determined that the relationship between maternal age and birth weight could vary across racial groups. It was demonstrated that for women in the white racial group, birth weight increased until the age of 30, followed by a slight decrease, whereas for women in the black racial group, there was a tendency for birth weight to decrease with age starting from adolescence (24). Vandekerckhove et al. (25) and Hochler et al. (26) reported an increased risk of low birth weight in older pregnancies compared to younger ones. In our study, there was no difference in average birth weight between the groups concerning maternal age, although this may be due to the insufficient number of premature patients.

In a study conducted in China with the participation of over 28,000 pregnant women, it was observed that those who received iron supplementation during pregnancy had higher birth weights for their newborns (27). A review and meta-analysis conducted by Haider et al. indicate that iron supplementation during pregnancy is associated with increased birth weight and a reduced risk of

low birth weight (28). In our country, iron supplements containing elemental iron are currently used during pregnancy and for a total of nine months postpartum as part of an ongoing iron support program for pregnant women.

Limitations

Our study has several limitations. First, among the 146 pregnant women included, 39 had no documented second-trimester hemoglobin values; therefore, while all participants were evaluated in the first trimester, only 107 could be analyzed in the second trimester. Second, although the number of premature births in the cohort was very small, we could not perform a gestational age-stratified analysis, and their inclusion may have influenced neonatal anthropometric measurements to a limited extent. Third, hemoglobin values were recorded only as continuous measurements, and anemia severity categories (mild vs. moderate) could not be evaluated separately. Information regarding iron supplementation (dose, timing, and adherence) was not available in our dataset and therefore could not be evaluated, which represents an additional limitation of the study. In addition, several potential confounding factors that may influence fetal growth such as maternal BMI, parity, interpregnancy interval, socioeconomic status, nutritional status, and tobacco or substance use were not assessed in this study, which may limit full adjustment for confounding. Furthermore, maternal nutritional status, including dietary iron intake, could not be assessed, although it is an important determinant of both maternal hemoglobin levels and fetal growth. Moreover, the sample size was relatively limited, which may have reduced the statistical power for subgroup analyses. Finally, the single-center design and inclusion of patients from only one family medicine unit may limit the generalizability of our findings.

CONCLUSION

Newborns of mothers with first-trimester anemia had significantly lower birth weights, shorter lengths, and smaller head circumferences compared to those of non-anemic mothers, a difference not observed in the second trimester. These findings suggest that early pregnancy anemia may adversely affects fetal development.

Although our study does not directly evaluate the effectiveness of iron supplementation, the observed association emphasizes the importance of early screening and timely management of anemia within routine prenatal care. Strengthening hemoglobin monitoring and ensuring access to appropriate preventive and therapeutic interventions in family health centers may contribute to improved maternal and neonatal outcomes.

Authorship Contributions: Conception – A.N.Ş., E.T., A.D.; Design – A.N.Ş., E.T., A.D.; Supervision – A.N.Ş., E.T., A.D.; Materials – A.N.Ş., A.D.; Data collection and/or processing – A.N.Ş., E.T.; Analysis and/or interpretation – A.N.Ş.; Literature review – A.N.Ş., A.D.; Writing – A.N.Ş., E.T.; Critical review – A.N.Ş., E.T., A.D.

Acknowledgment: This study was presented as a poster at the 12th Congress of Family Medicine with International Participation-AHEKON 2022.

Declaration of Conflicting Interests: The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding: The authors received no financial support for the research, authorship, and/or publication of this article.

Ethics Committee Approval: Approval was obtained from the ethics committee of Haydarpaşa Numune Training and Research Hospital (Approval date: May 30, 2022, and Approval number: 2022/KK/88). The administrative approval required for conducting the research was granted by the Evaluation Commission for Research, Printed Publications, and Announcement Content of the Provincial Health Directorate Health Services Department, in accordance with Decision No. 2022/05, dated February 25, 2022.

REFERENCES

1. Stevens GA, Finucane MM, De-Regil LM, Paciorek, CJ, Flaxman SR, Branca F. et al. Global, regional, and national trends in haemoglobin concentration and prevalence of total and severe anaemia in children and pregnant and non-pregnant women for 1995-2011: a systematic analysis of population-representative data. *Lancet Glob Health*. 2013;1(1):e16-e25. doi:10.1016/S2214-109X(13)70001-9
2. Bothwell TH. Iron requirements in pregnancy and strategies to meet them. *Am J Clin Nutr*. 2000;72(1 Suppl):257S-264S. doi:10.1093/ajcn/72.1.257S
3. Prakash S, Yadav K. Maternal Anemia in Pregnancy: An Overview. *Ijpr Human*, 2015; Vol. 4 (3): 164-79.
4. World Health Organization. Global anemia reduction efforts among women of reproductive age: impact, achievement of targets and the way forward for optimizing efforts. World Health Organization; 2020. Accessed October 12, 2024. Available from: <https://www.who.int/publications/item/9789240012202>
5. Horowitz KM, Ingardia CJ, Borgida AF. Anemia in pregnancy. *Clin Lab Med*. 2013;33(2):281-91. doi:10.1016/j.cl.2013.03.016
6. Sukrat B, Wilasrusmee C, Siribumrungwong B, McEvoy M, Okascharoen C, Attia J, et al. Hemoglobin concentration and pregnancy outcomes: a systematic review and meta-analysis. *Biomed Res Int*. 2013;2013:769057. doi:10.1155/2013/769057
7. Srimani P, Sengupta D, Bharati P, Bharati S. The effect of maternal anemia on different anthropometric parameters of newborns- A case-control study. *J Family Med Prim Care*. 2025;14(5):1735-1740. doi:10.4103/jfmpc.jfmpc_1229_24
8. Shankar V, Karthik S, Krishnappa J, Srikanth C. Effect of maternal anaemia on neonatal anthropometry: a cross-sectional study. *J Neonatal Surg*. 2025;14(24 Suppl):21-23.
9. Sifakis S, Pharmakides G. Anemia in pregnancy. *Ann N Y Acad Sci*. 2000;900:125-136. doi:10.1111/j.1749-6632.2000.tb06223.x
10. Shi H, Chen L, Wang Y, Sun M, Guo Y, Ma S. et al. Severity of anemia during pregnancy and adverse maternal and fetal outcomes. *JAMA Netw Open*. 2022;5(2):e2147046. doi:10.1001/jamanetworkopen.2021.47046
11. Haliloğlu B, Şahin FK, Gürbüz A, Peker H. Üçüncü trimester maternal total protein, albumin ve hemoglobin seviyelerinin doğum kilosuna etkisi. *Journal of Turkish Obstetric and Gynecology Society* 2007;4(4):254-8.
12. Lone FW, Qureshi RN, Emmanuel F. Maternal anaemia and its impact on perinatal outcome in a tertiary care hospital in Pakistan. *East Mediterr Health J*. 2004;10(6):801-7.
13. Malhotra M, Sharma JB, Batra S, Sharma S, Murthy NS, Arora R. Maternal and perinatal outcome in varying degrees of anemia. *Int J Gynaecol Obstet*. 2002;79(2):93-100. doi:10.1016/s0020-7292(02)00225-4

14. Allen LH. Anemia and iron deficiency: effects on pregnancy outcome. *Am J Clin Nutr*. 2000;71(5 Suppl):1280S-4S. doi:10.1093/ajcn/71.5.1280s
15. Tekbaş ÖF, Hasde M, Atay V. Bir tıp fakültesi kadın hastalıkları ve doğum polikliniğinde izlenen gebelerde anemi sıklığı. *GATA Bülteni*. 1997;39(1):20-5.
16. Öztürk M, Öztürk Ö, Ulubay M, Karasahin E, Özgürtaş T, Yenen M, et al. Anemia prevalence at the time of pregnancy detection. *Turk J Obstet Gynecol*. 2017;14(3):176-80. doi:10.4274/tjod.06337
17. Steer P, Alam MA, Wadsworth J, Welch A. Relation between maternal haemoglobin concentration and birth weight in different ethnic groups. *BMJ*. 1995;310(6978):489-91. doi:10.1136/bmj.310.6978.489
18. Schwartz WJ 3rd, Thurnau GR. Iron deficiency anemia in pregnancy. *Clin Obstet Gynecol*. 1995;38(3):443-54. doi:10.1097/00003081-199509000-00004
19. Xiong X, Buekens P, Alexander S, Demianczuk N, Wollast E. Anemia during pregnancy and birth outcome: a meta-analysis. *Am J Perinatol*. 2000;17(3):137-46. doi:10.1055/s-2000-9508
20. Lao TT, Pun TC. Anaemia in pregnancy--is the current definition meaningful?. *Eur J Obstet Gynecol Reprod Biol*. 1996;68(1-2):53-8. doi:10.1016/0301-2115(96)02479-7
21. Paiva Ade A, Rondó PH, Pagliusi RA, Latorre Mdo R, Cardoso MA, Gondim SS. Relationship between the iron status of pregnant women and their newborns. *Rev Saude Publica*. 2007;41(3):321-7. doi:10.1590/s0034-89102007000300001
22. Rahmati S, Delpishe A, Azami M, Hafezi Ahmadi MR, Sayehmiri K. Maternal anemia during pregnancy and infant low birth weight: A systematic review and Meta-analysis. *Int J Reprod Biomed*. 2017;15(3):125-34.
23. Çıtlı R, Yakıştıran Barut S, Eğri M, Önder Y. Devlet hastanesine başvuran gebelerde anemi görülme sıklığı ve etkileyen faktörler. *J Contemp Med*. 2014;4(2):76-83.
24. Shmueli A, Cullen MR. Birth weight, maternal age, and education: new observations from Connecticut and Virginia. *Yale J Biol Med*. 1999;72(4):245-58.
25. Vandekerckhove, M., Guignard, M., Civadier, MS. et al. Impact of maternal age on obstetric and neonatal morbidity: a retrospective cohort study. *BMC Pregnancy Childbirth*. 2021; 21, 732. doi:10.1186/s12884-021-04177-7
26. Hochler H, Lipschuetz M, Suissa-Cohen Y, Weiss A, Sela HY, Yagel S, et al. The impact of advanced maternal age on pregnancy outcomes: a retrospective multicenter study. *J Clin Med*. 2023;12(17):5696. doi:10.3390/jcm12175696
27. Shi G, Zhang Z, Ma L, Zhang B, Dang S, Yan H. Association between maternal iron supplementation and newborn birth weight: a quantile regression analysis. *Ital J Pediatr*. 2021;47(1):133. doi:10.1186/s13052-021-01084-7
28. Haider BA, Olofin I, Wang M, Spiegelman D, Ezzati M, Fawzi WW, et al. Anaemia, prenatal iron use, and risk of adverse pregnancy outcomes: systematic review and meta-analysis. *BMJ*. 2013;346:f3443. doi:10.1136/bmj.f3443

Impact of COVID-19 Measures on Neonatal Respiratory Tract Infections Across Different Pandemic Periods

Farklı Pandemi Dönemlerinde COVID-19 Önlemlerinin Yenidoğan Solunum Yolu Enfeksiyonlarına Etkisi

● Gökçe ÇIPLAK^{1*}, ● Evrim ALYAMAC DİZDAR², ● Cem BECERİR³, ● Halise MERCAN⁴, ● Isil ALTAN⁵, ● Aslinur OZKAYA PARLAKAY⁶,
● Fatma Nur SARI⁷

¹Specialist in Neonatology, MD, Ankara Bilkent City Hospital, University of Health Sciences, Department of Neonatology, Ankara, Türkiye

²Professor of Pediatrics and Neonatology, Ankara Bilkent City Hospital, University of Health Sciences, Department of Neonatology, Ankara, Türkiye

³Specialist in Neonatology, MD, Ankara Bilkent City Hospital, University of Health Sciences, Department of Neonatology, Ankara, Türkiye

⁴Specialist in Pediatrics, MD, Ankara Bilkent City Hospital, University of Health Sciences, Department of Pediatrics, Ankara, Türkiye

⁵Specialist in Pediatrics, MD, Ankara Bilkent City Hospital, University of Health Sciences, Department of Pediatrics, Ankara, Türkiye

⁶Professor of Pediatrics Infectious Disease, Ankara Bilkent City Hospital, Ankara Yıldırım Beyazıt University, Department of Pediatric Infectious Disease, Ankara, Türkiye

⁷Professor of Pediatrics and Neonatology, Ankara Bilkent City Hospital, University of Health Sciences, Department of Neonatology, Ankara, Türkiye

ABSTRACT

Aim: Infection control measures during the COVID-19 pandemic significantly reduced SARS-CoV-2 spread. These measures, widely implemented nationally and globally, also had a notable impact on the transmission of other viruses. We aimed to evaluate the effect of two different periods of the pandemic on viral respiratory agents and outcomes in newborns diagnosed with respiratory tract infections (RTI) in the neonatal intensive care unit (NICU).

Materials and Methods: Newborns admitted to the NICU with RTI were included in the study. Demographic, clinical and laboratory results of two separate 6-month periods (October 2020-March 2021 and October 2021-March 2022) were compared.

Results: Of the 141 newborns included in the study, 15 newborns were followed up during the period when infection precautions were strict (Period I) and 126 newborns were followed up during the period when restrictions were removed (Period II). There was no significant difference between the periods in terms of BW, GA, gender, length of hospitalization, radiologic findings and need for respiratory support. There was a significant difference in the distribution of all viral agents ($p=0.001$). The rate of detection of SARS-CoV-2 as the causative agent was 20% in Period I and 25% in Period II, with no statistically significant difference ($p=0.76$).

Conclusion: Relaxation of infection control measures was associated with increased diversity of viral agents causing RTIs in NICU-admitted newborns. These results suggest that strict infection control measures may have temporarily reduced the circulation of various respiratory viruses, highlighting the impact of these precautions on viral transmission dynamics and neonatal outcomes.

Keywords: COVID-19, newborns, respiratory tract infections, pandemic, public health measures

ÖZ

Amaç: COVID-19 pandemisi sırasında uygulanan enfeksiyon kontrol önlemleri, SARS-CoV-2'nin yayılımını önemli ölçüde azaltmıştır. Ulusal ve küresel düzeyde yaygın olarak uygulanan bu önlemler, diğer virüslerin bulaşında da dikkate değer bir etki yaratmıştır. Bu çalışmada, pandeminin iki farklı döneminin, yenidoğan yoğun bakım ünitesinde (YYBÜ) solunum yolu enfeksiyonu (SYE) tanısı alan yenidoğanlardaki viral solunum etkenleri ve klinik sonuçlar üzerindeki etkisini değerlendirmeyi amaçladık.

Gereç ve Yöntemler: SYE nedeniyle YYBÜ'ye yatırılan yenidoğanlar çalışmaya dâhil edildi. Ekim 2020-Mart 2021 ve Ekim 2021-Mart 2022 tarihlerini kapsayan iki ayrı 6 aylık döneme ait demografik, klinik ve laboratuvar verileri karşılaştırıldı.

Bulgular: Çalışmaya dâhil edilen 141 yenidoğandan 15'i enfeksiyon önlemlerinin sıkı uygulandığı dönemde (Dönem I), 126'sı ise kısıtlamaların kaldırıldığı dönemde (Dönem II) takip edildi. Doğum ağırlığı (BW), gebelik haftası (GA), cinsiyet, hastanede kalış süresi, radyolojik bulgular ve solunum desteği ihtiyacı açısından iki dönem arasında anlamlı fark bulunmadı. Tüm viral etkenlerin dağılımı açısından anlamlı fark saptandı ($p=0,001$). SARS-CoV-2'nin etken olarak saptanma oranı Dönem I'de %20, Dönem II'de %25 olup, bu fark istatistiksel olarak anlamlı değildi ($p=0,76$).

Sonuç: Enfeksiyon kontrol önlemlerinin gevşetilmesi, YYBÜ'ye yatırılan yenidoğanlarda SYE'ye neden olan viral etkenlerin çeşitliliğinde artış ile ilişkilidir. Bu sonuçlar, sıkı enfeksiyon kontrol önlemlerinin çeşitli solunum yolu virüslerinin dolaşımını geçici olarak azaltabileceğini ve bu önlemlerin viral bulaş dinamikleri ile yenidoğan sonuçları üzerindeki etkisini ortaya koymaktadır.

Anahtar Kelimeler: COVID-19, yenidoğan, solunum yolu enfeksiyonları, pandemi, halk sağlığı önlemleri

Cite as: Çıplak G, Alyamac Dizdar E, Becerir C, Mercan H, Altan I, Ozkaya Parlakay A et al. Impact of COVID-19 Measures on Neonatal Respiratory Tract Infections Across Different Pandemic Periods. Jinekoloji-Obstetrik ve Neonatoloji Tıp Dergisi 2026;23(2):118–123.

Geliş/Received: 08.10.2025 • Kabul/Accepted: 12.03.2026

Sorumlu Yazar/Corresponding Author: Gökçe Çıplak, Department of Neonatology, Ankara Bilkent City Hospital, University of Health Sciences, Türkiye

E-mail: gokchech@hotmail.com

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

INTRODUCTION

Infection control measures implemented during the COVID-19 pandemic have significantly prevented the spread of SARS-CoV-2. Extensive public health interventions, such as stay-at-home directives, physical distancing measures, travel restrictions, mandatory face mask usage, and the closure of educational institutions, were widely enforced both nationally and internationally. While these measures have effectively reduced COVID-19 transmission, their impact on other viruses is also noteworthy (1, 2).

During the pandemic, schools in our country were closed as a public health measure. From September 2020 to June 2021, education was online, and face-to-face learning resumed in the second year, with social distancing and mask mandates in place (3). Studies showed that these restrictions reduced emergency department and intensive care unit admissions for respiratory infections, and lowered the incidence of various viral infections beyond COVID-19 (4, 5).

Several investigators reported a significant decrease in the prevalence of non-SARS-CoV-2 viruses during the pandemic period (6-8). In the second year of the COVID-19 pandemic, the rollout of SARS-CoV-2 vaccines contributed to the progressive relaxation of public health and infection control measures. The relaxation of infection control measures led to a resurgence of respiratory infections among children. This highlights the complex interplay between public health measures and the epidemiology of respiratory viruses (9,10).

Although COVID-19 has been described primarily as a pandemic, it has also manifested in epidemic patterns within specific regions and time periods. Despite these insights, there is a striking scarcity of research specifically addressing the impact of these dynamics on newborns, leaving a critical gap in our understanding. This study evaluates the effects of two distinct periods of the pandemic -one with strict infection control measures and the other with relaxed measures- on viral agents and outcomes in newborns diagnosed with RTI in a tertiary NICU.

MATERIALS AND METHODS

Study design

The study was conducted at a single center. Our institution, a designated referral center for neonates during the COVID-19 pandemic, houses a 150-bed tertiary-level NICU. This retrospective analysis included infants who presented to the pediatric emergency department or neonatal outpatient clinics with symptoms suggestive of respiratory tract infection during the RSV season and

were subsequently admitted to the NICU with a clinical suspicion of community-acquired pneumonia. The study is single-center. Data from two consecutive six-month periods, October 2020–March 2021 and October 2021–March 2022, were evaluated and compared.

Study group

Data collected from patient charts and the hospital database included gestational age (GA), birth weight (BW), gender, age at presentation, oxygen support, initial laboratory results, respiratory virus screening, and radiological findings. Because of the retrospective design of the study, no formal sample size calculation was performed. All neonates admitted to the NICU with a diagnosis of respiratory tract infection during the defined RSV seasons (October 2020–March 2021 and October 2021–March 2022) who met the inclusion criteria were included in the analysis. Therefore, the sample size was determined by the number of eligible patients available in the hospital database during the study period.

Exclusion Criteria

Infants with neonatal septicemia or urinary tract infection were excluded from the study.

Screening for viral agents

Respiratory pathogens were analyzed using the QIAstat-Dx® Respiratory Panel (QIAGEN), a multiplex real-time PCR system designed for the qualitative detection of viral and bacterial nucleic acids from nasopharyngeal swab specimens. Each assay was performed on the QIAstat-Dx® Analyzer 1.0 with an input volume of 300 µL. The panel simultaneously screens for a broad range of respiratory agents, including coronaviruses, influenza A and B, respiratory syncytial virus (RSV), parainfluenza viruses, rhinovirus/enterovirus, adenovirus, human metapneumovirus, *Mycoplasma pneumoniae*, *Chlamydomphila pneumoniae*, and *Bordetella pertussis*. To ensure assay reliability, an internal control was incorporated in every reaction to monitor extraction quality and PCR inhibition. Negative controls were run to detect potential contamination, while positive controls were included to verify amplification performance. Data acquisition and interpretation were automatically carried out by the QIAstat-Dx® Analyzer software (version 1.0, Hilden, Germany).

Statistical Analysis

Statistical analyses were conducted using the Statistical Package for the Social Sciences (SPSS), version 22.0. Continuous variables were first evaluated for normality using the Shapiro–Wilk test. Normally distributed variables were expressed as mean $\pm$ standard deviation (SD), while non-normally distributed variables were reported as median and interquartile range (IQR). Comparisons between groups were performed using Student's *t*-test for normally

distributed continuous variables or the Mann–Whitney *U* test for non-normally distributed variables. Categorical variables were expressed as numbers and percentages and compared using the Fisher's exact test or the χ^2 test as appropriate. A *p*-value of <0.05 was considered indicative of statistical significance.

Ethics approval statement

Ethics approval has been obtained with letter number E2-22-1308 dated 19/01/2022.

RESULTS

The study include 141 newborns with RTI admitted to the NICU. Of those, 15 were monitored during strict infection precautions (Period I: October 2020–March 2021), and 126 during the period with lifted restrictions (Period II: October 2021–March 2022).

The median (IQR) BW and GA for the group were 2900 (2347–3400) grams and 37 (34–39) weeks, respectively. The median (IQR) age at admission was 23 (17–32) days, and length of hospitalization was 7 (5–10) days. The median (IQR) BW was 2522 (1880–3250) g for Period I and 2861 (2515–3400) g for Period II (*p*=0.991). The median (IQR) GA at birth was 34 (32–38) and 36 (34–39) weeks (*p*=0.14), the median (IQR) postnatal age at admission was 16 (7–

23) and 15 (7–22) days (*p*=0.56), and the median (IQR) length of hospital stay was 7 (6–8) and 8 (5–10) days (*p*=0.84) respectively. No significant difference were found between the periods in terms of BW, GA, gender, length of hospitalization, radiologic findings, need for respiratory support, and mortality (Table 1).

Throughout the study period, at least one virus was identified in 88.6% of the patients and more than one virus in 4.2%. No viral agents were detected in 46.7% of patients during the Period I, compared with 7.1% during the Period II (*p* <0.001). There was a significant difference in the distribution of all viral agents (*p*<0.001). Respiratory syncytial virus (RSV), influenza, adenovirus, bocavirus, metapneumovirus, which were not found in Period I, were found in Period II. However, the rate of detection of SARS-CoV-2 as the causative agent was 20% in Period I and 25% in Period II, with no statistically significant difference (*p*=0.76). The viral distribution in the two periods is shown in Table 2.

Upon comparison of the rates of NICU hospitalization due to RTIs, it was observed that there was an 8.4% increase in the overall hospitalization rate during Period II. Notably, while there were no NICU admissions in December during Period I, the months of November and December exhibited the highest number of NICU admissions in Period II. Distribution of the NICU admissions by months is shown in Figure 1.

Table 1. Demographic and clinical characteristics of the study infants

Variable	Period I n=15	Period II n=126	p
Patient characteristics			
Gestational age	34 (32–38)	36 (34–39)	0.35 ^b
Birthweight	2522 (1880–3250)	2861 (2515–3400)	0.15 ^b
Gender, male	9 (60)	79 (63)	0.52
Age at presentation (days)	16 (7–23)	15 (7–22)	0.41 ^b
Hematological and Biochemical parameters			
White blood cells (x10 ⁶ /L)	9654 (7590–11950)	9172 (7130–10895)	0.35 ^b
Neutrophils (x10 ⁶ /L)	2724 (1600–3220)	2976 (1650–3800)	0.99 ^b
Lymphocytes (x10 ⁶ /L)	4977±2151	4212±1923	0.15 ^a
Systemic inflammatory index	157460 (1200–236948)	443110 (148152–540964)	0.13 ^b
C-reactive protein (mg/L)	5.6 (0.003–11.75)	3.3 (0.001–0.5)	0.15 ^b
pH	7.42 (7.37–7.49)	7.33 (7.37–7.44)	0.29 ^b
pCO ₂ (mmHg)	36.5 (30–43)	40.2 (34.8–44.7)	0.25 ^b
HCO ₃ (mmol/L)	23.4 (22–25)	23.5 (22–26)	0.64 ^b
Base excess (mmol/L)	1.66±2.5	1.16±2.4	0.52 ^a
Lactate (mmol/L)	2.3 (2.17–3.82)	2.0 (1.6–2.72)	0.15 ^b
Clinical characteristics			
Duration of hospitalization	7 (6–8)	9 (5–10)	0.84
Radiologic findings	8 (53)	71 (56)	0.79
Requirement of oxygen supplement	6 (40)	74 (59)	0.24
Mortality	0 (0)	2 (1.5)	0.79

Data are presented as mean ± standard deviation (±SD), median (IQR) or n (%). Continuous variables were compared using Student's *t*-test or Mann–Whitney *U* test depending on distribution. Categorical variables were compared using Fisher's exact test.

a: Student's *t*-test b: Mann–Whitney *U*

Table 2. Distribution of viral agents during study periods

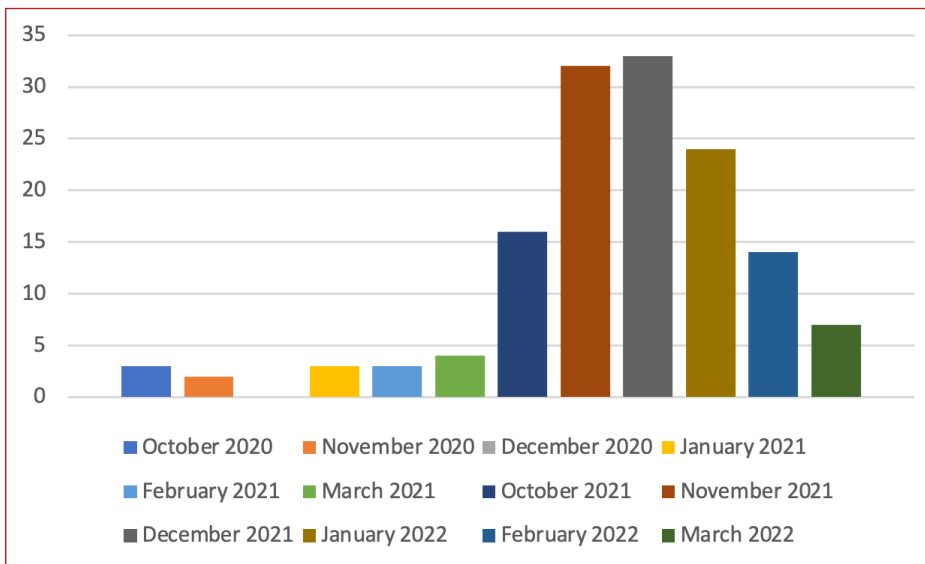
Variable	Overall (n= 141)	Period I (n=15)	Period II (n=126)	p
RSV	56 (39.7)	0 (0)	56 (44)	<0.001 ^a
SARS-CoV-2	34 (24.1)	3 (20)	31 (25)	0.76 ^a
SARS-CoV-2 (Delta)	1 (0.7)	0 (0)	1 (0.8)	0.89 ^a
Rhinovirus	18 (12.7)	3 (20)	16 (12.7)	0.32 ^a
Adenovirus	1 (0.7)	0 (0)	3 (2.4)	0.89 ^a
Metapneumoniae	3 (2.1)	0 (0)	1 (0.8)	0.71 ^a
Influenza	2 (1.4)	0 (0)	2 (1.6)	0.79 ^a
Parainfluenza	3 (2.1)	1 (6.7)	2 (1.6)	0.28 ^a
Bocavirus	1 (0.7)	0 (0)	1 (0.8)	0.89 ^a
Multiple agent	6 (4.2)	1 (6.7)	5 (4)	0.49 ^a
Negative PCR test	16 (11.3)	7 (46.7)	9 (7.1)	<0.001 ^b

Data are presented as n (%).

Comparisons between groups were performed using χ^2 test or Fisher's exact test.

a: Fisher's exact test b: χ^2 test

RSV: Respiratory syncytial virus; SARS-CoV-2: Severe Acute Respiratory Syndrome Coronavirus 2

**Figure 1.** NICU admissions during study periods

DISCUSSION

The findings suggest that NICU admissions for RTIs caused by non-SARS-CoV-2 viral agents increased following the relaxation of infection control measures. A shift in the distribution of viral agents was observed, with viruses not detected during first year of the pandemic emerging in the second year. This change may be linked to the relaxation of public health measures, low vaccination rates, and weakened immun systems.

Several investigators have reported that incidence of respiratory viral infections decreased during the first year of the COVID-19 pandemic. For instance, a study in Turkey reported a significant

decrease in the prevalence of respiratory viruses such as influenza and respiratory syncytial virus (RSV) during the pandemic period (6). Similarly, research from Kuwait indicated a reduction in severe lower RTIs caused by non-SARS-CoV-2 viruses during the same period (7). A study from Argentina reported that the rate of hospitalization due to acute lower RTIs decreased significantly compared with 2019, coinciding with the absence of seasonal respiratory virus circulation in the pediatric population (8).

In contrast to the declines observed during periods of strict public health measures, several studies have reported a marked increase in RTIs following the relaxation of restrictions and increased after the relaxation of restrictions. A Danish study, which include a huge

number of patients under the age of 17 years, showed higher hospital admissions for RSV after the relaxation of restrictions. However, the severity remained unchanged (11). A retrospective study from England observed an unexpected reduction in RSV during the first year of pandemic at children under 5 years of age (12). Breinig et al. conducted an evaluation of pediatric intensive care unit admissions data from 14 centers across France, comparing the pandemic lockdown with corresponding period of the previous year (13). Their results revealed a significant reduction in admissions due to RTIs. Data from four countries indicated a notable reduction in the incidence of respiratory infections requiring admission to the PICU during the COVID-19 pandemic compared to previous years (14). Similar results were found in a study from Spain comparing hospital admission rates due to RSV during the pandemic and previous seasons in children under 2 years of age (15). These findings are consistent with the results of the present study.

Recent studies also analysed the impact of the pandemic on the etiology of respiratory infections. Kurskaya et al. examined three seasons between November 2019 and April 2022 (16). While RSV, Influenza and Parainfluenza were the most common agents in 2019-2020, metapneumovirus, rhinovirus and coronavirus were common in 2020-2021, and RSV, SARS-CoV-2, influenza, and rhinovirus dominated in the third season. Similarly, our study observed a marked re-emergence of RSV, influenza, adenovirus, bocavirus, metapneumovirus, whereas these pathogens were not detected in 2020-2021. A surveillance study from China collected data of children that hospitalized due to respiratory infections from 2015 to 2021 (17). The study compared the distribution of respiratory viral agents during the periods before and after the onset of the pandemic. It is observed that COVID-19 prevention measures affected the incidence of all viral agents except for RSV and rhinovirus. Our study demonstrated a significant difference in the distribution of all viral agents, including RSV, between the two periods. Another study from China evaluated the impact of public health measures on the rate of respiratory viral agents by collecting data from 10.396 hospitalized children (18). Rhinovirus was the most common viral agent causing respiratory infections during the period of pandemic restrictions. In contrast to the Chinese study, which evaluated only single period, the present study conducted a comparative analysis of two periods during pandemics. Based on the findings, rhinovirus and SARS-CoV-2 were identified as the most prevalent causative agents during the first period. In contrast, the results of a prospective surveillance study indicate that there was no significant difference in the viral etiologies of neonatal RTIs between the pre-pandemic and post-pandemic periods (19).

The impact of COVID-19 pandemic on the behaviour of the respiratory viruses has also reported. Compared with previous

seasons, the peak of RSV epidemic has shifted to early summer instead of autumn-winter. While the incidence of the disease increased in some age groups, no change was observed in the severity of disease (20-22). A retrospective study from Italy compared the trend of RSV infections among hospitalized infants during the epidemic season of 2022-2023 with the trend from the last pre-pandemic season of 2018-2019 (20). Results from a large database covering all age groups in Turkey suggested that when public health measures were strict, an unusual seasonal peak of all viral respiratory agents was observed (21). Scarponi et al. reported that the rate of respiratory infections in preterm infants with bronchopulmonary dysplasia decreased during the pandemic (22). The results demonstrated an increase in NICU admissions for viral respiratory infections following the relaxation of pandemic precautions. A rapid rise was observed in the incidence of viral agents including RSV, rhinovirus and influenza.

Data regarding the behavior and detection of other respiratory viruses in neonates in the context of COVID-19 pandemic is currently insufficient. An observational study analyzing data from 208 neonates at a tertiary center in Turkey evaluated three periods: prior to the pandemic, during the period of strict restrictions, and following the removal of those restrictions. After the COVID-19 pandemic, there has been an increase in both the frequency and severity of RSV infections among newborns (23). A study comparing five years of data for preterm infants with a gestational age <32 weeks, both before and after the pandemic, reported a significant reduction in post-pandemic RSV infection rates (24). The results indicate a significant decrease in hospitalizations due to viral infections during the first year of the pandemic. Notably, there were no NICU admissions for RSV during restrictions, while the rate rose to 40% after restrictions were lifted.

The main limitations of the present study are its retrospective design and single-center nature. The study focused on the period from October to March, corresponding to the peak incidence of viral RTIs are most common in the region, and included only hospitalized infants. Despite these limitations, the findings provide valuable insights into the impact of infection control measures on viral agents and NICU admissions among newborns.

CONCLUSION

In conclusion, the findings indicate an increase in the number of infants admitted to the NICU with RSV during the 2021–22 period compared to 2020–21. However, there was a notable change in the distribution of viral agents. In the second year of the pandemic, the widespread use of vaccines and the easing of infection control

measures coincided with a rise in NICU hospitalizations for RTIs, as well as a broader range of non-SARS-CoV-2 viral agents. This increase in cases and viral diversity may reflect the influence of public health interventions on the immune system. Although COVID-19 is no longer perceived as an immediate global crisis, COVID-related respiratory infections continue to be detected. While extensive data are available for children and adults, studies focusing specifically on newborns remain scarce, underscoring the importance of the present work in addressing this critical gap.

Ethics Approval Statement: Ethics approval has been obtained with letter number E2-22-1308 dated 19/01/2022.

Author Contributions: GC: Conceptualization, Data curation, Validation, Writing – original draft. EAD: Formal analysis, Methodology, Supervision, Writing – review & editing. CB: Data curation, Methodology, Writing – review & editing. HM: Data curation. IA: Data curation. AOP: Formal analysis, Methodology, Supervision. FNS: Formal analysis, Methodology, Supervision.

Conflict of Interest: The authors declare no conflict of interest

REFERENCES

- Van Brusselen D, De Troeyer K, Ter Haar E, Vander Auwera A, Poschet K, Van Nuijs S, et al. Bronchiolitis in COVID-19 times: a nearly absent disease? *Eur J Pediatr*. 2021;180(6):1969-1973.
- Baker RE, Park SW, Yang W, Vecchi GA, Metcalf CJE, Grenfell BT. The impact of COVID-19 nonpharmaceutical interventions on the future dynamics of endemic infections. *Proc Natl Acad Sci U S A*. 2020;117(48):30547-30553.
- Devrim İ, Bayram N. Infection control practices in children during COVID-19 pandemic: Differences from adults. *Am J Infect Control*. 2020;48(8):933-939.
- Di Mattia G, Nenna R, Mancino E, Rizzo V, Pierangeli A, Villani A et al. During the COVID-19 pandemic where has respiratory syncytial virus gone? *Pediatr Pulmonol*. 2021;56(10):3106-3109.
- Guitart C, Bobillo-Perez S, Alejandro C, Armero G, Launes C, Cambra FJ et al. surveillance in Catalonia. Bronchiolitis, epidemiological changes during the SARS-CoV-2 pandemic. *BMC Infect Dis*. 2022;22(1):84.
- Mese S, Allahverdiyeva A, Onel M, Uysal HK, Agacfidan A. Investigation of the Effect of the COVID-19 Pandemic Period on Respiratory Tract Viruses at Istanbul Medical Faculty Hospital, Turkey. *Infect Dis Rep*. 2024;16(5):992-1004.
- Altawalrah H, Alfouzan W, Al-Fadallah T, Zalzal MA, Ezzikouri S. Viral etiology of severe lower respiratory tract infections in SARS-CoV-2 negative hospitalized patients during the COVID-19 pandemic in Kuwait. *Heliyon*. 2024;10(8):e29855.
- Lucion MF, Del Valle Juárez M, Pejito MN, Orqueda AS, Romero Bollón L, Mistchenko AS et al. Impact of COVID-19 on the circulation of respiratory viruses in a children's hospital: an expected absence. *Arch Argent Pediatr*. 2022;120(2):99-105.
- Magalhães Bronze K, Dos Santos UR, Barbosa Costa G, Sevá ADP, Guimarães Kersul M, Sacramento Pinto C et al. The Impact of the COVID-19 Pandemic on the Clinical and Epidemiological Profile of Severe Acute Respiratory Infection in Bahia, Brazil: A Comparative Analysis of Pre- and Post-Pandemic Trends. *Viruses*. 2025;17(3):389.
- Bedir Demirdag T, Ozcicek M, Polat M, Kavas FC, Demir F, Atay Unal N et al. Effects of COVID-19 pandemic on epidemiological features of viral respiratory tract infections in children: a single-centre study. *Epidemiol Infect*. 2024;152:e128.
- Nygaard U, Hartling UB, Nielsen J, Vestergaard LS, Dungu KHS, Nielsen JSA et al. Hospital admissions and need for mechanical ventilation in children with respiratory syncytial virus before and during the COVID-19 pandemic: a Danish nationwide cohort study. *Lancet Child Adolesc Health*. 2023;7(3):171-179.
- Bardsley M, Morbey RA, Hughes HE, Beck CR, Watson CH, Zhao H et al. Epidemiology of respiratory syncytial virus in children younger than 5 years in England during the COVID-19 pandemic, measured by laboratory, clinical, and syndromic surveillance: a retrospective observational study. *Lancet Infect Dis*. 2023;23(1):56-66.
- Breinig S, Mortamet G, Brossier D, Amadieu R, Claudet I, Javouhey E et al. Impact of the French National Lockdown on Admissions to 14 Pediatric Intensive Care Units During the 2020 COVID-19 Pandemic-A Retrospective Multicenter Study. *Front Pediatr*. 2021;9:764583.
- Vásquez-Hoyos P, Diaz-Rubio F, Monteverde-Fernandez N, Jaramillo-Bustamante JC, Carvajal C, Serra A et al. Reduced PICU respiratory admissions during COVID-19. *Arch Dis Child*. 2021;106(8):808-811.
- Bermúdez Barrezueta L, Matías Del Pozo V, López-Casillas P, Brezmes Raposo M, Gutiérrez Zamorano M, Pino Vázquez MA. Variation in the seasonality of the respiratory syncytial virus during the COVID-19 pandemic. *Infection*. 2022;50(4):1001-1005.
- Kurskaya OG, Prokopyeva EA, Sobolev IA, Solomatina MV, Saroyan TA, Dubovitskiy NA et al. Changes in the Etiology of Acute Respiratory Infections among Children in Novosibirsk, Russia, between 2019 and 2022: The Impact of the SARS-CoV-2 Virus. *Viruses*. 2023;15(4):934.
- Cao R, Du Y, Tong J, Xia D, Song Q, Xia Z et al. Influence of COVID-19 pandemic on the virus spectrum in children with respiratory infection in Xuzhou, China: a long-term active surveillance study from 2015 to 2021. *BMC Infect Dis*. 2023;23(1):467.
- Shi T, Huang L. Prevalence of respiratory pathogens and risk of developing pneumonia under non-pharmaceutical interventions in Suzhou, China. *Epidemiol Infect*. 2023;151:e82.
- Bravo-Queipo-de-Llano B, Sánchez García L, Casas I, Pozo F, La Banda L, Alcolea S et al. Surveillance of Viral Respiratory Infections in the Neonatal Intensive Care Unit-Evolution in the Last 5 Years. *Pathogens*. 2023;12(5):644.
- Vittucci AC, Antilici L, Russo C, Musolino AMC, Cristaldi S, Cutrera R et al. Respiratory syncytial virus: can we still believe that after pandemic bronchiolitis is not a critical issue for public health? *Eur J Pediatr*. 2023;182(12):5303-5313.
- Kırca F, Aydoğan S, Gozalan A, Güler E, Uyan Erten AZ, Özşen Uygur AS et al. Impact of non-pharmaceutical interventions on circulating respiratory viruses during the COVID-19 pandemic in Turkey. *Ann Saudi Med*. 2023;43(3):143-153.
- Scarponi D, Bedetti L, Zini T, Di Martino M, Cingolani GM, Spaggiari E et al. COVID-19 restrictions and hygiene measures reduce the rates of respiratory infections and wheezing among preterm infants. *Acta Biomed*. 2023;94(1):e2023032.
- Akbay Ak S, Soysal B, Yangin Ergon E, Kalkanlı OH, Ayhan Y, Alkan Ozdemir S et al. The Impact of the COVID-19 Pandemic on Respiratory Syncytial Virus Infection in the Neonatal Period. *Am J Perinatol*. 2024;41(12):1706-1713.
- Abu-Raya B, Viñeta Paramo M, Reichert F, Lavoie PM. Why has the epidemiology of RSV changed during the COVID-19 pandemic? *E Clinical Medicine*. 2023;61:102089.

Predictive Value of First-Trimester Inflammatory Hematological Indices for Gestational Hypertension

Birinci Trimesterde Ölçülen İnflamatuvar Hematolojik İndekslerin Gestasyonel Hipertansiyonu Öngörmekdeki Prediktif Değeri

¹Aykut KINDAN¹, ²Ahmet KURT², ³Özgür Volkan AKBULUT³, ¹Sait ERBEY³, ¹Alican SAPMAZ³, ¹Murat POLAT³

¹Department of Obstetrics and Gynecology, Pursaklar State Hospital, Ankara, Türkiye

²Department of Obstetrics and Gynecology, Gemlik State Hospital, Bursa, Türkiye

³Department of Obstetrics and Gynecology, Etlik City Hospital, Ankara, Türkiye

ABSTRACT

Aim: This study aimed to evaluate the predictive value of first-trimester hematological and inflammatory indices derived from complete blood count (CBC) parameters in gestational hypertension (GHT).

Materials and Methods: A retrospective observational study was conducted on 80 pregnant women who were followed up between January 2019 and December 2024. Participants were divided into two groups: women who remained normotensive (control, n=40) and those who developed isolated GHT after 20 weeks (GHT, n=40). First-trimester CBC results (≤ 14 weeks) were analyzed. Inflammatory indices, including neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), monocyte-to-lymphocyte ratio (MLR), and systemic immune-inflammation index (SII), were calculated. Group comparisons were performed using t-tests or Mann-Whitney U-tests. Receiver operating characteristic (ROC) analysis was used to assess the diagnostic performance, and logistic regression was used to identify independent predictors.

Results: Women with GHT had significantly higher WBC, neutrophil, monocyte, hemoglobin, hematocrit, PDW, RDW, NLR, PLR, MLR, and SII values than the controls (all $p < 0.05$), whereas lymphocyte counts were lower ($p = 0.046$). Platelet counts did not differ significantly ($p = 0.453$). ROC analysis demonstrated that NLR (AUC=0.871, cut-off=2.14, sensitivity 78%, specificity 82%), RDW (AUC=0.787, cut-off=12.7, sensitivity 73%, specificity 77%), and SII (AUC=0.836, cut-off=513, sensitivity 83%, specificity 75%) had the strongest predictive value for GHT (all $p < 0.001$). Logistic regression confirmed that NLR, RDW, and PDW were independent predictors. No significant differences were observed in gestational age at delivery or birth weight; however, neonates of hypertensive mothers required longer NICU stays ($p = 0.025$).

Conclusion: First-trimester inflammatory indices, particularly NLR, RDW, and PDW, are independent predictors of gestational hypertension. CBC-derived parameters, which are simple and widely accessible, may assist in the early identification of women at risk for hypertensive disorders during pregnancy.

Keywords: Gestational hypertension, neutrophil-to-lymphocyte ratio, red cell distribution width, platelet distribution width, systemic immune-inflammation index, predictive marker

ÖZ

Amaç: Bu çalışmanın amacı, tam kan sayımı (TKS) parametrelerinden elde edilen birinci trimester hematolojik ve inflamatuvar indekslerin gestasyonel hipertansiyon (GH) öngörüsündeki değerini değerlendirmektir.

Gereç ve Yöntemler: Ocak 2019 – Aralık 2024 tarihleri arasında takip edilen 80 gebe kadın üzerinde retrospektif gözlemsel bir çalışma yürütüldü. Katılımcılar iki gruba ayrıldı: normotansif kalanlar (kontrol, n=40) ve 20. gebelik haftasından sonra izole GH gelişenler (GH, n=40). Birinci trimester TKS sonuçları (≤ 14 hafta) incelendi. Nötrofil/lenfosit oranı (NLR), trombosit/lenfosit oranı (PLR), monosit/lenfosit oranı (MLR) ve sistemik immün-inflamasyon indeksi (SII) hesaplandı. Grup karşılaştırmaları t-testi veya Mann-Whitney U testi ile yapıldı. Alıcı işletim karakteristik (ROC) analizi tanısal performansı değerlendirdi ve lojistik regresyon bağımsız prediktörleri belirledi.

Bulgular: GH gelişen kadınlarda; WBC, nötrofil, monosit, hemoglobin, hematokrit, PDW, RDW, NLR, PLR, MLR ve SII değerleri anlamlı olarak daha yüksek saptandı (tümü $p < 0,05$), lenfosit sayıları ise daha düşüktü ($p = 0,046$). Trombosit sayıları açısından fark izlenmedi ($p = 0,453$). ROC analizinde NLR (AUC=0,871, cut-off=2,14, duyarlılık %78, özgüllük %82), RDW (AUC=0,787, cut-off=12,7, duyarlılık %73, özgüllük %77) ve SII (AUC=0,836, cut-off=513, duyarlılık %83, özgüllük %75) GH için en güçlü öngörücü değerleri gösterdi (tümü $p < 0,001$). Lojistik regresyon analizinde NLR, RDW ve PDW bağımsız prediktörler olarak doğrulandı. Doğum haftası ve doğum ağırlığı açısından gruplar arasında fark bulunmazken, hipertansif annelerin yenidoğanlarının yenidoğan yoğun bakım ünitesinde (YYBÜ) kalış süreleri daha uzundu ($p = 0,025$).

Sonuç: Birinci trimester inflamatuvar indeksler, özellikle NLR, RDW ve PDW, gestasyonel hipertansiyon için bağımsız prediktörlerdir. TKS'den türetilen bu parametreler, basit ve kolay erişilebilir olmaları nedeniyle gebelikte hipertansif bozukluklar açısından risk altındaki kadınların erken dönemde belirlenmesine katkı sağlayabilir.

Anahtar Kelimeler: Gestasyonel hipertansiyon, nötrofil/lenfosit oranı, eritrosit dağılım genişliği, trombosit dağılım genişliği, sistemik immün-inflamasyon indeksi, prediktif belirteç.

Cite as: Kindan A, Kurt A, Akbulut ÖV, Erbey S, Sapmaz A, Polat M. Predictive Value of First-Trimester Inflammatory Hematological Indices for Gestational Hypertension. Jinekoloji-Obstetrik ve Neonatoloji Tıp Dergisi 2026;23(2):124–131.

Geliş/Received: 17.09.2025 • Kabul/Accepted: 10.02.2026

Sorumlu Yazar/Corresponding Author: Aykut Kindan, Department of Obstetrics and Gynecology, Pursaklar State Hospital, Ankara, Türkiye
E-mail: aykutkindan33@hotmail.com

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

INTRODUCTION

Pregnancy is a dynamic period characterized by comprehensive physiological, hormonal, and immunological alterations in the maternal body (1). During this stage, hemodynamic parameters are reorganized, cardiac output increases, and vascular tone undergoes significant modification (2). On a hormonal level, the secretion of placental hormones facilitates maternal adaptation to pregnancy, while the immune system undergoes adjustments in both cellular and humoral responses to ensure maternal-fetal tolerance (3). However, insufficient or dysregulated adaptive processes may predispose individuals to pregnancy-related complications. Among these, hypertensive disorders emerge as one of the most critical conditions threatening both maternal and fetal health (4).

Gestational hypertension is a condition that develops in the second half of pregnancy in women with no prior history of hypertension (5). The elevation of blood pressure observed in expectant mothers poses risks for both maternal and perinatal outcomes (6, 7). Early recognition and close monitoring are critical to prevent progression to severe complications, such as preeclampsia (PE), eclampsia, or organ damage.

Assessments conducted in the early stages of pregnancy provide a valuable opportunity to predict high-risk pregnancies and implement appropriate preventive measures. In this context, easily accessible biological markers, such as blood parameters and hematological indices, have the potential to serve as practical and cost-effective screening tools in clinical practice (8-10). In particular, hematological indices associated with inflammation are thought to offer predictive value for the development of pregnancy-related complications (11).

This study aimed to investigate the predictive value of inflammatory hematological indices measured in the first trimester of pregnancy for the development of gestational hypertension. This study aimed to identify high-risk cases at an early stage and support preventive strategies aimed at improving maternal and fetal health.

MATERIAL AND METHODS

Study Design

This was a retrospective, descriptive, and analytical study. Ethical approval was obtained from the Ethics Committee of the Ankara Etlik City Hospital Scientific Research Evaluation Board (Approval No: AEŞH-BADEK-2025-0125, Date: 12/02/2025). Study data were collected from pregnant women who were followed up between January 2019 and December 2024 at the Departments of Obstetrics

and Gynecology of Ankara Etlik City Hospital and Pursaklar State Hospital. The study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki (1964) and its subsequent revisions.

Study Groups

A total of 80 pregnant women were included in the study and were divided into two groups. The control group (n=40) comprised healthy pregnant women with complete blood count (CBC) results available in the first trimester, who remained normotensive throughout pregnancy and did not develop any hypertensive disorders. The gestational hypertension group (n=40) included previously normotensive women who developed systolic blood pressure ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg after the 20th week of gestation. Blood pressure measurements were confirmed by at least two separate recordings taken 4 h apart. Women without proteinuria or evidence of organ dysfunction were classified as having "isolated gestational hypertension." Diagnosis was established in accordance with the criteria of the American College of Obstetricians and Gynecologists (ACOG) Practice Bulletin (12).

Inclusion and Exclusion Criteria

The study included women with singleton viable pregnancies who had complete blood count (CBC) results available in the first trimester ($\leq 14+0$ weeks), were between 18 and 45 years of age, and had complete antenatal follow-up and delivery data available. In the gestational hypertension group, only cases of isolated gestational hypertension diagnosed according to ACOG criteria were included. The exclusion criteria comprised women with chronic hypertension (present before pregnancy, diagnosed before 20 weeks of gestation, or persisting beyond 12 weeks postpartum), PE or HELLP syndrome, current smoking, multiple pregnancies, a history or clinical findings of acute infection in the first trimester, CBC measurements obtained after 14+0 weeks, or incomplete essential data. Furthermore, pregnancies ending in spontaneous or elective abortion, preterm delivery before 37 weeks, or intrauterine fetal demise were excluded from the study.

Patient Selection Process

Within the scope of the study, the records of a total of 326 pregnant women who were followed between January 2019 and December 2024 at the Departments of Obstetrics and Gynecology of Ankara Etlik City Hospital and Pursaklar State Hospital were reviewed. In the preliminary evaluation, 48 cases were excluded because of missing essential data (complete blood count parameters or obstetric follow-up information). Among the remaining 278 women, those with chronic hypertension (n=32), PE or HELLP syndrome (n=21), multiple pregnancies (n=18), smoking (n=24), and a history or findings of acute infection in the first trimester (n=15)

were excluded. In addition, cases in which the CBC was obtained after 14+0 weeks (n=19) and pregnancies that ended in abortion, intrauterine fetal demise, or preterm delivery before 37 weeks (n=21) were also excluded. After these exclusions, 80 pregnant women who met the inclusion criteria were enrolled in the study. Of these, 40 constituted the control group, consisting of women who remained normotensive throughout pregnancy, while 40 constituted the gestational hypertension group, defined as isolated gestational hypertension diagnosed according to the ACOG of Obstetricians and Gynecologists criteria. The patient selection process is summarized in Figure 1 as a flow diagram.

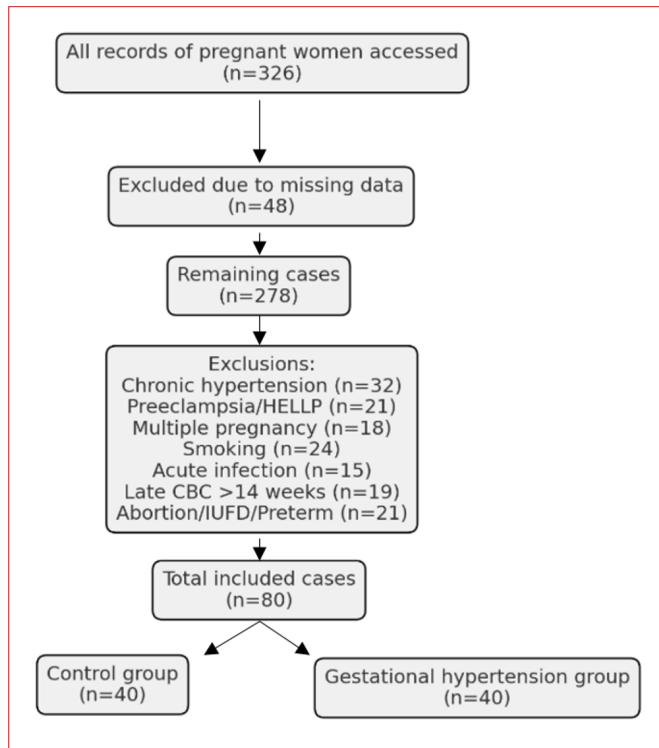


Figure 1. Flow diagram of patient inclusion and exclusion

Data Collection

Demographic variables (age, body mass index (BMI), gravida) and obstetric information of all participants were recorded. Laboratory parameters obtained from complete blood count (CBC) included leukocyte, neutrophil, lymphocyte, monocyte, platelet, hemoglobin, hematocrit, platelet distribution width (PDW), and red cell distribution width (RDW) values. The perinatal outcomes assessed were gestational age at delivery, birth weight, and length of stay in the neonatal intensive care unit (NICU).

Calculation of Inflammatory Parameters

The following inflammatory indices were calculated from the CBC data:

- Neutrophil-to-Lymphocyte Ratio (NLR): Absolute neutrophil count / Absolute lymphocyte count
- Platelet-to-Lymphocyte Ratio (PLR): Absolute platelet count / Absolute lymphocyte count
- Monocyte-to-Lymphocyte Ratio (MLR): Absolute monocyte count / Absolute lymphocyte count
- Systemic Immune-Inflammation Index (SII): (Platelet × Neutrophil) / Lymphocyte

Statistical Analysis

Statistical analyses were performed using SPSS version 27.0 (IBM Corp., Armonk, NY, USA). The Kolmogorov–Smirnov test was used to assess the normality of the distribution. The selection of hypothesis testing methods was based on the data distribution and underlying test assumptions. Parametric tests were applied when the assumptions of normal distribution and independence of observations were met, whereas non-parametric tests were used for variables that did not meet the normality assumptions. For continuous variables, the independent samples t-test was used for normally distributed data, while the Mann–Whitney U test was used for non-normally distributed data. Categorical variables were compared using the chi-square test. To evaluate the diagnostic performance of hematological and inflammatory indices in predicting the development of gestational hypertension, receiver operating characteristic (ROC) curve analysis was conducted, and the cut-off values, sensitivity, and specificity were calculated. The associations between perinatal outcomes and hematological indices were analyzed using Pearson's correlation analysis. Statistical significance was set at $p < 0.05$. The sample size was determined based on an a priori power analysis. Using G*Power software (version 3.1.9.7), assuming a medium effect size (Cohen's $d = 0.65$), significance level of $\alpha = 0.05$, and statistical power of 80%, the minimum required sample size was calculated as 36 participants per group. After accounting for potential data loss and incomplete records, 40 participants were ultimately included in each group.

RESULTS

There were no significant differences between the control and gestational hypertension groups in terms of maternal age, BMI, gravida, or gestational week at diagnosis (all $p > 0.05$) (Table 1).

Women with gestational hypertension had significantly higher WBC, neutrophil, monocyte, hemoglobin, hematocrit, PDW, RDW, NLR, PLR, MLR, and SII values than those in the control group (all

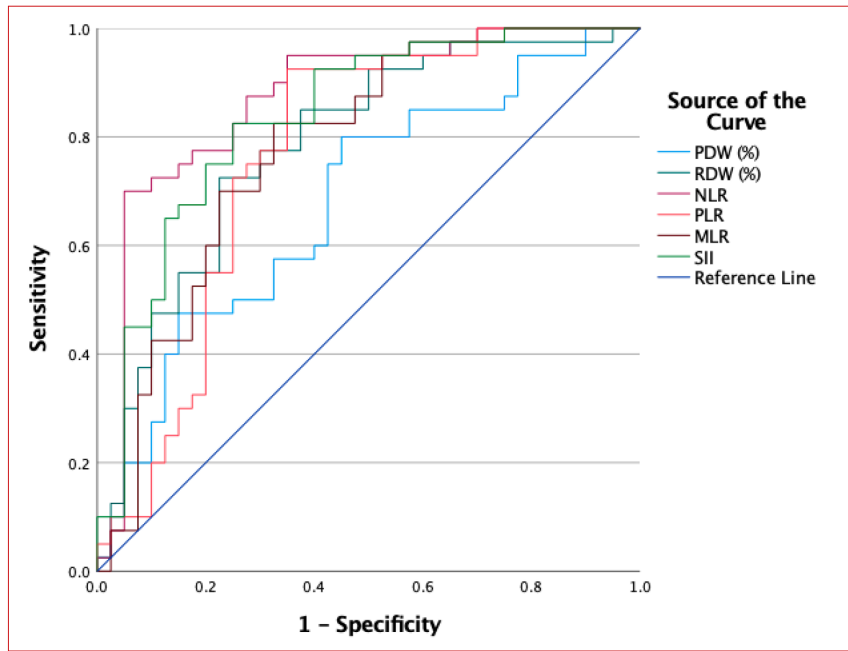


Figure 2. Receiver operating characteristic (ROC) curves of hematological and inflammatory indices (PDW, RDW, NLR, PLR, MLR, and SII) for predicting gestational hypertension.

Table 1. Comparison of Baseline Demographic and Clinical Characteristics between Control and Gestational Hypertension Groups

	Control (n=40)	GHT (n=40)	p value
	Mean±S.D.	Mean±S.D.	
Age (years)	27.0 (23.0–31.5)	27.3 (24.0–30.0)	0.780 ^b
BMI (kg/m ²)	23.1 (22.0–25.0)	22.7 (21.5–24.0)	0.186 ^b
Gravida (n)	1.2 (0.0–2.0)	1.6 (1.0–2.5)	0.126 ^b
GHT Diagnosis Week	9.7±1.4	10.1±1.4	0.212 ^a

Data are presented as mean ± standard deviation (SD) and median (IQR). Abbreviations: BMI, body mass index; GHT, gestational hypertension. a Independent samples t-test; b Mann-Whitney U test. Statistical significance was set at $p < 0.05$. Statistically significant values are bolded.

Table 2. Comparison of Hematological and Inflammatory Parameters between Control and Gestational Hypertension Groups

	Control (n=40)	GHT (n=40)	p value
WBC Count ($\times 10^9/L$)	7.7±1.1	9.3±1.4	<0.001^a
Neutrophil ($\times 10^9/L$)	4.0±0.7	4.6±0.5	<0.001^a
Lymphocyte ($\times 10^9/L$)	2.2±0.3	2.1±0.2	0.046^a
Monocyte ($\times 10^9/L$)	0.4 (0.3–0.5)	0.4 (0.4–0.5)	0.044^b
Platelet ($\times 10^9/L$)	252.6±36.6	258.1±27.2	0.453 ^a
Hemoglobin (g/dL)	12.1±0.8	12.5±0.8	0.038^a
Hematocrit (%)	35.7±2.7	37.8±3.1	0.002^a
PDW (%)	12.2±0.8	12.7±0.7	0.004^a
RDW (%)	12.5±0.4	12.9±0.4	<0.001^a
NLR	1.8 (1.6–2.1)	2.5 (2.2–2.8)	<0.001^b
PLR	117.6±25.9	138.8±18.1	<0.001^a
MLR	0.2±0.1	0.2±0.1	<0.001^a
SII	469.5±137.6	655.7±130.8	<0.001^a

Data are presented as mean ± standard deviation (SD) and median (IQR). Abbreviations: WBC, white blood cell; PDW, platelet distribution width; RDW, red cell distribution width; NLR, neutrophil-to lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; MLR, monocyte-to-lymphocyte ratio; SII, systemic immune-inflammation index; GHT, gestational hypertension. a Independent samples t-test; b Mann-Whitney U test. $p < 0.05$ was considered statistically significant. Statistically significant values are bolded.

$p < 0.05$). Lymphocyte counts were slightly lower in the gestational hypertension group ($p = 0.046$), whereas platelet counts did not differ significantly between the groups ($p = 0.453$) (Table 2).

There were no significant differences between the groups in terms of gestational age at delivery or birth weight ($p = 0.480$ and $p = 0.644$, respectively). However, neonates born to mothers with gestational hypertension had a significantly longer NICU stay than those in the control group ($p = 0.025$) (Table 3).

ROC curve analysis demonstrated that NLR (AUC=0.871), SII (AUC=0.836), and RDW (AUC=0.787) had the highest predictive accuracy for gestational hypertension. NLR with a cutoff of 2.14 showed 78% sensitivity and 82% specificity, whereas SII at a cutoff of 513 demonstrated 83% sensitivity and 75% specificity. RDW with a cut-off of 12.7 had 73% sensitivity and 77% specificity, respectively. Other indices, including PLR, MLR, and PDW, also

showed significant but lower discriminative power (all $p < 0.05$) (Table 4).

Correlation analysis revealed that RDW was positively correlated with birth weight ($r = 0.253$, $p = 0.024$). In addition, MLR showed a significant positive correlation with NICU stay ($r = 0.238$, $p = 0.033$). No significant correlations were found between the other hematological indices and perinatal outcomes (all $p > 0.05$) (Table 5).

In the multivariate logistic regression analysis, higher PDW (OR=5.55, 95% CI: 1.349–22.834, $p = 0.018$), RDW (OR=10.572, 95% CI: 1.128–99.049, $p = 0.039$), and NLR (OR=66.561, 95% CI: 2.395–1849.953, $p = 0.013$) were independently associated with an increased risk of gestational hypertension. Other variables, including age, BMI, gravida, PLR, MLR, and SII, were not significant predictors (all $p > 0.05$) (Table 6).

Table 3. Comparison of Perinatal Outcomes between Control and Gestational Hypertension Groups

	Control (n=40)	GHT (n=40)	p value
Gestational Age at Delivery (weeks)	39.0 (37.0–41.0)	38.8 (37.0–40.0)	0.480 b
Birth Weight (grams)	3275.2 (2880.0–3626.5)	3308.1 (2869.5–3683.0)	0.644 b
NICU (days)	0.1 (0.0–0.0)	0.7 (0.0–0.5)	0.025 b

Data are presented as medians (IQR). Abbreviations: NICU, neonatal intensive care unit; GHT, gestational hypertension. b Mann-Whitney U test. Statistical significance was set at $p < 0.05$. Statistically significant values are bolded.

Table 4. Receiver Operating Characteristic (ROC) Analysis of Hematological and Inflammatory Indices for Predicting Gestational Hypertension

	Area	Sensitivity	Specificity	p value	Cut-off	Asym. 95% CI	
						Low. Bound	Up. Bound
PDW (%)	0.681	60	60	0.005	12.6	0.564	0.799
RDW (%)	0.787	73	77	<0.001	12.7	0.686	0.888
NLR	0.871	78	82	<0.001	2.14	0.789	0.954
PLR	0.767	78	70	<0.001	128	0.657	0.876
MLR	0.779	75	70	<0.001	0.21	0.675	0.882
SII	0.836	83	75	<0.001	513	0.747	0.925

Data are expressed as area under the curve (AUC) with 95% confidence intervals (CI), sensitivity, specificity, and cutoff values. Abbreviations: PDW, platelet distribution width; RDW, red cell distribution width; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; MLR, monocyte-to-lymphocyte ratio; SII, systemic immune-inflammation index; GHT, gestational hypertension. Statistical significance was set at $p < 0.05$. Statistically significant values are bolded.

Table 5. Correlation Analysis of Hematological and Inflammatory Indices with Perinatal Outcomes

		Gestational Age at Delivery (weeks)	Birth Weight (grams)	NICU Stay (days)
PDW (%)	Pearson Corr.	-0.030	-0.084	0.130
	p value	0.790	0.459	0.251
RDW (%)	Pearson Corr.	-0.127	0.253	0.106
	p value	0.263	0.024	0.351
NLR	Pearson Corr.	0.071	0.022	0.132
	p value	0.534	0.845	0.245
PLR	Pearson Corr.	0.126	0.079	0.089
	p value	0.267	0.486	0.433
MLR	Pearson Corr.	0.119	-0.008	0.238
	p value	0.293	0.945	0.033
SII	Pearson Corr.	0.058	-0.059	0.168
	p value	0.612	0.604	0.136

Data are expressed as Pearson correlation coefficients (r) with corresponding p values.

Abbreviations: PDW, platelet distribution width; RDW, red cell distribution width; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; MLR, monocyte-to-lymphocyte ratio; SII, systemic immune-inflammation index; NICU, neonatal intensive care unit. $p < 0.05$ was considered statistically significant. Statistically significant correlations are bolded.

Table 6. Multivariate Logistic Regression Analysis of Hematological and Inflammatory Indices for Predicting Gestational Hypertension

	B	p value	OR (Exp(B))	95% CI
Age (years)	0.015	0.871	1.015	0.851–1.210
BMI (kg/m ²)	0.003	0.992	1.003	0.588–1.708
Gravida (n)	0.038	0.905	1.039	0.553–1.954
PDW (%)	1.714	0.018	5.55	1.349–22.834
RDW (%)	2.358	0.039	10.572	1.128–99.049
NLR	4.198	0.013	66.561	2.395–1849.953
PLR	0.008	0.709	1.008	0.965–1.054
MLR	10.715	0.205	45.71	0.003–6.98
SII	-0.002	0.645	0.998	0.988–1.008
Constant	0.015	0.871	1.015	0.851–1.210

B: Regression coefficient; OR (Exp(B)): Odds ratio; CI: Confidence interval. PDW, RDW, and NLR remained statistically significant independent predictors of gestational hypertension. Statistical significance was set at $p < 0.05$ and is shown in bold.

DISCUSSION

The findings of this study demonstrated that hematological parameters reflecting inflammatory responses showed significant alterations in pregnant women who developed gestational hypertension. In particular, increased levels of white blood cells, neutrophils, and monocytes suggest an accentuated systemic inflammatory state in these cases. Moreover, the observed elevations in hemoglobin, hematocrit, PDW, and RDW indicate disruption of hematological homeostasis and increased vascular

stress. Higher values of combined inflammatory indices, such as NLR, PLR, MLR, and SII, further support the notion that the immune-inflammatory balance during pregnancy shifts in favor of gestational hypertension. These results highlight that simple and readily accessible hematological parameters may be clinically valuable for the early prediction of gestational hypertension.

Jeon et al. investigated the predictive value of NLR and the newly proposed PNR in differentiating gestational hypertension from

PE and reported that NLR levels were elevated, whereas PLR demonstrated only limited discriminative power (13).

Özkan et al. reported significant alterations in hematological parameters, such as NLR, PLR, and PDW, among patients with gestational hypertension and PE, with particularly marked elevations observed in severe PE cases (14). Similarly, in our study, the inflammatory indices, including NLR, RDW, PDW, PLR, and SII, were significantly higher in the gestational hypertension group than in the control group. However, Özkan et al. noted that NLR levels were comparable between the gestational hypertension and control groups, with a more pronounced increase observed in PE and severe PE, suggesting a potential association between this parameter and disease severity. In contrast, the fact that our study demonstrated elevated indices even in cases of isolated gestational hypertension is noteworthy, as it indicates that the inflammatory response may begin before the progression to PE.

A large retrospective study involving 2050 pregnant women (164 with PE and 1886 controls) demonstrated that NLR and PLR values did not differ before 20 weeks of gestation; however, at the time of delivery, the PE group exhibited higher NLR and lower PLR values (15). Similarly, Gezer et al. observed significantly elevated NLR and PLR in women with PE compared to controls and identified NLR as the most robust predictor in a multivariate regression analysis (16). Wang et al. further supported these findings, reporting through ROC analysis that NLR could discriminate PE from healthy pregnancies and predict disease severity (cut-off 4.198, sensitivity 53%, specificity 83%) (17). Zheng et al. also found increased inflammatory indices in PE cases and suggested that both NLR and PLR may be useful markers for predicting PE (18). Conversely, Yavuzcan et al. noted that these parameters did not effectively predict the progression from PE to severe PE (SPE) (19). This is consistent with the results of Targońska-Ste Rpnia et al., who concluded that NLR and PLR were not reliable for identifying SPE in otherwise healthy subjects (20). In another investigation, Kurtoglu et al. proposed an NLR cut-off value of 4.48 with a sensitivity of 58% and specificity of 63%; however, no significant link to disease severity was established (21). In line with these reports, our study also demonstrated significantly higher NLR values in women with gestational hypertension than in controls, supporting the concept that inflammatory activation is involved even in the earlier hypertensive spectrum of pregnancy disorders. Moreover, unlike several previous studies, we found that not only NLR but also RDW and SII emerged as strong independent predictors of gestational hypertension, with NLR showing the highest diagnostic accuracy in the present study. These findings suggest that the systemic inflammatory burden, reflected by the NLR and composite indices such as the SII, may provide a superior predictive capacity compared to conventional markers alone.

Importantly, the identification of these indices in the first trimester highlights their potential utility for early risk stratification before the clinical onset of PE, thereby adding novel evidence to the growing literature on the hematological predictors of hypertensive disorders during pregnancy.

Recent evidence supports the role of inflammatory and hematological indices in the pathophysiology of hypertensive disorders of pregnancy. In a recent study (22), alterations in inflammation-related biomarkers were shown to be closely associated with disease severity and adverse perinatal outcomes. Consistent with these findings, our study demonstrated that first-trimester inflammatory indices, particularly NLR, RDW, and PDW, were significantly elevated in women who later developed gestational hypertension. These results suggest that systemic inflammatory activation may precede the clinical onset of gestational hypertension and contribute to its development. Moreover, the independent predictive value of NLR and RDW observed in our multivariate analysis highlights the potential clinical utility of these easily accessible parameters for early risk stratification.

The meta-analysis conducted by Kang et al., which included 15 studies with a total of 3,982 pregnant women, demonstrated that NLR was significantly higher in PE cases than in healthy pregnancies (23). Moreover, NLR values were more markedly elevated in the severe PE group than in the control and mild PE groups. This methodologically robust study, which combined data from diverse populations, suggests that NLR may serve as a reliable biomarker for disease severity. In line with these findings, our study also revealed elevated NLR in the gestational hypertension group. However, in contrast to the analysis by Kang et al., our study focused on first-trimester data and exclusively examined isolated cases of gestational hypertension. Additionally, we demonstrated that NLR, RDW, and SII had independent predictive values. These differences highlight that inflammatory markers may rise during the gestational hypertension stage even before progression to PE, and that more complex indices could provide stronger tools for early risk prediction.

This study has certain limitations that should be considered when interpreting its findings. It should be noted that the relatively wide confidence intervals observed in the multivariate logistic regression analysis, particularly for NLR and RDW, may reflect the limited sample size of this study. Although statistically significant associations were identified, these wide intervals indicate a degree of uncertainty in the effect size estimates and should be interpreted with caution. Its retrospective design may have introduced selection bias, as the analysis was based on previously recorded data. In addition, the study was conducted at a single tertiary

center, which may restrict the external validity of the results and limit their applicability to populations with different demographic or ethnic characteristics of the study population. Although strict exclusion criteria were applied, residual confounding factors such as subclinical infections, nutritional status, and genetic predispositions could not be completely eliminated. Furthermore, only first-trimester hematological indices were evaluated, and longitudinal changes throughout pregnancy were not assessed, which may have provided further insights into the temporal relationship between inflammatory markers and the development of gestational hypertension.

In summary, this study demonstrated that first-trimester hematological inflammatory indices, particularly NLR, RDW, and SII, were significantly associated with the subsequent development of gestational hypertension. Among these, NLR exhibited the highest diagnostic accuracy, while RDW and SII emerged as independent predictors in the multivariate analysis. These findings suggest that simple, cost-effective, and widely available blood parameters obtained from routine complete blood count testing may serve as practical tools for early risk stratification of gestational hypertension in daily obstetric practice and help identify women who may benefit from closer monitoring. However, further large-scale prospective studies are warranted to validate these results and to support their integration into routine first-trimester screening programs.

Conflict of Interest: The authors declare that they have no conflict of interest related to this study.

Funding: This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Author Contributions: A.K.I. contributed to study conception, design, data acquisition, statistical analysis, and drafting of the manuscript. A.H.K. participated in data collection, literature review, and critical revision of the manuscript. Ö.V.A. was involved in data interpretation, supervision, and manuscript editing. S.E. contributed to patient recruitment, data management, and discussion. A.I.S. assisted with methodology and critical revision of the manuscript. M.P. provided supervision, validation of results, and final approval of the manuscript. All authors read and approved the final version of the manuscript and agree to be accountable for all aspects of the work.

Data Availability Statement: The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

REFERENCES

- Komijani E, Parhizkar F, Abdolmohammadi-Vahid S, Ahmadi H, Nouri N, Yousefi M, et al. Autophagy-mediated immune system regulation in reproductive system and pregnancy-associated complications. *J Reprod Immunol*. 2023;158:103973.
- Barr LC, Liblik K, Johri AM, Smith GN. Maternal Cardiovascular Function Following a Pregnancy Complicated by Preeclampsia. *Am J Perinatol*. 2022;39(10):1055-64.
- Yüzen D, Graf I, Diemert A, Arck PC. Climate change and pregnancy complications: From hormones to the immune response. *Front Endocrinol (Lausanne)*. 2023;14:1149284.
- Deer E, Herrock O, Campbell N, Cornelius D, Fitzgerald S, Amaral LM, et al. The role of immune cells and mediators in preeclampsia. *Nat Rev Nephrol*. 2023;19(4):257-70.
- Cifková R. Hypertension in Pregnancy: A Diagnostic and Therapeutic Overview. *High Blood Press Cardiovasc Prev*. 2023;30(4):289-303.
- Sunita, Kaushik R, Gaur PK, Verma KK. Gestational Hypertension: A Contemporary Review of Epidemiology, Pathophysiology, and Therapeutic Approaches. *Curr Hypertens Rev*. 2024;20(3):117-26.
- Antza C, Cifkova R, Kotsis V. Hypertensive complications of pregnancy: A clinical overview. *Metabolism*. 2018;86:102-11.
- Gao J, Jiang N, Chen Q, Zhao M, Tang Y. Systemic Immune-Inflammation Indices Could Be Additional Predictive Markers for Cesarean Scar Pregnancy. *Am J Reprod Immunol*. 2024;92(3):e13924.
- Han VX, Patel S, Jones HF, Nielsen TC, Mohammad SS, Hofer MJ, et al. Maternal acute and chronic inflammation in pregnancy is associated with common neurodevelopmental disorders: a systematic review. *Transl Psychiatry*. 2021;11(1):71.
- Kindan A, Kurt DS, Nalbantçılar DR, Ulusoy CO, Yücel KY. Evaluation of albumin-based inflammatory markers as diagnostic tools in HELLP syndrome. *Sci Rep*. 2025;15(1):22125.
- Soysal C, Sarı H, Işıksalan MM, Özkaya EB, Ulaş Ö, Taşçı Y, et al. Role of the systemic immune-inflammation index in threatened abortion patients and predicting of abortion. *J Obstet Gynaecol Res*. 2023;49(7):1723-8.
- Gestational Hypertension and Preeclampsia: ACOG Practice Bulletin, Number 222. *Obstet Gynecol*. 2020;135(6):e237-e60.
- Jeon Y, Lee WI, Kang SY, Kim MH. Modified Complete Blood Count Indices as Predicting Markers of Preeclampsia from Gestational Hypertension: Neutrophil to Lymphocyte Ratio, Platelet to Lymphocyte Ratio, and Platelet to Neutrophil Ratio. *Clin Lab*. 2017;63(11):1897-902.
- Ozkan D, İbanoglu MC, Adar K, Ozkan M, Lutfi Tapisiz O, Engin-Ustun Y, et al. Efficacy of blood parameters in predicting the severity of gestational hypertension and preeclampsia. *J Obstet Gynaecol*. 2023;43(1):2144175.
- Mannaerts D, Heyvaert S, De Cordt C, Macken C, Loos C, Jacquemyn Y. Are neutrophil/lymphocyte ratio (NLR), platelet/lymphocyte ratio (PLR), and/or mean platelet volume (MPV) clinically useful as predictive parameters for preeclampsia? *J Matern Fetal Neonatal Med*. 2019;32(9):1412-9.
- Gezer C, Ekin A, Ertas IE, Ozeren M, Solmaz U, Mat E, et al. High first-trimester neutrophil-to-lymphocyte and platelet-to-lymphocyte ratios are indicators for early diagnosis of preeclampsia. *Ginekolo Pol*. 2016;87(6):431-5.
- Wang J, Zhu QW, Cheng XY, Liu JY, Zhang LL, Tao YM, et al. Assessment efficacy of neutrophil-lymphocyte ratio and monocyte-lymphocyte ratio in preeclampsia. *J Reprod Immunol*. 2019;132:29-34.
- Zheng WF, Zhan J, Chen A, Ma H, Yang H, Maharjan R. Diagnostic value of neutrophil-lymphocyte ratio in preeclampsia: A PRISMA-compliant systematic review and meta-analysis. *Medicine (Baltimore)*. 2019;98(51):e18496.
- Yavuzcan A, Çağlar M, Ustün Y, Dilbaz S, Ozdemir I, Yildiz E, et al. Mean platelet volume, neutrophil-lymphocyte ratio and platelet-lymphocyte ratio in severe preeclampsia. *Ginekolo Pol*. 2014;85(3):197-203.
- Targońska-Stępnik B, Zwolak R, Piotrowski M, Grzechnik K, Majdan M. The Relationship between Hematological Markers of Systemic Inflammation (Neutrophil-To-Lymphocyte, Platelet-To-Lymphocyte, Lymphocyte-To-Monocyte Ratios) and Ultrasound Disease Activity Parameters in Patients with Rheumatoid Arthritis. *J Clin Med*. 2020;9(9).
- Kurtoglu E, Kokcu A, Celik H, Tosun M, Malatyalioglu E. May ratio of neutrophil to lymphocyte be useful in predicting the risk of developing preeclampsia? A pilot study. *J Matern Fetal Neonatal Med*. 2015;28(1):97-9.
- Agaoglu Z, Bastemur AG, Bal AA, Kayaalp H, Serbetci H, Agaoglu MO, et al. Placental microvascular flow imaging as a predictor of disease severity and adverse perinatal outcomes in preeclampsia: An observational study. *Int J Gynaecol Obstet*. 2026.
- Kang Q, Li W, Yu N, Fan L, Zhang Y, Sha M, et al. Predictive role of neutrophil-to-lymphocyte ratio in preeclampsia: A meta-analysis including 3982 patients. *Pregnancy Hypertens*. 2020;20:111-8.

Evaluation of AST/Platelet Ratio Index, AST/Creatinine Ratio Index, and AST/ALT Ratio (De Ritis) in Type 2 Diabetes Mellitus: A Tertiary Center Case–Control Study

Tip 2 Diabetes Mellitus Tanılı Gebe Hastaların AST/Platelet Ratio İndeks ve AST/Kreatinin Ratio İndeks, AST/ALT Ratio İndekslerinin Değerlendirilmesi. Bir Tersiye Merkez Vaka -Kontrol Çalışması

 Hüseyin KAYAALP¹,  Sertaç AYÇİÇEK²

¹University of Health Sciences, Ankara Bilkent City Hospital, Department of Obstetrics and Gynecology, Perinatology Unit, Ankara, Türkiye

²University of Health Sciences, Gazi Yaşargil Training and Research Hospital, Department of Obstetrics and Gynecology, Diyarbakır, Türkiye

ABSTRACT

Aim: The aim of this study was to compare the aspartate aminotransferase/platelet ratio index (APRI), aspartate aminotransferase/creatinine ratio index (ACRI), and AST/ALT ratio (De Ritis) between pregnant women diagnosed with tip 2 diabetes mellitus (DM) and healthy controls.

Materials and Methods: This retrospective, single-center study was conducted in a tertiary referral hospital between January 2023 and January 2025. A total of 190 pregnant women were included: 95 with tip 2 DM (group 1) and 95 without (group 2). The APRI and ACRI indices, as well as the maternal and fetal outcomes, were compared between the groups.

Results: In the study group, first-trimester (tr) creatinine ($p<0.001$) and leukocyte (WBC) counts ($p=0.003$), as well as third-tr AST ($p<0.001$) and creatinine ($p<0.001$), were significantly higher. In the study group, first-tr ACRI ($p=0.006$) and De Ritis ratio ($p=0.008$) were significantly lower, whereas third-tr APRI ($p<0.001$), ACRI ($p=0.040$), and De Ritis ratio ($p=0.002$) were significantly higher.

Conclusions: In this study, first-tr ACRI and De Ritis ratios were significantly lower, while third-tr APRI, ACRI, and De Ritis ratios were significantly higher in patients with tip 2 DM compared to controls. Although first- and third-tr APRI, ACRI, and De Ritis indices differed significantly from those of the control group, they did not demonstrate predictive value for NICU admission. These indices may reflect metabolic and hepatic changes in tip 2 DM but lack independent predictive value, though they could support multivariate models.

Keywords: Pregnancy, Diabetes Mellitus, Type 2, Aspartate Aminotransferases, Creatinine, Intensive Care Units, Neonatal

ÖZ

Amaç: Bu çalışmanın amacı tip 2 diabetes mellitus (DM) tanılı hastaların AST/platelet ratio indeksi (APRI) ve AST/kreatinin ratio indeksi (ACRI), AST/ALT ratio (De Ritis)'lerinin sonuçlarını sağlıklı gebelerle karşılaştırmak ve bu indekslerin yeni doğan yoğun bakıma yatış (NICU)'ları öngörücü etkinliğini araştırmaktır.

Gereç ve Yöntemler: Bu çalışma tek merkezli, üçüncü basamak bir merkezde retrospektif olarak tasarlandı. Çalışmaya ocak 2023 ile ocak 2025 tarihleri arasında tip 2 DM tanılı 95 ve tip 2 DM tanılı olmayan 95 toplamda 190 gebe hasta dahil edildi. Çalışmaya dahil edilen hastalar tip 2 DM (grup 1) ve kontrol (grup 2) olacak şekilde 2 grup oluşturuldu. Grupların maternal laboratuvar sonuçları sonrası oluşturulan APRI ve ACRI indeksleri ve maternal, fetal sonuçları karşılaştırıldı.

Bulgular: Çalışma grubunda 1. trimester (tr) kreatinin ($p<0.001$), lökosit (wbc) ($p=0.003$), 3. tr AST ($p<0.001$), kreatinin ($p<0.001$) anlamlı ve yüksek izlendi. Çalışma grubunda 1. tr ACRI ($p=0.006$), De Ritis ($p=0.008$) anlamlı, düşük izlenirken, 3. tr APRI ($p<0.001$), ACRI ($p=0.040$), De Ritis ($p=0.002$) anlamlı, yüksek izlenmiştir.

Sonuç: Bu çalışmada tip 2 DM'li hastalarda 1. tr ACRI, De Ritis anlamlı ve düşük 3. tr APRI, ACRI, De Ritis ise kontrol gruplarına göre anlamlı ve yüksek izlenmiştir. 1. tr ve 3. tr APRI, ACRI, De Ritis sonuçları kontrol grubuna göre anlamlı çıkmasına rağmen NICU'yu öngörü etkinliğinin olmadığı sonucuna vardık. Tip 2 DM'de bu indekslerin etkili olabileceği yerler olabilir ancak öngörücü olarak kullanımı uygun görülmemektedir. Bununla birlikte daha anlamlı kılabilen çok parametrelili modellere dahil edilebilirler.

Anahtar Kelimeler: Gebelik, Tip 2 diyabetes mellitus, Aspartat Aminotransferaz, Kreatinin, yeni doğan yoğun bakım

Cite as: Kayaalp H and Ayçiçek S. Evaluation of AST/Platelet Ratio Index, AST/Creatinine Ratio Index, and AST/ALT Ratio (De Ritis) in Type 2 Diabetes Mellitus: A Tertiary Center Case–Control Study. Jinekoloji-Obstetrik ve Neonatoloji Tıp Dergisi 2026;23(2):132–138.

Geliş/Received: 13.12.2025 • **Kabul/Accepted:** 15.01.2026

Sorumlu Yazar/Corresponding Author: Hüseyin Kayaalp, University of Health Sciences, Ankara Bilkent City Hospital, Department of Obstetrics and Gynecology, Perinatology Unit, Ankara, Türkiye
E-mail: huseyinkayaalp.2121@gmail.com

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

INTRODUCTION

Pregestational diabetes mellitus (PreGDM) refers to type 1 diabetes mellitus (DM) or type 2 DM diagnosed before pregnancy and is associated with significant risks for both maternal and fetal outcomes. In type 2 DM, processes such as insulin resistance, inflammation, and oxidative stress induced by hyperglycemia affect not only glucose metabolism but also liver and renal functions, thereby predisposing patients to systemic complications (1–3). In recent years, there has been increasing interest in simple and noninvasive biochemical indices that may reflect these systemic effects. In this context, the aspartate aminotransferase (AST) -to-platelet ratio index (APRI), AST-to-creatinine ratio index (ACRI), and the De Ritis ratio (AST / alanine aminotransferase (ALT) have emerged as promising indicators.

The aspartate APRI was originally developed to assess liver fibrosis in patients with chronic hepatitis C and is calculated based on the ratio between AST and platelet count. This index can noninvasively reflect the degree of fibrosis by its association with increased AST and decreased platelet counts (4). The ACRI is a relatively novel parameter calculated by dividing AST by creatinine and is considered to be helpful particularly in the diagnosis of nonalcoholic steatohepatitis (NASH). Since creatinine may be influenced by metabolic factors such as muscle mass, renal function, and insulin resistance, ACRI has the potential to reflect both hepatic and renal metabolic dysfunction simultaneously (5).

The De Ritis ratio was first described in 1957 and has been widely used in the differential diagnosis of liver diseases. Higher ALT compared with AST are typically observed in conditions such as acute hepatitis, whereas an AST to ALT ratio greater than 1 suggests alcoholic hepatitis or fibrotic processes (6). Moreover, several studies have shown that this ratio may also be associated with type 2 DM and metabolic syndrome (7). These findings suggest that liver enzyme patterns may serve not only as indicators of hepatic disease but also as markers of systemic metabolic burden.

During pregnancy, serum creatinine levels physiologically decrease, while AST and ALT enzymes generally remain within normal ranges. Therefore, in the presence of additional stressors such as type 2 DM, deviations in these parameters may indicate underlying metabolic disturbances. Recent evidence suggests that these ratios may reflect not only hepatic involvement but also have an impact on neonatal prognosis (8,9). In this context, we aimed to compare APRI, ACRI, and De Ritis ratios in pregnant women with type 2 DM and healthy pregnant controls, and to evaluate their potential role in predicting adverse outcomes.

MATERIALS AND METHODS

Study Population

This study was designed as a single center retrospective case control study. Pregnant women aged 18 to 45 years with a diagnosis of type 2 DM who were followed and treated at the Department of Obstetrics and Gynecology of Gazi Yaşargil Training and Research Hospital between January 2023 and January 2025 were included. The diagnosis of type 2 DM was established before pregnancy based on at least one of the following criteria: hemoglobin A1c level of 6.5 percent or higher, fasting plasma glucose level of 126 mg/dL or higher, 2 hour plasma glucose level of 200 mg/dL or higher during an oral glucose tolerance test, or random plasma glucose level of 200 mg/dL or higher (3).

The exclusion criteria were the presence of major fetal anomalies, multiple pregnancies, pregnant women with additional chronic diseases, cases with preterm premature rupture of membranes (PPROM), and patients who smoked or consumed alcohol. Participants were matched into a study (group 1) and a control (group 2). The study group consisted of pregnant women with type 2 DM, while the control group included low risk pregnant women without systemic diseases such as neurological, cardiovascular, respiratory, gastrointestinal, genitourinary, endocrine, or gastrointestinal disorders, and without obstetric complications including preeclampsia, gestational diabetes mellitus (GDM), or PPRM.

Homogeneity was ensured between the study and control groups with respect to blood parameters obtained during the first trimester (tr), defined as 0 to 14 weeks of gestation, and the third tr, defined as 28 to 36 weeks of gestation. Clinical and demographic data of the participants were recorded, including age, body mass index (BMI), gravidity, parity, gestational age at delivery, birth weight, mode of delivery, umbilical cord pH, 1 minute and 5 minute Apgar scores, neonatal intensive care unit (NICU) admission and indications, hemoglobin (hgb), platelet (PLT), creatinine, white blood cell (WBC), ALT, AST, APRI, ACRI, and De Ritis ratio. Hgb, WBC, PLT levels were measured using the Mindray BC-6000 device (China); ALT, AST, creatinine level was analyzed using the Architect C8000 system (Abbott, USA).

APRI was calculated by accepting the upper limit of AST as 35 U/L and dividing AST by the platelet count. ACRI was calculated by accepting the upper limit of AST as 35 U/L and dividing AST by the creatinine level. The De Ritis ratio was calculated as the ratio of AST to ALT. All statistical analyses were performed using SPSS version 25.0 (SPSS Inc., Chicago, IL, USA). The study was conducted in accordance with the principles of the Declaration of Helsinki, and ethical approval was obtained from the Ethics Committee of the

Gazi Yaşargil Training and Research Hospital on July 25, 2025, with decision number 575.

Statistical Analysis

Statistical analyses were performed using SPSS version 25.0 (SPSS Inc., Chicago, IL, USA). The normality of data distribution was assessed using the Kolmogorov Smirnov test and the Shapiro Wilk test. The Mann Whitney U test was used to compare variables that did not show a normal distribution. Descriptive statistics for non normally distributed variables were presented as median and interquartile range. Receiver operating characteristic (ROC) curve analysis was performed to evaluate the predictive value of type 2 DM for NICU admission. The chi square test was used to compare categorical variables. A $p < 0.05$ was considered statistically significant.

RESULTS

A total of 190 patients were included in this study, with 95 patients in the type 2 DM group and 95 patients in the control group. There were no significant differences between the groups in terms of age, gravidity, parity, BMI, mode of delivery, or fetal birth weight ($p > 0.05$). However, significant differences were observed between

the groups with respect to gestational age at delivery, 1st and 5th minute Apgar scores, and cord pH ($p < 0.001$) (Table 1). The gestational weeks at which laboratory parameters were obtained in the first and third tr were similar between the groups (Table 1). NICU admission was significantly more frequent in the type 2 DM group ($p < 0.001$) (Table 1). The NICU indications of the type 2 DM and control groups are presented in Table 1. The median hemoglobin A1c in the study group was 7.0 (Table 1).

No significant differences were observed between the groups regarding first tr hemoglobin, PLT, ALT and AST ($p > 0.05$). In contrast, first tr creatinine ($p < 0.001$) and WBC ($p = 0.003$) differed significantly between the groups (Table 2). In the third tr, no significant differences were found in hemoglobin ($p = 0.093$), WBC ($p = 0.809$), PLT ($p = 0.941$), or ALT levels ($p = 0.003$), whereas AST ($p < 0.001$) and creatinine ($p < 0.001$) showed significant differences between the groups (Table 2).

Regarding inflammatory indices, no significant difference was observed in first tr APRI values between the groups ($p = 0.088$). However, significant differences were detected in first tr ACRI ($p < 0.006$) and De Ritis ratio ($p = 0.008$), as well as in third tr APRI ($p < 0.001$), ACRI ($p = 0.040$), and De Ritis ratio ($p = 0.002$) (Table 2).

Table 1. Evaluation of the clinicodemographic characteristics of the type 2 DM and control groups.

		Group1 (Type 2 DM) (n:95)	Group 2 control (n:95)	p value
Age(years), Median (IQR)		32.0(7.0)	30.0(4.0)	0.089
Gravidy, Median (IQR)		2.0(3.0)	2.0(1.0)	0.247
Parity, Median (IQR)		1.0(2.0)	1.0(1.0)	0.848
BMI (kg/m ²), Median (IQR)		27.2(4.55)	26.7(2.86)	0.169
hbA1c, Median (IQR)		7.0(2.3)		
Week of blood sampling, Median (IQR)	1st tr	10.4(2.95)	10.1(3.05)	0.501
	3rd tr	32.0(3.50)	31.5(3.75)	0.827
Weeks of birth, Median (IQR)		37.0(2.0)	39.0(2.0)	<0.001
Weigth of birth(gr), Median (IQR)		3270.0(680.0)	3190.0(600.0)	0.184
Apgar 1st minute, Median (IQR)		7.0(1.0)	8.0(1.0)	<0.001
Apgar 5th minute, Median (IQR)		9.0(1.0)	9.0(0.0)	<0.001
Cord pH, Median (IQR)		7.4(0.01)	7.4(0.0)	<0.001
NICU indications (n/%)	Respiratory problems	6.0 (%40)	2.0(%100)	<0.001
	Hypoglycemia	4.0 (%26)	0.0 (%0)	
	Hyperbilirubinemia	3.0 (%20)	0.0 (%0)	
	Prematurity	2.0 (%14)	0.0 (%0)	
NICU, (n/%)		15.0(15.8%)	2.0(2.1%)	<0.001
Mode of delivery(n/%)	Nvd	41.0(43.2%)	53.0(55.8%)	0.082
	C/S	54.0(56.8%)	42.0(44.2%)	

NICU: Neonatal intensive care unit, IQR: Interquartile range, 1st: first, 3rd: third, Nvd: vaginal delivery c/s: sezaryen sectio, BMI: Body mass index, Statistical Test: Mann-whitney U, Significant value $p < 0.05$

Table 2. Evaluation of maternal laboratory parameters, APRI, ACRI, and De Ritis ratios in the type 2 DM and control groups.

	Group1 (type 2 DM) (n:95) Median(IQR)	Group 2(control) (n:95) Median (IQR)	p value
1st tr Hgb (g/dL)	12.3(1.9)	12.5(1.3)	0.493
1st tr wbc (10 ⁹ /L)	8.9(2.5)	8.3(2.46)	0.003
1st tr plt (10 ⁹ /L)	265.0(88.0)	256.0(80.0)	0.823
1st tr creatinine (mg/dl)	0.56(0.14)	0.5(0.1)	<0.001
1st tr ALT (U/L)	15.5(13.5)	15.0(5.0)	0.629
1st tr AST (U/L)	12.0(9.0)	14.0(5.0)	0.152
3rd tr Hgb (g/dL)	11.7(1.6)	11.9(2.0)	0.093
3rd tr wbc (10 ⁹ /L)	9.8(4.4)	9.98(2.98)	0.809
3rd tr plt (10 ⁹ /L)	245.0(133.0)	235.0(88.0)	0.941
3rd tr creatinine (mg/dl)	0.57(0.18)	0.49(0.13)	<0.001
3rd tr ALT (U/L)	14.5(9.8)	15.0(6.0)	0.664
3rd tr AST (U/L)	21.0(10.0)	13.0(7.0)	<0.001
1st tr APRI	0.42(0.03)	0.52(0.03)	0.190
1st tr ACRI	21.8(9.99)	26.3(10.5)	0.006
1st tr DE Ritis	0.80(0.41)	0.93(0.31)	0.008
3rd tr APRI	0.10(0.09)	0.05(0.04)	<0.001
3rd tr ACRI	39.3(10.3)	26.8(18.5)	0.040
3rd tr De Ritis	1.2(1.43)	0.87(0.75)	0.002

APRI: AST/ PLT ratio, ACRI: AST/ creatinine ratio, wbc: white blood cell, plt: Platelet, Hgb: hemoglobin, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase
De Ritis : AST/ALT ratio, Statistical test: Mann- whitney U, Significant value p<0.05, tr: trimester, 1st: first, 3rd: third

Table 3. ROC curve results of significant laboratory parameters and indices for predicting NICU admission in the type 2 DM group

		Area	Standard deviation	p value	AUC %95 lower	AUC %95 upper	Cut off-value	sensitivity (%)	specificity (%)
NICU	3rd tr AST	0.546	0.088	0.597	0.374	718	15.5	58.3	56.7
	3rd tr ALT	0.489	0.094	0.900	0.304	0.674	14.5	58.3	55.4
	1st tr creatinine	0.528	0.094	0.750	0.328	728	0.53	58.2	41.8
	3rd tr creatinine	0.627	0.102	0.144	0.443	811	0.54	66.7	63.4
	3rd tr APRI	0.530	0.084	0.732	0.366	0.694	0.063	50.0	49.6
	1st tr ACRI	0.418	0.085	0.346	0.254	0.582	24.09	50.0	49.6
	3rd tr ACRI	0.494	0.084	0.946	0.329	0.659	30.80	50.1	46.7
	1st tr De Ritis	0.534	0.097	0.699	0.343	0.724	0.87	50.0	49.6
	3rd tr De Ritis	0.564	0.092	0.462	0.384	0.744	0.97	58.3	51.1

AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, APRI: AST/ PLT ratio, ACRI: AST/kreatinin ratio, NICU: neonatal intensive care unit, De Ritis : AST/ALT Ratio
significant value p<0.05, tr: trimester, 1st: first, 3rd: third

ROC curve analyses performed to evaluate the predictive value of first and third tr APRI, ACRI, and De Ritis ratios, as well as third tr ALT and AST, for NICU admission in the type 2 DM group did not yield statistically significant results ($p > 0.05$). The results are presented in Table 3, and the ROC curve is shown in Figure 1.

DISCUSSION

The aim of this study was to compare APRI, ACRI, and De Ritis indices in patients with type 2 DM and healthy pregnant women, and to evaluate their predictive value for NICU admission.

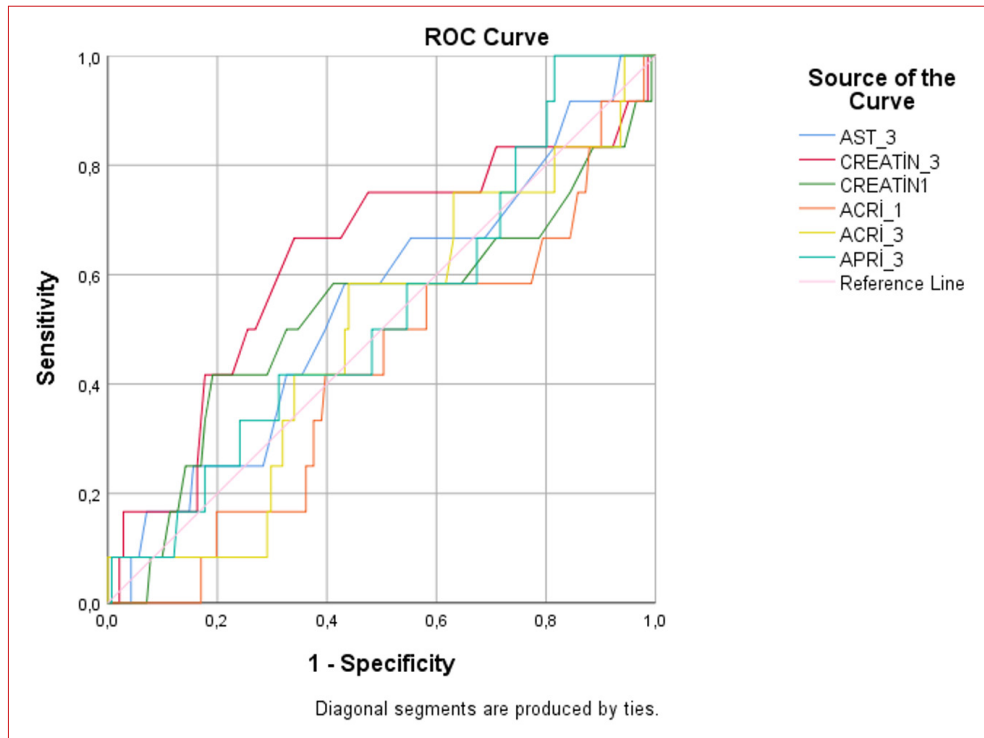


Figure 1. ROC curves of laboratory parameters and indices for predicting NICU admission in the type 2 DM group

In our study, gestational age at delivery, 1st and 5th minute Apgar scores, and cord pH were significantly lower in the type 2 DM group, while NICU admission was more frequent in this group. In the study group, first tr ACRI and De Ritis ratios were significantly lower, whereas third tr APRI, ACRI, and De Ritis ratios were significantly higher.

APRI is a simple index that was initially defined in patients with chronic hepatitis C to noninvasively assess liver fibrosis (10). As AST levels increase and PLT counts decrease with higher degrees of fibrosis, APRI reflects these opposing changes and has been shown to be effective in identifying significant fibrosis, with reported area under the curve values of approximately 0.80 for fibrosis and 0.89 for cirrhosis in hepatitis C patients (10). Although data on the use of APRI in obstetrics are limited, recent studies, particularly those focusing on intrahepatic cholestasis of pregnancy, are noteworthy. For example, Saadi et al. reported that third trimester APRI scores were significantly higher in pregnant women with intrahepatic cholestasis compared with healthy controls, with a cutoff value of approximately 0.42, sensitivity of 65%, and specificity of 73% (11). Similarly, Eyisoy et al. demonstrated that APRI scores were associated with disease severity in intrahepatic cholestasis of pregnancy, with significantly higher values observed in severe cases compared with mild cases. They also reported that elevated APRI levels were associated with meconium stained amniotic fluid, NICU and preterm birth, with a cutoff value of approximately 1.06 (12). These findings suggest that APRI may reflect the severity of pregnancy related liver involvement.

In our study, no significant difference was observed between the groups in first tr APRI values. However, third tr APRI values were significantly higher in diabetic pregnancies compared with controls. This finding may indicate mild hepatic stress or enzyme elevation in the later stages of pregnancy. Nevertheless, ROC curve analysis showed that APRI did not demonstrate significant predictive performance for NICU with an area under the curve of approximately 0.53 and a $p > 0.05$. Overall, APRI may reflect metabolic stress in diabetic pregnancies, but it appears to have limited predictive value for neonatal outcomes.

ACRI is not a widely established biochemical index in the literature, and data regarding its use during pregnancy are scarce. This ratio combines AST, a marker of hepatic function, with creatinine, a marker of renal function, and aims to reflect potential hepatorenal alterations. In normal pregnancy, serum creatinine decrease significantly due to increased glomerular filtration rate, which represents a physiological adaptation. The reference range for creatinine in pregnancy is generally accepted as approximately 0.4 to 0.8 mg/dL, which is lower than that in the nonpregnant population (13). In diabetic pregnancies, serum creatinine may remain above this physiological range due to long standing diabetes related renal involvement.

One of the few studies evaluating ACRI was conducted by Mohamed et al. in patients with cirrhosis, where the index was used to predict the presence of esophageal varices. In that study, an ACRI cutoff value greater than 40 demonstrated good diagnostic accuracy,

with sensitivity of 80%, specificity of 82.5%, and an area under the curve of approximately 0.85 (14). The authors also emphasized that ACRI had not been previously used for this purpose (14). Additionally, several studies have indirectly reported associations between AST and creatinine and metabolic disturbances in diabetic individuals (15). In this context, our study represents one of the first investigations to evaluate the ACRI index during pregnancy, particularly in a diabetic population.

According to our findings, first trimester ACRI values were significantly lower in the type 2 DM group compared with controls. This difference may be explained by the physiologically lower creatinine levels observed in healthy pregnancies. In the third tr, however, ACRI values were significantly higher in the diabetic group. This increase may be attributed to elevated AST combined with relatively higher creatinine in diabetic pregnancies, possibly reflecting mild hepatic enzyme elevation and early diabetic nephropathy. Despite these biochemical differences, ACRI showed weak clinical predictive performance, as neither first nor third tr ACRI values significantly predicted NICU with area under the curve values ranging from approximately 0.42 to 0.49 and $p > 0.05$. Therefore, although ACRI reflects biochemical alterations, it does not appear to be a useful practical predictor of NICU admission.

The De Ritis ratio, also known as the AST to ALT ratio, has long been used in hepatology. First described by Fernando De Ritis in 1957, this ratio is particularly useful in differentiating various types of liver injury (7). In acute viral hepatitis, ALT are typically higher than AST, resulting in a De Ritis ratio below 1, whereas in alcoholic hepatitis or advanced fibrosis, AST exceed ALT, leading to a ratio greater than 1 (16).

In recent years, the De Ritis ratio has also been associated with conditions beyond liver disease. Elevated De Ritis ratios have been linked to metabolic syndrome, insulin resistance, type 2 DM, and cardiovascular diseases (17). For instance, Li et al. demonstrated increased De Ritis ratios in the presence of preGDM and metabolic syndrome (18). In pregnancy related research, Dinçgez et al. reported that pregnant women with lower De Ritis ratios had a higher risk of developing gestational diabetes mellitus (19). These findings suggest that liver enzyme patterns may provide insights into metabolic risk even in early pregnancy.

In our study, the course of the De Ritis ratio in type 2 diabetic pregnancies was evaluated. While the ratio remained below 1 in all groups during the first tr, it increased significantly in the third tr in the diabetic group, exceeding 1. This increase may be explained by a greater rise in AST compared with ALT and may be associated with hepatic stress or nonalcoholic steatohepatitis (16). Our findings indicate altered liver enzyme dynamics in diabetic pregnancies

and are consistent with data related to metabolic syndrome (9). However, the De Ritis ratio did not show significant predictive value for NICU admission, with an area under the curve of approximately 0.56 and a p value greater than 0.4. Thus, the De Ritis ratio may be better interpreted as a marker of maternal metabolic status rather than a predictor of neonatal outcomes.

This study is among the first to simultaneously evaluate changes in APRI, ACRI, and De Ritis indices during both the first and third tr in type 2 DM and to assess their role in predicting NICU admission. The main strengths of the study include the comparative analysis between distinct groups and a relatively larger sample size compared with similar studies. The limitations of the study include its single center and retrospective design.

In conclusion, our study demonstrates that indices based on hepatic function tests show systematic differences in diabetic pregnancies compared with healthy controls. In the third trimester, increases in AST levels were accompanied by significant changes in APRI, ACRI, and De Ritis scores, highlighting the importance of monitoring liver enzymes in diabetic pregnancies. However, these indices were not sufficient predictors of NICU admission. Therefore, these parameters should be interpreted with caution in clinical decision making. Our findings provide a foundation for future large scale prospective studies.

Author Contributions: H.K: Oversaw the overall coordination of the study, contributed to the conception and study design, supervised data collection processes, ensured the accuracy and integrity of the data, and guided the statistical and methodological workflow. Reviewed all stages of manuscript development, provided critical intellectual input, ensured compliance with ethical and publication standards, and approved the final version of the manuscript for submission. S.A: Led the conception and design of the study, contributed to data acquisition, performed statistical analyses, and drafted the original manuscript.

Acknowledgments: The authors would like to thank the clinical staff and sonographers who supported data collection throughout the study. We also express our gratitude to the biostatistics team for their contributions to the statistical analyses. We acknowledge the assistance of the Obstetrics and Gynecology Department for providing technical and logistical support during the research process. The authors extend their appreciation to all individuals who contributed to the study but did not meet the criteria for authorship.

Conflict of Interest: The authors declare that there is no conflict of interest.

REFERENCES

1. Catalano PM. Trying to understand gestational diabetes. *Diabet Med*. 2014;31(3):273-81. DOI: [10.1111/dme.12381](https://doi.org/10.1111/dme.12381)
2. ACOG Practice Bulletin No. 201: Pregestational Diabetes Mellitus. *Obstet Gynecol*. 2018;132(6):e228-e248. doi:10.1097/AOG.0000000000002960.
3. American Diabetes Association (ADA). Standards of Medical Care in Diabetes—2024. *Diabetes Care*. 2024;47(Suppl 1):S1–S167. doi:10.2337/dc24-SINT
4. Shin WG, Park SH, Jang MK, Hahn TH, Kim JB, Lee MS, et al. Aspartate aminotransferase to platelet ratio index (APRI) can predict liver fibrosis in chronic hepatitis B. *Dig Liver Dis*. 2008 Apr;40(4):267-74. doi:10.1016/j.dld.2007.10.011. Epub 2007 Dec 4.

5. Kim YS, Jung ES, Hur W, Bae SH, Choi JY, Song MJ, et al. Noninvasive predictors of nonalcoholic steatohepatitis in Korean patients with histologically proven nonalcoholic fatty liver disease. *Clin Mol Hepatol*. 2013 Jun 27;19(2):120–130. doi:10.3350/cmh.2013.19.2.120.
6. Giannini E, Risso D, Testa R. Serum ALT/AST ratio: useful diagnostic tool in chronic hepatitis C? *Dig Dis Sci*. 2003;48(7):1445–50. DOI: [10.1111/j.1572-0241.2001.03646.x](https://doi.org/10.1111/j.1572-0241.2001.03646.x)
7. Zhang Y, Li H, Li Y, Zhang Y, Wang F, Zhao Y, et al. Nonlinear relationship between AST-to-ALT ratio and the incidence of type 2 diabetes mellitus: results from a population-based cohort study. *Front Endocrinol (Lausanne)*. 2022;13:1041616. doi:10.3389/fendo.2022.1041616.
8. Yamamoto JM, Kellett JE, Balsells M, García-Patterson A, Hadar E, Solà I et al. Gestational diabetes and neonatal outcomes: systematic review and meta-analysis. *BMJ*. 2018;362:k3478. PMID: 29934478 DOI: [10.2337/dc18-0102](https://doi.org/10.2337/dc18-0102)
9. Song S, Zhang Y, Qiao X, Duo Y, Xu J, Peng Z, et al. ALT/AST as an independent risk factor of gestational diabetes mellitus. *Int J Gen Med*. 2022;15:7665–7673. doi:10.2147/IJGM.S366508.
10. Wai CT, Greenson JK, Fontana RJ, Kalbfleisch JD, Marrero JA, Conjeevaram HS, et al. A simple noninvasive index can predict both significant fibrosis and cirrhosis in patients with chronic hepatitis C. *Hepatology*. 2003;38(2):518–26. PMID: 12883497 DOI: [10.1053/jhep.2003.50346](https://doi.org/10.1053/jhep.2003.50346)
11. Saadi R, Saban A, Weintraub AY, Yardeni D, Eşkoli T. Association between aspartate aminotransferase/platelet ratio index (APRI) and intrahepatic cholestasis of pregnancy and other related complications. *Arch Gynecol Obstet*. 2024 Jul;310(1):427–432. doi:10.1007/s00404-024-07383-8.
12. Eyisoy ÖG, Taşdemir Ü, Eriç Özdemir M, Eyisoy S, Kahramanoğlu Ö, Öçal A, et al. Aspartate aminotransferase/platelet ratio index (APRI) score: Is it useful in patients with intrahepatic cholestasis of pregnancy? *J Matern Fetal Neonatal Med*. 2022 Dec;35(25):10137–10142
13. Kac G, Mendes RH, Farias DR, Eshriqui I, Rebelo F, Benaim C, et al. Hepatic, renal and inflammatory biomarkers are positively associated with blood pressure changes in healthy pregnant women: a prospective cohort study. *Medicine (Baltimore)*. 2015 May;94(20):e683. doi:10.1097/MD.0000000000000683.
14. Mohamed AA, Elsadek HM, Abdel Aziz MM, Abo El-Fotoh WM. AST/creatinine ratio: A new index for prediction of esophageal varices in cirrhotic patients. *J Egypt Soc Parasitol*. 2020;50(2):469–474. <https://doi.org/10.21608/jesp.2020.47260.1202>
15. Yao X, Liu C, Luo Y, Peng J, Wu Y, Chen L, et al. Relationship between renal and liver function with diabetic retinopathy in patients with type 2 diabetes mellitus: a study based on cross-sectional data. *Sci Rep*. 2022;12:9363. doi:10.1038/s41598-022-13164-7.
16. De Ritis F, Coltorti M, Giusti G. An enzymic test for the diagnosis of viral hepatitis: the transaminase serum activities. *Clin Chim Acta*. 1957;2(1):70–74. doi:10.1016/0009-8981(57)90049-7.
17. Botros M, Sikaris KA. The De Ritis ratio: the test of time. *Clin Biochem Rev*. 2013;34(3):117–130. Available from: <https://pmc.ncbi.nlm.nih.gov/articles/PMC3866949/>
18. Li S, Xie X, Zeng X, Wang S, Lan J. Association of serum albumin/serum creatinine ratio with mortality risk in patients with heart failure. *Clin Transl Sci*. 2024;16(11):2345–2355. doi:10.1111/cts.13636.
19. Dinçgez C, Koç A, Kaya AE, Yalçinkaya M, Kaya B. Third-trimester AST/ALT and APRI scores in intrahepatic cholestasis of pregnancy and neonatal outcomes. *J Matern Fetal Neonatal Med*. 2024;37(1):155–161. doi:10.1080/14767058.2022.2122036.

Unmasking Age or Condition? A Retrospective Analysis of Neonatal Outcomes in Advanced Maternal Age Pregnancies

Yaş mı Etken, Eşlik Eden Durumlar mı? İleri Anne Yaşında Neonatal Sonuçların Retrospektif Değerlendirmesi

 Halil DEGİRMENCİOĞLU¹,  Enes KARAMAN²

¹Department of Pediatrics, Niğde Ömer Halisdemir University, Maternity and Teaching Hospital, Niğde, Türkiye

²Department of Obstetrics and Gynecology, Niğde Ömer Halisdemir University, Maternity and Teaching Hospital, Niğde, Türkiye

ABSTRACT

Aim: This study aimed to determine whether advanced maternal age (≥ 35 years) independently increases the risk of adverse neonatal outcomes compared to younger mothers, and to clarify the extent to which maternal age versus comorbidities influences neonatal morbidity and mortality.

Materials and Methods: We conducted a retrospective cohort study at Niğde Ömer Halisdemir University Training and Research Hospital between September 2023 and March 2024. Singleton live births to mothers aged ≥ 20 years were grouped by maternal age: < 35 years old (younger control group) and ≥ 35 years old (AMA group). Maternal demographics, obstetric complications, and neonatal outcomes—including low birth weight (LBW), prematurity, Apgar scores, neonatal intensive care unit (NICU) admission, early-onset neonatal sepsis, and mortality—were compared between groups. Multivariable logistic regression identified independent predictors of adverse neonatal outcomes.

Results: Among 413 mother–infant pairs, AMA mothers had significantly higher gravidity, parity, and neonatal mortality than younger mothers (9.4% vs. 2.3% neonatal death rate, $p=0.004$). However, rates of prematurity, LBW, neonatal sepsis, and NICU admission were similar between the two age groups. In multivariate analysis, maternal age ≥ 35 years old was an independent predictor of neonatal mortality (adjusted OR 18.48, 95% CI 2.61–130.67, $p=0.003$) even after controlling for parity, gestational diabetes, and preeclampsia. Conversely, AMA was not an independent risk factor for other adverse outcomes such as low Apgar scores, prematurity, or LBW.

Conclusions: Although pregnancies in women of AMA were associated with higher neonatal mortality, maternal age alone did not independently predict other key neonatal complications. Our findings suggest that the elevated neonatal risks often attributed to AMA are mediated primarily through age-related comorbid conditions and birth-related complications rather than age itself. This distinction holds clinical significance for risk stratification and patient counseling. Optimized prenatal care targeting modifiable risk factors may help mitigate neonatal risks in AMA pregnancies.

Keywords: Advanced maternal age, Neonatal mortality, NICU admission, Low birth weight, Prematurity, Preeclampsia, Gestational diabetes, Retrospective cohort study.

ÖZ

Amaç: Bu çalışmanın amacı, ileri anne yaşının (≥ 35 yıl) olumsuz yenidoğan sonuçlarını genç annelerle karşılaştırıldığında bağımsız olarak artırıp artırmadığını belirlemek ve yenidoğan morbidite ve mortalitesi üzerinde yaş ile komorbiditelerin etkisini ayırt etmektir.

Gereç ve Yöntemler: Bu retrospektif kohort çalışması, Eylül 2023 ile Mart 2024 tarihleri arasında Niğde Ömer Halisdemir Üniversitesi Eğitim ve Araştırma Hastanesi'nde yürütüldü. Yaşı ≥ 20 olan annelerin tekil canlı doğumları, anne yaşına göre < 35 (kontrol) ve ≥ 35 (İAY) olarak iki gruba ayrıldı. Anne demografisi, obstetrik komplikasyonlar ve neonatal sonuçlar—düşük doğum ağırlığı (DDA), prematürite, Apgar skorları, yenidoğan yoğun bakım (YYBÜ) ihtiyacı, erken başlangıçlı neonatal sepsis ve mortalite—iki grup arasında karşılaştırıldı. Advers neonatal sonuçların bağımsız belirleyicilerini saptamak için çok değişkenli lojistik regresyon analizleri yapıldı.

Bulgular: Toplam 413 anne-bebek çiftinde, İAY grubunda gravide, parite ve neonatal mortalite oranları anlamlı olarak daha yüksekti (%9,4 vs. %2,3; $p=0,004$). Ancak prematürite, DDA, sepsis ve YYBÜ'ye yatış oranları her iki grupta benzer bulundu. Çok değişkenli analizde, parite, gestasyonel diyabet ve preeklampsi kontrol edildikten sonra bile, anne yaşının ≥ 35 olmasının neonatal mortalitenin bağımsız bir belirleyicisi olduğu görüldü (düzeltilmiş OR: 18,48; %95 GA: 2,61–130,67; $p=0,003$). Buna karşın İAY, düşük Apgar skoru, prematürite veya DDA açısından bağımsız bir risk faktörü değildi.

Sonuç: İleri anne yaşı gebelikleri neonatal mortalite açısından daha yüksek risk taşımakla birlikte, anne yaşının kendisi diğer temel neonatal komplikasyonların bağımsız bir belirleyicisi değildir. Bulgularımız, İAY ile ilişkili artmış neonatal risklerin esasen bu yaş grubunda daha sık görülen komorbiditelere ve doğumla ilgili komplikasyonlara bağlı olduğunu düşündürmektedir. Bu ayırım, risk sınıflandırması ve hasta danışmanlığında klinik olarak önemlidir. Modifiye edilebilir faktörlere odaklanan optimize edilmiş doğum öncesi bakım, İAY gebeliklerinde neonatal riskleri azaltmaya yardımcı olabilir.

Anahtar Kelimeler: İleri anne yaşı, Neonatal mortalite, YYBÜ yatışı, Düşük doğum ağırlığı, Prematürite, Preeklampsi, Gestasyonel diyabet, Retrospektif kohort çalışması.

Cite as: Degirmencioglu H and Karaman E. Unmasking Age or Condition? A Retrospective Analysis of Neonatal Outcomes in Advanced Maternal Age Pregnancies. Jinekoloji-Obstetrik ve Neonatoloji Tıp Dergisi 2026;23(2):139–146.

Geliş/Received: 16.06.2025 • **Kabul/Accepted:** 01.12.2026

Sorumlu Yazar/Corresponding Author: Halil Degirmencioglu, Department of Pediatrics, Niğde Ömer Halisdemir University, Maternity and Teaching Hospital, Niğde, Türkiye
E-mail: hdegirmencioglu@gmail.com

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

INTRODUCTION

Advanced maternal age (AMA) is typically defined as pregnancy at 35 years or older, a threshold historically used because maternal and perinatal risks begin to rise beyond this age (1). Clinically, AMA is considered a distinct high-risk category due to its association with increased obstetric complications and neonatal risks. Women in their late 30s and early 40s are more prone to conditions such as gestational diabetes, hypertension (preeclampsia, PE), placenta previa, and miscarriage (1). These maternal complications can in turn adversely affect neonatal outcomes. Indeed, infants of AMA mothers have been linked to higher rates of preterm birth, low birth weight (LBW), need for neonatal intensive care unit (NICU) admission, and even a higher likelihood of stillbirth compared to infants of younger mothers (1). Given these concerns, pregnancies at age 35 years old and above have long been approached with extra caution in prenatal care.

Globally, childbearing is shifting to later ages, driven by sociocultural factors and improved contraception and fertility treatments (1). In the United States, the birth rate among women aged 35–39 years old increased from 45.9 per 1,000 in 2010 to 52.7 in 2019 (1). Türkiye shows a parallel trend: the average age at first birth rose from around 22 years in 2010 to about 27 years in 2023, and the mean maternal age at any birth reached ~29 years by 2020 (2,3). Consequently, a larger share of pregnancies now falls into the advanced maternal age range, underscoring the need to understand the implications for maternal and neonatal health (2,3). Although AMA is often associated with higher neonatal risk, recent studies report mixed findings and suggest that the elevated risk is at least partly due to comorbid conditions rather than age alone (4,5). Notably, professional guidelines acknowledge that even at age 35 years old there is a small but significant increase in adverse neonatal outcomes, with risks escalating further at more advanced ages (6). A substantial body of recent research has examined how AMA affects neonatal outcomes. Many studies indicate that AMA is associated with higher odds of adverse neonatal outcomes in general. For example, a large cohort study in Turkey reported that mothers aged ≥ 35 years old had significantly higher rates of preterm delivery and small-for-gestational-age (SGA) infants, as well as increased NICU admission and perinatal mortality, compared to mothers in their 20s (7). Similarly, a recent study from Iran found that after adjusting for other factors, women ≥ 35 years old still faced greater risks of gestational diabetes (adjusted OR ~3.2) and PE (aOR ~2.9), which contributed to higher odds of preterm birth (aOR ~2.4) and stillbirth in this age group (8). Across different populations, similar trends have been observed. The effects of maternal age are also age-dependent: risk is higher in women aged ≥ 40 years old than in those 35–39 years old, and parity appears

to play a role. For instance, one nationwide analysis of nulliparous (first-time) mothers showed that those ≥ 35 years old had greater likelihood of cesarean delivery and NICU admission than younger first-time mothers (7), underscoring that an older mother's parity status may interact with age in determining outcomes.

Given the rising prevalence of AMA pregnancies and the mixed findings in the literature, our study was designed to clarify the relationship between advanced maternal age and neonatal outcomes in a Turkish cohort. The primary objective was to determine whether AMA (defined as maternal age ≥ 35 years old) independently increases the risk of adverse neonatal outcomes compared to younger maternal age (< 35 years old). Key neonatal outcomes of interest included low birth weight, preterm birth, 5-minute Apgar scores, NICU admission, neonatal morbidity (such as respiratory distress or neonatal sepsis), and neonatal or perinatal mortality. A secondary objective was to assess whether parity modifies the association between AMA and neonatal outcomes (by comparing outcomes in nulliparous vs. multiparous older mothers), and to evaluate the contribution of age-related comorbidities—gestational diabetes, preexisting diabetes, and hypertensive disorders such as PE—through stratified analyses and multivariable models. By isolating the independent effect of maternal age, we aimed to determine if advanced age itself is a risk factor when controlling for these conditions. The findings of this study will provide region-specific evidence from Türkiye and help discern whether the risks often associated with AMA are due to maternal age alone or predominantly driven by comorbid conditions. Such knowledge is vital for improving prenatal counseling and optimizing perinatal care for the growing population of older mothers, ensuring that risk management is appropriately focused. Ultimately, distinguishing the effects of maternal age from those of associated conditions could refine clinical practice and lead to healthier outcomes for both mothers and newborns.

MATERIALS AND METHODS

Study Design and Setting

This study was a retrospective observational cohort analysis conducted at Niğde Ömer Halisdemir University Training and Research Hospital. All procedures followed institutional and international ethical standards. The study population included women who delivered at this hospital between September 1, 2023 and March 31, 2024. The cohort was divided based on maternal age into two groups: an AMA group (mothers who were aged ≥ 35 years old at the time of delivery) and a control group (mothers aged 20–34 years old). The study protocol was approved by the Niğde Ömer Halisdemir University Clinical Research Ethics Committee

(Approval No: 2025/07-101), and all procedures were performed in accordance with the latest Declaration of Helsinki. Because of the retrospective design and use of de-identified data, the need for informed consent was waived by the ethics committee.

Inclusion criteria

(maternal–infant pairs were eligible if all criteria were met):

- Maternal age ≥ 20 years old.
- Singleton pregnancy resulting in a live birth.
- Delivery at ≥ 24 completed weeks' gestation (viable gestational age).
- Complete prepartum and postpartum clinical and obstetric records available.
- Availability of neonatal clinical and laboratory data (including neonatal blood test results) within the first 24 hours after birth.

Exclusion criteria

- Multiple gestation pregnancies (twins, triplets, or higher-order multiples).
- Newborns with major congenital anomalies.
- Stillbirths (intrauterine fetal demise).
- Births before 24 weeks of gestation.
- Incomplete or insufficient medical records for either the mother or the newborn.
- Mothers with active systemic diseases (e.g., lupus, malignancy, or active infections) that could directly affect neonatal outcomes.

Data Collection

All data were obtained retrospectively from the hospital's electronic medical record system. A comprehensive, structured data form was used to extract relevant information. Maternal variables collected included maternal age, gravidity, parity, obstetric history, gestational age at delivery (in weeks), mode of delivery (vaginal or cesarean section), and any pregnancy complications (with particular attention to gestational diabetes mellitus and PE). Recorded neonatal variables included infant sex, birth weight, Apgar scores at 1 and 5 minutes, need for NICU admission (and length of NICU stay, in days), diagnosis of early neonatal sepsis, and perinatal mortality status (early neonatal death). All personal identifiers were removed during data collection, and patient confidentiality was strictly maintained.

Statistical Analysis:

All statistical analyses were performed using IBM SPSS Statistics (version 25.0; IBM Corp., Armonk, NY, USA). Descriptive statistics

were first calculated for the two study groups. Continuous variables were assessed for normality using the Kolmogorov–Smirnov and Shapiro–Wilk tests. For approximately normally distributed continuous data, results are presented as mean $\pm$ standard deviation (SD), and independent-samples t-tests were used to compare group means. For non-normally distributed continuous data, medians with range (minimum–maximum) are reported, and the Mann–Whitney U test was employed for group comparisons. Categorical variables were summarized as frequencies and percentages (%), and compared between the AMA and control groups using the chi-square test or Fisher's exact test, as appropriate.

To evaluate whether advanced maternal age was an independent risk factor for adverse neonatal outcomes, multivariable logistic regression analyses were performed. Each key neonatal outcome (such as low birth weight, preterm delivery <37 weeks, NICU admission, early neonatal sepsis, and neonatal mortality) was modeled as a dependent variable in separate logistic regression models. Maternal age group (AMA ≥ 35 years old vs. <35 years old) was included as the primary predictor, along with potential confounders selected *a priori* based on clinical relevance and literature (1,2). These covariates included maternal parity, gestational diabetes mellitus, and preeclampsia (hypertensive disorder of pregnancy), among others. Adjusted odds ratios (aOR) with 95% confidence intervals (CI) were calculated to estimate the independent effect of AMA on each neonatal outcome. A two-tailed p-value <0.05 was considered statistically significant for all analyses.

RESULTS

A total of 413 mothers were included in the study: 349 (84.5%) were under 35 years of age and 64 (15.5%) were 35 years old or older. By design, maternal age differed significantly between the groups (median approximately 29 years in the <35 years old group vs. 37 years in the ≥ 35 years old group, $p<0.001$). Mothers aged ≥ 35 years old had significantly higher parity and gravidity on average compared to younger mothers (mean parity 3.92 vs. 2.62; mean gravidity 3.92 vs. 2.60; $p<0.001$ for both) (Table 1). Consistently, the older group had more living children on average (mean 3.30 vs. 2.22, $p<0.001$). The number of prior abortions (pregnancy losses) was slightly greater in the ≥ 35 group (mean 0.55 vs. 0.41), but this difference did not reach statistical significance ($p=0.106$). There were no significant differences in mode of delivery between the age groups: the vaginal delivery rate was 21.9% in mothers ≥ 35 vs. 30.4% in those <35 years old ($p=0.169$), with cesarean section being the predominant mode in both groups (~ 70 – 78% , $p=0.169$) (Table 1). Similarly, the incidence of gestational diabetes (7.8%

Table 1. Maternal demographic and obstetric characteristics of the study population, stratified by maternal age group.

Characteristic	< 35 years (n = 349)	≥ 35 years (n = 64)	p-value
Maternal age (years)	27.8 ± 5.3 (29)	37.5 ± 2.4 (37)	<0.001**
Parity (number)	2.62 ± 1.5 (2)	3.92 ± 1.8 (4)	<0.001**
Gravidity (number)	2.60 ± 1.5 (2)	3.92 ± 1.8 (4)	<0.001**
Living children (number)	2.22 ± 1.2 (2)	3.30 ± 1.5 (3)	<0.001**
Abortions (number)	0.41 ± 0.8 (0)	0.55 ± 0.9 (0)	0.106
Vaginal delivery (%)	106 (30.4%)	14 (21.9%)	0.169
Cesarean section (%)	243 (69.6%)	50 (78.1%)	0.169
Gestational diabetes (%)	13 (3.7%)	5 (7.8%)	0.141
Preeclampsia (%)	12 (3.4%)	3 (4.7%)	0.623

Note: Continuous variables are presented as mean ± SD (median); categorical variables as n (%). Comparisons by Mann-Whitney U test (continuous) or chi-square test (categorical). $p < 0.05$ considered statistically significant.

Table 2. Maternal hematologic parameters by maternal age group.

Maternal Parameter	< 35 years old (n = 349)	≥ 35 years old (n = 64)	p-value
Hemoglobin (g/dL)	11.3 ± 1.7	11.5 ± 1.4	0.333
Hematocrit (%)	33.3 ± 4.8	34.1 ± 3.8	0.214
White blood cell count ($\times 10^9/L$)	13.3 ± 4.7	12.5 ± 3.8	0.475
Neutrophils ($\times 10^9/L$)	10.8 ± 6.0	9.74 ± 3.9	0.291
Lymphocytes ($\times 10^9/L$)	1.93 ± 1.3	1.99 ± 1.3	0.635
Platelet count ($\times 10^9/L$)	215.2 ± 65.5	233.2 ± 93.8	0.362
Mean platelet volume (fL)	10.7 ± 1.1	10.8 ± 1.1	0.780
Platelet distribution width (fL)	13.1 ± 2.3	13.3 ± 2.0	0.389

Abbreviations: SD, standard deviation; fL, femtoliter. No significant differences were observed between groups for any parameter (Mann-Whitney U tests, $p > 0.05$ for all).

vs. 3.7%, $p=0.141$) and PE (4.7% vs. 3.4%, $p=0.623$) was higher in the older mothers, but these differences were not statistically significant. Notably, no cases of obstetric cholestasis or maternal obesity were recorded in either group during the study period.

Maternal laboratory profiles were comparable between the two age groups (Table 2). There were no significant differences in maternal hemoglobin levels (mean ~ 11.3 g/dL in both groups, $p=0.333$) or hematocrit ($\sim 33\text{--}34\%$, $p=0.214$). Likewise, maternal white blood cell counts were within high-normal ranges and similar between groups (13.3 ± 4.7 vs. $12.5 \pm 3.8 \times 10^9/L$, $p=0.475$), and there were no differences in differential counts (neutrophils or lymphocytes, $p > 0.2$ for both). Platelet counts and indices also did not differ significantly: mean platelet count was $\sim 215 \times 10^9/L$ in the <35 group vs. $\sim 233 \times 10^9/L$ in the ≥ 35 group ($p=0.362$), and mean platelet volume and platelet distribution width were similar ($p=0.780$ and $p=0.389$, respectively). In summary, the maternal baseline hematologic values showed no appreciable differences by age group.

Neonatal hematologic and biochemical parameters at birth were also broadly similar regardless of maternal age (Table 3). Mean hemoglobin levels in newborns were high (as expected for healthy term neonates) and did not differ between groups (17.8 ± 2.5

vs. 17.9 ± 2.5 g/dL, $p=0.589$). Hematocrit values were likewise comparable (approximately 53% in both, $p=0.874$). There were no significant differences in neonatal white blood cell counts or differentials by maternal age; for instance, the total WBC count was $\sim 15.5 \times 10^9/L$ in both groups ($p=0.740$), with similar neutrophil and lymphocyte counts ($p=0.601$ and $p=0.269$, respectively). Platelet counts showed a trend toward being lower in infants of older mothers (mean 292.8 vs. $302.2 \times 10^9/L$), but this difference was not statistically significant ($p=0.061$). Markers of neonatal inflammation or infection were low in both groups and did not differ: mean C-reactive protein was ~ 1 mg/L in both ($p=0.192$) and procalcitonin ~ 0.8 ng/mL ($p=0.710$). In summary, we found no clinically meaningful differences in neonatal laboratory values between the two maternal age categories.

Key neonatal clinical outcomes are summarized in Table 4. Gestational age at birth was similar between groups: the mean gestational age was ~ 37 weeks in both (37.1 ± 3.0 weeks in <35 vs. 36.3 ± 3.9 weeks in ≥ 35 , $p=0.417$). Accordingly, the rate of preterm birth (<37 weeks' gestation) did not differ significantly, occurring in roughly one-third of deliveries in each group (35.8% vs. 34.4%, $p=0.825$). Birth weight distributions were likewise comparable: mean birth weight was about 2.9 kg in both groups

Table 3. Neonatal hematologic and laboratory parameters by maternal age group.

Neonatal Parameter	Born to < 35 y mothers (n = 349)	Born to ≥ 35 y mothers (n = 64)	p-value
Hemoglobin (g/dL)	17.8 ± 2.5	17.9 ± 2.5	0.589
Hematocrit (%)	52.6 ± 7.7	52.8 ± 7.2	0.874
White blood cell count (×10 ⁹ /L)	15.4 ± 5.5	15.9 ± 6.8	0.740
Neutrophils (×10 ⁹ /L)	8.43 ± 5.8	8.84 ± 5.7	0.601
Lymphocytes (×10 ⁹ /L)	5.53 ± 2.9	5.19 ± 2.2	0.269
Platelet count (×10 ⁹ /L)	302.2 ± 83.4	292.8 ± 107.7	0.061
Mean platelet volume (fL)	9.73 ± 0.9	9.9 ± 1.0	0.111
Platelet distribution width (fL)	11.1 ± 1.9	11.3 ± 2.0	0.246
C-reactive protein (mg/L)	1.08 ± 3.6	1.10 ± 2.3	0.192
Procalcitonin (ng/mL)	0.72 ± 2.9	0.89 ± 2.7	0.710

Abbreviations: WBC, white blood cell; CRP, C-reactive protein; PCT, procalcitonin. No significant intergroup differences were observed in neonatal laboratory values ($p > 0.05$ for all comparisons).

Table 4. Neonatal clinical outcomes and complications by maternal age group.

Outcome	Infants of < 35 y (n = 349)	Infants of ≥ 35 y (n = 64)	p-value
Gestational age at birth (weeks)	37.1 ± 3.0	36.3 ± 3.9	0.417
Preterm birth (<37 weeks)	125 (35.8%)	22 (34.4%)	0.825
Birth weight (g)	2897 ± 729	2920 ± 920	0.391
Low birth weight (≤2500 g)	101 (28.9%)	14 (21.9%)	0.246
1-min Apgar score	8.5 ± 1.2 (median 9)	8.5 ± 1.2 (median 9)	0.991
Apgar <7 at 1 min	19 (5.9%)	4 (6.3%)	0.785
5-min Apgar score	9.6 ± 0.9 (median 10)	9.6 ± 0.9 (median 10)	0.778
Apgar <7 at 5 min	8 (2.5%)	2 (3.1%)	0.683
RDS requiring surfactant	62 (17.8%)	11 (17.2%)	0.911
Any mechanical ventilation	73 (20.9%)	14 (21.9%)	0.840
MV duration (days)	2.35 ± 4.6 (median 1)	2.14 ± 3.2 (median 1)	0.923
Oxygen therapy duration (days)	2.88 ± 3.7 (median 1)	2.82 ± 3.6 (median 1)	0.891
Any neonatal sepsis	49 (14.0%)	6 (9.4%)	0.359
Neonatal mortality	8 (2.3%)	6 (9.4%)	0.004**

Abbreviations: RDS, respiratory distress syndrome; MV, mechanical ventilation. Data are mean ± SD (with median where shown) or n (%). Neonatal complications (including RDS, sepsis, etc.) did not differ significantly by maternal age group ($p > 0.05$), with the exception of neonatal mortality, which was significantly higher in the ≥35 years group ($p = 0.004$).

(2897 ± 729 g vs. 2920 ± 920 g, $p = 0.391$), and the incidence of low birth weight (LBW, defined as ≤2500 g) was not significantly different (28.9% in <35 vs. 21.9% in ≥35, $p = 0.246$).

Neonatal Apgar scores were generally high in both groups and showed no significant variation by maternal age. The median 1-minute Apgar score was 9 in both groups, with only around 6% of infants in each group having a 1-minute Apgar <7 (5.9% vs. 6.8%, $p = 0.785$). By 5 minutes, the median Apgar was 10 in both groups; only about 2–3% of infants had a low 5-minute Apgar (<7) in either group (2.5% vs. 3.4%, $p = 0.683$). Thus, maternal age ≥35 was not associated with depressed Apgar scores in newborns.

The need for and duration of neonatal respiratory support were also similar across groups. Approximately 20% of newborns overall developed respiratory distress syndrome (RDS), with no significant difference between groups (21.9% vs. 20.1%, $p = 0.740$). Correspondingly, mechanical ventilation (MV) was required in

a subset of infants in both groups; the median duration on MV was 1 day in each group (mean ~2.3 days in <35 vs. ~2.1 days in ≥35, $p = 0.923$). Non-invasive respiratory support needs were comparable as well: the median duration of continuous positive airway pressure (CPAP) support was 0 days in both groups (very few infants required any CPAP; $p = 0.837$), and supplemental oxygen days were similar (median 1 day in both, $p = 0.891$). There were also no significant differences in the use of surfactant therapy (~18% of infants in each group received surfactant, $p = 0.911$) or the need for vasopressor/inotropic support (~11% in both, $p = 0.462$). The median NICU length of stay was 4 days in both groups (mean ~6.4 days in <35 vs. ~6.2 days in ≥35, $p = 0.606$), indicating that prolonged neonatal hospitalization was not related to maternal age in this cohort.

Importantly, the incidence of major neonatal morbidities was largely comparable between the two groups. Rates of conditions

such as intraventricular hemorrhage (~1.6% in each group), bronchopulmonary dysplasia (~1% in each), necrotizing enterocolitis (~3% severe NEC in each), and neonatal sepsis (early-onset sepsis ~11% vs. 6%, and late-onset sepsis ~3% in both) were not significantly different (all p -values >0.1). The proportion of infants who were SGA was around 10% in each group ($p=0.872$). One notable difference did emerge in neonatal survival: neonatal mortality was significantly higher in the ≥ 35 maternal age group. The neonatal mortality rate among infants of AMA mothers was 9.4% (6/64), compared to 2.3% (8/349) among infants of mothers <35 , which represents a more than four-fold difference ($p=0.004$). Although the absolute numbers of neonatal deaths were small, a disproportionately higher share of these deaths occurred in the advanced maternal age group. No other neonatal outcome differed significantly between the two groups (Table 4).

In the multivariable models, maternal age ≥ 35 years was an independent predictor of neonatal mortality (aOR 18.48, $p=0.003$), even after adjusting for prematurity, birth weight, Apgar scores, and other covariates. By contrast, AMA was not independently associated with preterm birth, LBW or low Apgar scores. These outcomes appeared more strongly influenced by clinical factors such as gestational maturity and neonatal condition at birth, underscoring the complex interplay between prematurity, low Apgar scores, and birth weight in determining neonatal risk.

DISCUSSION

In this study, we found that AMA, defined as ≥ 35 years old, was associated with worse neonatal outcomes in our cohort—most notably a higher neonatal mortality rate—compared to younger mothers. Infants born to mothers aged 35 and above had an elevated risk of neonatal death, consistent with the general understanding that maternal age over 35 increases perinatal risks (7,9). This adverse outcome could be attributed to age-related biological factors, such as diminished placental perfusion or the higher incidence of pregnancy complications in older women (e.g., preeclampsia or diabetes), which can negatively affect neonatal survival. Our findings underscore that, even in a modern obstetric setting, advanced maternal age remains a significant risk factor that can translate into greater neonatal morbidity and mortality if not carefully managed.

We observed that AMA mothers in our cohort had higher gravidity and parity than younger mothers, reflecting prior pregnancies and more living children. Increased parity may itself affect outcomes, as grand multiparity (≥ 5 births) has been linked to complications such as hemorrhage, placental problems, and perinatal mortality

(10). However, a recent study in women over 35 reported that grand multiparity alone was not an independent predictor of adverse neonatal outcomes, with similar complication rates across parity groups (11). Still, AMA combined with high parity may increase risk, particularly through cumulative stresses like repeat cesarean deliveries (10). Parity status may also modify risk: in one Turkish study, NICU admissions were more frequent in primiparous AMA mothers compared with multiparous AMA mothers (11). These findings suggest that advanced maternal age is associated with higher neonatal mortality, but the impact may vary depending on parity, underscoring the complexity of the age–parity interaction.

Our results are consistent with recent Turkish and international data. Multiple studies from Türkiye in the last five years confirm that pregnancies in women ≥ 35 carry higher neonatal risks. For example, Elçi et al. reported significantly more NICU admissions and perinatal deaths among nulliparous mothers >35 compared to younger women (7), echoing our finding of increased neonatal mortality. Similarly, Günkaya et al. observed higher rates of preterm birth, LBW, low Apgar scores, and other complications in mothers 35–39 and ≥ 40 , with outcomes particularly worse at ≥ 40 (12). These findings align with national and international guidelines: the American College of Obstetricians and Gynecologists emphasizes that even at 35 years, risks of LBW, preterm birth, low Apgar scores, and NICU admission are elevated, rising further with age (6). In sum, our study's signal of greater neonatal risk with maternal age is supported by robust Turkish and global evidence.

Beyond mortality, older mothers are consistently shown to experience more pregnancy complications that affect neonatal outcomes. Recent studies (2019–2024) link AMA with higher rates of hypertensive disorders, gestational diabetes, placental problems, and cesarean delivery, which contribute to preterm birth and growth restriction, thereby raising neonatal risks. Our finding of more comorbid conditions in older mothers (e.g., PE, diabetes) aligns with these reports. A 2019 Turkish study from Haseki similarly found PE and gestational diabetes more frequent in mothers ≥ 35 , with higher intrauterine fetal death rates, although Apgar scores, prematurity, and NICU admission did not differ between groups (11). Overall, the evidence indicates that AMA is associated with increased obstetric complications, and when these lead to prematurity or growth restriction, neonatal morbidity and mortality increase accordingly.

It is worth noting that not all research is concordant. Some earlier studies did not show worse neonatal outcomes with AMA, raising debate about the true impact of maternal age (13). Several recent analyses suggest that once comorbidities common in older mothers (hypertension, diabetes, obesity, assisted reproduction) are considered, differences in neonatal morbidity or mortality diminish,

particularly in the 35–39 age range (4,5). By contrast, studies defining AMA at ≥ 40 years consistently show increased risks even after adjustment (4). These findings imply that maternal age is a marker of risk accumulation, with the magnitude depending on comorbidities and age threshold (4,5). Importantly, a 2018 study restricted to healthy nulliparous women still found higher odds of late preterm birth and SGA in those >35 , confirming that the age effect is not solely due to confounding (13). On the other hand, data from the EPICE cohort showed that with high-quality neonatal care, AMA did not independently worsen outcomes in very preterm infants after adjustment (5). Such results suggest that adverse effects of AMA are context-dependent and can be mitigated by proactive management strategies (6). Population differences and selection bias (e.g., healthier older mothers) may also explain variability across studies.

In summary, our finding of higher neonatal mortality in mothers ≥ 35 is consistent with Turkish and international reports, which show more NICU admissions, perinatal deaths, and elevated mortality at extreme maternal ages (7–9). Yet, some studies note that when healthcare quality is high or analyses adjust for comorbidities, the effect of age diminishes (5). These variations highlight the role of context and may explain why in certain settings, including ours, the age effect appears smaller. Overall, the evidence confirms that advanced maternal age remains a significant risk factor for neonatal health, while underscoring the importance of optimal care to mitigate risks.

Our study has several strengths. We analyzed over 400 mother–infant pairs from a single institution, providing adequate power to detect even rare outcomes like neonatal mortality. By including essentially all deliveries over a defined period, we obtained a comprehensive and unselected picture of both younger and advanced-age mothers. We also used rigorous methods, applying bivariable tests and multivariable logistic regression to adjust for confounders, which strengthens the validity of observed associations. Furthermore, the study assessed a broad set of maternal and neonatal variables, allowing us to link parity and comorbidities with neonatal outcomes in detail. Finally, we focused on a clinically relevant cutoff (<35 vs. ≥ 35 years), directly aligning with obstetric guidelines. Together, the robust sample, statistical rigor, comprehensive dataset, and clear study design enhance the reliability and applicability of our findings.

This study has several limitations. Its retrospective, single-center design limits generalizability, as care practices and patient profiles may differ elsewhere. Reliance on medical records raises the possibility of missing or inaccurate data, and some confounders (e.g., socio-economic status, assisted reproduction) were not captured. The smaller size of the ≥ 35 group compared to the <35

group may also have reduced statistical power or exaggerated percentage differences. As an observational study, causality cannot be established, and residual confounding (such as maternal health or antenatal care quality) may remain. We also focused only on short-term neonatal outcomes; stillbirths were excluded, leaving our perinatal mortality measure incomplete despite AMA being a known risk factor for stillbirth (7). In addition, lack of information on interventions like antenatal corticosteroid use further constrains interpretation. Overall, these limitations temper our conclusions and highlight the need for larger, prospective studies.

Further research is needed to better understand AMA and neonatal outcomes. Larger, multi-center prospective studies are required to validate whether the higher neonatal mortality observed in our cohort applies at national and international levels. Future work should also assess how parity modifies risk—for instance, whether first-time AMA mothers have worse outcomes than multiparous counterparts (11). Mechanistic research could clarify whether the excess risk is mainly mediated by prematurity, age-related complications like preeclampsia, or placental changes. Interventional studies are also warranted, testing strategies such as low-dose aspirin for preeclampsia prevention (14), enhanced monitoring for gestational diabetes, or elective delivery at 39 weeks in women ≥ 40 to reduce stillbirth risk (6). Comparing outcomes in AMA mothers under targeted versus standard care would show how much risks can be mitigated. In addition, longitudinal studies should examine whether AMA affects child health beyond the neonatal period. Finally, international collaborations could compare outcomes across different healthcare systems, highlighting best practices that minimize the age-related gap.

CONCLUSION

In our cohort, advanced maternal age (≥ 35 years) was associated with significantly higher neonatal mortality, even after adjusting for obstetric complications. By contrast, prematurity, LBW, and low Apgar scores appeared more closely linked to comorbidities than to age itself. These findings suggest that while AMA should remain a high-risk category, most neonatal risks arise through modifiable factors such as hypertension or diabetes. Thus, vigilant prenatal care and targeted management of comorbidities are essential. With appropriate interventions, much of the neonatal risk in AMA pregnancies can be mitigated, offering reassurance that maternal age alone does not inevitably determine poor outcomes.

Ethics Committee Approval: The study protocol was approved by the Niğde Ömer Halisdemir University Clinical Research Ethics Committee (Approval No: 2025/07-101)

Conflict of Interest Statement: The authors declare that they have no conflicts of interest related to the content of this manuscript. No financial, personal, or professional relationships have influenced the design, conduct, or reporting of this research.

CRedit Authorship Contribution Statement: HD: Conceptualization, Methodology, Data curation, Investigation, Writing – review & editing, Visualization. EK: Conceptualization, Methodology, Resources, Data curation, Formal analysis.

REFERENCES

- Glick I, Kadish E, Rottenstreich M. Management of pregnancy in women of advanced maternal age: improving outcomes for mother and baby. *Int J Womens Health*. 2021;13:751-759. doi:10.2147/IJWH.S283216
- Krzyżanowska Z. Turkey: a looming demographic crisis. OSW Commentary. 7 Aug 2024. (Institute of Central Europe, Warsaw – commentary on demographic trends in Turkey; no DOI available)
- Turkish Statistical Institute (TurkStat). World Population Day 2021 press release: "Turkey ranks 19th in population size, age for 1st birth rises." *Daily Sabah*. 6 Jul 2021. (Press release; no DOI)
- Rodrigues I, Soares H, Rocha G, Azevedo I. Impact of advanced maternal age on neonatal morbidity: a systematic review. *J Matern Fetal Neonatal Med*. 2023; [Epub ahead of print]. doi:10.1080/14767058.2023.2287981
- Nourkani-Tutdibi N, Tutdibi E, Faas T, Hoehn T, Zemlin M, Hummers E, et al. Neonatal morbidity and mortality in advanced-aged mothers – maternal age is not an independent risk factor for infants born very preterm. *Front Pediatr*. 2021;9:747203. doi:10.3389/fped.2021.747203
- American College of Obstetricians and Gynecologists' Committee on Clinical Consensus–Obstetrics; Society for Maternal-Fetal Medicine, et al. Pregnancy at age 35 years or older (Obstetric Care Consensus No. 11). *Obstet Gynecol*. 2022;140:348-366. doi:10.1097/AOG.0000000000004873
- Elçi G, Çakmak A, Elçi E, Sayan S. The effect of advanced maternal age on perinatal outcomes in nulliparous pregnancies. *J Perinat Med*. 2022;50:1087-1095. doi:10.1515/jpm-2021-0298
- Shekari M, Shirzadfarjahromi M, Ranjbar A, Mehrnough V, Darsareh F, Roozbeh N. Advanced maternal age and adverse obstetrical and neonatal outcomes of singleton pregnancies. *Gynecol Obstet Clin Med*. 2022;2:175-180. doi:10.1016/j.gocm.2022.10.004
- Tamir TT, Abebe A, Kumar M, Olayinka O, Teshome B, Alvarez G, et al. Neonatal mortality rate and determinants among births of mothers at extreme ages of reproductive life in low- and middle-income countries. *Sci Rep*. 2024;14:12596. doi:10.1038/s41598-024-61867-w
- Atlıhan U, Yavuz O, Aşar HA, Ata C, Erkinç S, Bildacı TB. The impact of grand multiparity on perinatal and neonatal results in females over 35 years of age. *Cyprus J Med Sci*. 2025;10:33-37. doi:10.4274/cjms.2024.2024-77
- Çakmak BD, Dünder B, Türker ÜA. Perinatal outcomes of advanced and extremely advanced maternal age pregnancies. *Med Bull Haseki*. 2019;57:366-371. doi:10.4274/haseki.galenos.2019.5003
- Günkaya E, Şahin D, Şahin HE, Özcan O, Karaaslan İ, Yıldızhan R, ve ark. Adverse perinatal outcomes at advanced pregnancy ages. *Clin Exp Obstet Gynecol*. 2025;52:303-309. doi:10.31083/CEOG31319
- Kahveci B, Melekoglu R, Evruke IC, Çetin C. The effect of advanced maternal age on perinatal outcomes in nulliparous singleton pregnancies. *BMC Pregnancy Childbirth*. 2018;18:343. doi:10.1186/s12884-018-1984-x
- Rolnik, D. L., Wright, D., Poon, L. C., O'Gorman, N., Syngelaki, A., de Paco Matallana, C., et.al (2017). Aspirin versus Placebo in Pregnancies at High Risk for Preterm Preeclampsia. *The New England journal of medicine*, 377(7), 613–622. <https://doi.org/10.1056/NEJMoa1704559>

The Effect of Diurnal Rhythm on Fetal Biophysical Profile in Term and Postterm Pregnancies

Diurnal Ritmin Term ve Postterm Gebeliklerde Fetal Biyofizik Profil Üzerine Etkisi

 Muhammed Alperen ALAYBEYOĞLU ²,  Mehmet ÇINAR ¹,  İbrahim TAŞKUM ²,  Cennet Meltem ALAYBEYOĞLU ³,  Selcan SINACI ²

¹Department of Obstetrics and Gynecology, Ankara Bilkent City Hospital, University of Health Sciences, Ankara, Türkiye

²Department of Obstetrics and Gynecology, Gaziantep City Hospital, Gaziantep, Türkiye

³Department of Obstetrics and Gynecology, Cengiz Gökcek Gynecology and Pediatrics Hospital, Gaziantep, Türkiye

ABSTRACT

Aim: The biophysical profile (BPP) is a non-invasive and reliable test used to assess fetal well-being. This study aimed to evaluate the diurnal variations in BPP parameters in term and postterm pregnancies.

Materials and Methods: This prospective observational study included 75 term and 75 postterm pregnant women. Participants with systemic diseases, fetomaternal risk factors, smoking habits, or social/occupational conditions that could affect the diurnal rhythm were excluded. BPP and non-stress test (NST) evaluations were performed in the morning (08:00–10:00) and evening (20:00–22:00). The collected data were analyzed both within groups and between groups.

Results: Evening assessments revealed significantly higher scores for fetal movements, breathing, NST findings, and mean BPP scores compared to morning evaluations. This pattern was observed both in the overall study population and within term and postterm groups separately. In the morning measurements, mean BPP scores were significantly lower in postterm pregnancies than in term pregnancies. Although the number of fetal breathing was lower in the postterm group, the difference was not statistically significant. In the evening measurements, the postterm group also had lower mean BPP scores.

Conclusion: Diurnal rhythm has a significant impact on fetal biophysical parameters. Further large-scale studies with quantitative assessment of hormonal levels are needed to clarify the underlying biological mechanisms.

Keywords: Biophysical profile; circadian rhythm; pregnancy, post-term; pregnancy, term

ÖZ

Amaç: Biyofizik profil (BFP), fetal iyilik hâlinin değerlendirilmesinde kullanılan, non-invaziv ve güvenilir bir testtir. Bu çalışmada, term ve postterm gebeliklerde BFP parametrelerinin gün içi (diurnal) değişimlerini değerlendirmek amaçlanmıştır.

Gereç ve Yöntemler: Bu prospektif gözlemsel çalışmaya, 75 term ve 75 postterm gebe dahil edilmiştir. Sistemik hastalığı, fetomaternal risk faktörleri bulunanlar, sigara kullananlar ve diurnal ritmi etkileyebilecek sosyal ya da mesleki alışkanlıkları olanlar dışlanmıştır. Katılımcıların BFP ve non-stres test (NST) değerlendirmeleri sabah (08.00–10.00) ve akşam (20.00–22.00) saatlerinde gerçekleştirilmiştir. Elde edilen veriler hem grup içi hem gruplar arası olarak analiz edilmiştir.

Bulgular: Fetal hareket, solunum, NST bulguları ve ortalama BFP skorları açısından, akşam saatlerinde yapılan değerlendirmelerde sabah saatlerine kıyasla anlamlı düzeyde daha yüksek skorlar elde edilmiştir. Bu durum hem genel hasta grubunda hem de term ve postterm gruplarda ayrı ayrı gözlenmiştir. Sabah saatlerinde postterm gebelerde ortalama BFP skorları, term gebelere göre anlamlı düzeyde daha düşük bulunmuştur. Fetal solunum sayısı postterm grupta daha az olmakla birlikte istatistiksel olarak anlamlı değildir. Akşam ölçümlerinde de postterm grubun ortalama BFP skorları daha düşük bulunmuştur.

Sonuç: Diurnal ritmin fetal biyofizik parametreler üzerinde anlamlı etkileri bulunmaktadır. Hormon düzeylerinin kantitatif olarak değerlendirildiği daha geniş örneklemli çalışmalarla bu etkinin biyolojik mekanizmaları daha net ortaya konabilir.

Anahtar Kelimeler: Biyofizik profil; gebelik, post-term; gebelik, term; sirkadiyen ritim

Cite as: Alaybeyoğlu MA, Çınar M, Taşkum İ, Alaybeyoğlu CM, Sinacı S. The Effect of Diurnal Rhythm on Fetal Biophysical Profile in Term and Postterm Pregnancies. Jinekoloji-Obstetrik ve Neonatoloji Tıp Dergisi 2026;23(2):147–153.

Geliş/Received: 28.06.2025 • **Kabul/Accepted:** 25.12.2026

Sorumlu Yazar/Corresponding Author: İbrahim Taşkum, Department of Obstetrics and Gynecology, Gaziantep City Hospital, Gaziantep, Türkiye

E-mail: ibrahimtaskum@gmail.com

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

INTRODUCTION

The fetal biophysical profile (BPP) test is one of the fundamental antenatal methods used to assess fetal well-being and predict perinatal risks such as hypoxemia and acidemia (1). The test evaluates fetal breathing, movements, tone, and amniotic fluid volume via ultrasonography, while the non-stress test (NST) is assessed using cardiotocography. Each parameter is scored as 0 or 2, with a total score of 8–10 considered normal, 6 as borderline, and 4 or below as abnormal (2,3). Although the BPP has high specificity, in some cases low scores may not accurately reflect fetal distress, potentially influencing clinical decisions (4,5). The method's non-invasive nature and ease of application support its widespread use in obstetric practice. However, the physiological or environmental factors that may influence BPP scores have not yet been clearly defined.

Circadian rhythm is closely associated with the secretion patterns of various hormones, particularly melatonin and cortisol, and may have significant effects on fetal physiology (6–9). For instance, while insulin and cortisol levels fluctuate throughout the day, melatonin levels rise during nighttime and can cross the placenta, potentially influencing the fetal biological rhythm (10–14). Furthermore, the tendency for labor to begin during the night or early morning supports the link between this internal rhythm and the physiology of childbirth. Sleep disturbances observed in late pregnancy, increased daytime sleepiness, and hormonal fluctuations may further accentuate this rhythm. In the literature, studies directly examining the variation of BPP scores at different times of day are limited, and comparative analyses between term and postterm pregnancies in this context are particularly scarce (7–9).

This study aimed to evaluate the effect of diurnal rhythm on fetal biophysical parameters by comparing morning (08:00–10:00) and evening (20:00–22:00) BPP assessments in term and postterm pregnancies.

MATERIALS AND METHODS

Study Design

This single-center, prospective observational study was conducted at the Department of Obstetrics and Gynecology, Ankara Bilkent City Hospital, University of Health Sciences. The aim of the study was to evaluate the effect of diurnal rhythm on BPP parameters. The study was approved by the Academic Board (decision number 188295, dated 28/11/2022) and the Ethics Committee (approval number E2-22-2185, dated 20/07/2022). Written informed consent was obtained from all participants. The study was

conducted in accordance with the principles of the Declaration of Helsinki.

The sample size was calculated using the mean and standard deviation values of BPP scores reported in similar studies (15). Based on these data, and using the G*Power 3.1 software, a two-tailed alpha of 0.05 and a power of 80% indicated that at least 64 cases were required in each group. Considering potential data loss, 75 cases were planned for each group. A total of 150 pregnant women who met the study criteria were included from among 168 candidates followed in the antenatal delivery unit. Of these, 75 were classified as postterm pregnancies ($\geq 42+0$ weeks) and 75 as term pregnancies (37+0 to 41+6 weeks). Eighteen patients were excluded based on the exclusion criteria.

Gestational age was determined for all participants based on the concordance between first- and second-trimester ultrasonography findings and the last menstrual period (LMP); those with inconsistencies were excluded from the study. Each participant underwent two BPP assessments, one in the morning (08:00–10:00) and one in the evening (20:00–22:00). All assessments were performed using the same ultrasound device (GE Voluson S10) and the same NST monitor, by the same physician blinded to group allocation. NST recordings were standardized to 20 minutes and conducted while the fetus was in an active state. All assessments were carried out in a quiet, well-lit room and at least one hour after a meal.

Patient Selection

The study population consisted of women with live, singleton intrauterine pregnancies. Participants were divided into two groups: the term group, comprising women between 37+0 and 41+6 weeks of gestation based on the last menstrual period (LMP), and the postterm group, consisting of those at 42+0 weeks or later. All participants had consistent gestational age estimates (a discrepancy of less than 7 days) between their first- or second-trimester ultrasound measurements and their LMP. Additionally, all participants agreed to remain under hospital observation for at least 24 hours and consented to undergo two BPP evaluations—one in the morning and one in the evening. Written informed consent was obtained from all patients.

Patients were excluded if they had maternal systemic diseases (e.g., diabetes, hypertension, thyroid disorders, autoimmune diseases, epilepsy, or cardiac conditions), a history of high-risk pregnancy (e.g., preeclampsia, gestational diabetes, placental abruption, placenta previa), or any fetal risk factors (e.g., structural anomalies, suspected genetic syndromes, intrauterine growth restriction, polyhydramnios or oligohydramnios, or abnormal screening test results).

Exclusion criteria also included smoking or alcohol use, maternal infections such as TORCH that may lead to fetal anomalies, night shift work, or any social or occupational habits that could disrupt biological rhythms. Furthermore, multiple pregnancies and non-cephalic presentations were excluded from the study.

Statistical Analysis

The normality of continuous variables was evaluated using histogram plots and the Shapiro–Wilk test. Categorical variables were presented as frequencies and percentages, while continuous variables were expressed as mean, standard deviation (SD), and 95% confidence intervals (CI) if normally distributed, or as median, interquartile range (IQR), and 95% CI if not normally distributed. Categorical data were compared using Fisher's exact test or the chi-square test, as appropriate. For continuous variables, normally distributed data were analyzed using the independent samples t-test for between-group comparisons and the paired samples t-test for within-group comparisons, while non-normally distributed data were analyzed using the Mann–Whitney U test or the Wilcoxon signed-rank test, respectively. All analyses were carried out using SPSS version 25.0 (IBM Corp., Armonk, NY, USA). A p-value of <0.05 was considered statistically significant.

RESULTS

A total of 150 pregnant women were included in the study, comprising 75 term and 75 postterm cases. BPP parameters were evaluated for all participants in both the morning (08:00–10:00) and evening (20:00–22:00) time periods. When comparing morning and evening BPP assessments in the term group, fetal movement, fetal breathing, and NST parameters were found to be significantly increased in the evening ($p<0.001$, $p<0.001$, and $p=0.006$, respectively). The mean BPP score was 8.5 ± 0.9 in the

morning and 10.0 ± 0.0 in the evening, with this difference being statistically significant ($p<0.001$). Detailed data are presented in Table 1. In the postterm group, a similar pattern was observed: fetal movement, fetal breathing, and NST parameters were significantly higher in the evening compared to the morning ($p<0.001$ for each and $p=0.006$). The mean BPP score was 8.2 ± 0.5 in the morning and 9.9 ± 0.5 in the evening, and this difference was statistically significant ($p<0.001$). The findings for the postterm group are summarized in Table 2.

When comparing the term and postterm groups in the morning assessments, no statistically significant differences were found in fetal movement, breathing, NST, or amniotic fluid index parameters ($p>0.05$ for all). However, the proportion of patients with a perfect BPP score of 10 was significantly higher in the term group than in the postterm group (24.0% vs. 8.8%; $p=0.013$). Additionally, the mean BPP score was higher in the term group compared to the postterm group (8.5 ± 0.9 vs. 8.2 ± 0.5 ; $p=0.007$). Relevant findings are presented in Table 3.

In the evening assessments, all patients in both groups received full scores (2 points) for fetal movement, breathing, tone, and NST; therefore, statistical comparisons for these parameters were not feasible. Although the rates of normal amniotic fluid index and perfect BPP scores appeared higher in the term group, these differences did not reach statistical significance ($p=0.058$ for both). However, the mean BPP score was significantly higher in the term group than in the postterm group (10.0 ± 0.0 vs. 9.9 ± 0.5 ; $p=0.024$). Detailed comparisons are presented in Table 4.

When morning (08:00–10:00) and evening (20:00–22:00) mean BPP scores were compared within both groups, significantly higher scores were observed in the evening for both term and postterm pregnancies ($p<0.001$ for both groups) (Figure 1).

Table 1. Comparison of BPP Parameters Measured in the Morning (08:00–10:00) and Evening (20:00–22:00) in Term Pregnancies

Parameter	Morning (08:00–10:00)	Evening (20:00–22:00)	p value
Fetal movement (2 points)	43 (%57,3)	75 (%100)	<0.001*
Fetal breathing (2 points)	58 (%77,3)	75 (%100)	<0.001*
Fetal tone (2 points)	75 (%100)	75 (%100)	0.999*
Amniotic fluid index (2 points)	75 (%100)	75 (%100)	0.999*
NST (2 points)	67 (%89,3)	75 (%100)	0.006*
BPP score (10 points)	18 (%24,0)	75 (%100)	<0.001*
Mean BPP score	8.5 ± 0.9 (95% CI: 8.29–8.71)	10.0 ± 0.0 (95% CI: 10.0–10.0)	<0.001**

Abbreviations: BPP: Biophysical Profile; NST: Non-Stress Test

*Chi-square or Fisher's exact test was used for categorical variables.

**Paired samples t-test was used for continuous variables.

Data are presented as mean $\pm$ standard deviation (SD) with 95% confidence intervals (CI) for continuous variables, and as frequency (percentage) for categorical variables.

Table 2. BPP Parameters Measured at 08:00–10:00 and 20:00–22:00 in Postterm Pregnancies

Parameter	Morning (08:00–10:00)	Evening (20:00–22:00)	p value
Fetal movement (2 points)	41 (%54,7)	75 (%100)	<0.001*
Fetal breathing (2 points)	55 (%73,3)	75 (%100)	<0.001*
Fetal tone (2 points)	75 (%100,0)	75 (%100,0)	0.999*
Amniotic fluid index (2 points)	70 (%93,3)	70 (%93,3)	0.999*
NST (2 points)	65 (%86,7)	75 (%100,0)	0,006*
BPP score (10 points)	6 (%8,0)	5 (%6,7)	<0.001*
BPP score (8 points)	69 (%92,0)	70 (%93,3)	
Mean BPP score	8.2 ± 0.5 (95% CI: 8.09–8.32)	9.9 ± 0.5 (95% CI: 9.79–10.01)	<0.001**

Abbreviations: BPP: Biophysical Profile; NST: Non-Stress Test

*Chi-square or Fisher's exact test was used for categorical variables.

**Paired samples t-test was used for continuous variables.

Data are presented as mean ± standard deviation (SD) with 95% confidence intervals (CI) for continuous variables, and as frequency (percentage) for categorical variables.

Table 3. Comparison of BPP Measurements at 08:00–10:00 Between Term and Postterm Pregnancies

Parameter	Term (n=75)	Post-term (n=75)	p value
Fetal movement (2 points)	43 (%57,3)	41 (%54,7)	0,869*
Fetal breathing (2 points)	58 (%77,3)	55 (%73,3)	0,705*
Fetal tone (2 points)	75 (%100,0)	75 (%100,0)	***
Amniotic fluid index (2 points)	75 (%100,0)	70 (%93,3)	0.058*
NST (2 points)	67 (%89,3)	65 (%86,7)	0.802*
BPP score (10 points)	18 (%24,0)	6 (%8,8)	0,013*
BPP score (8 points)	57 (%76,0)	69 (%92,0)	
Mean BPP score	8.5 ± 0.9 (95% CI: 8.29–8.71)	8.2 ± 0.5 (95% CI: 8.09–8.32)	0,007**

Abbreviations: BPP: Biophysical Profile; NST: Non-Stress Test

*Chi-square or Fisher's exact test was used for categorical variables.

*Independent samples t-test was used for continuous variables.

Data are presented as mean ± standard deviation (SD) with 95% confidence intervals (CI) for continuous variables, and as frequency (percentage) for categorical variables.

Table 4. Comparison of BPP Measurements at 20:00–22:00 Between Term and Postterm Pregnancies

Parameter	Term (n=75)	Post-term (n=75)	p value
Fetal movement (2 points)	75 (%100,0)	75 (%100,0)	***
Fetal breathing (2 points)	75 (%100,0)	75 (%100,0)	***
Fetal tone (2 points)	75 (%100,0)	75 (%100,0)	***
Amniotic fluid index (2 points)	75 (%100,0)	70 (%93,3)	0,058*
NST (2 points)	75 (%100,0)	75 (%100,0)	***
BPP score (10 points)	75 (%100,0)	70 (%93,3)	0,058*
BPP score (8 points)	0 (%0,0)	5 (%6,7)	
Mean BPP score	10.0 ± 0.0 (95% CI: 10.0–10.0)	9.9 ± 0.5 (95% CI: 9.79–10.01)	0,024**

Abbreviations: BPP: Biophysical Profile; NST: Non-Stress Test

*Chi-square or Fisher's exact test was used for categorical variables.

*Independent samples t-test was used for continuous variables.

Data are presented as mean ± standard deviation (SD) with 95% confidence intervals (CI) for continuous variables, and as frequency (percentage) for categorical variables.

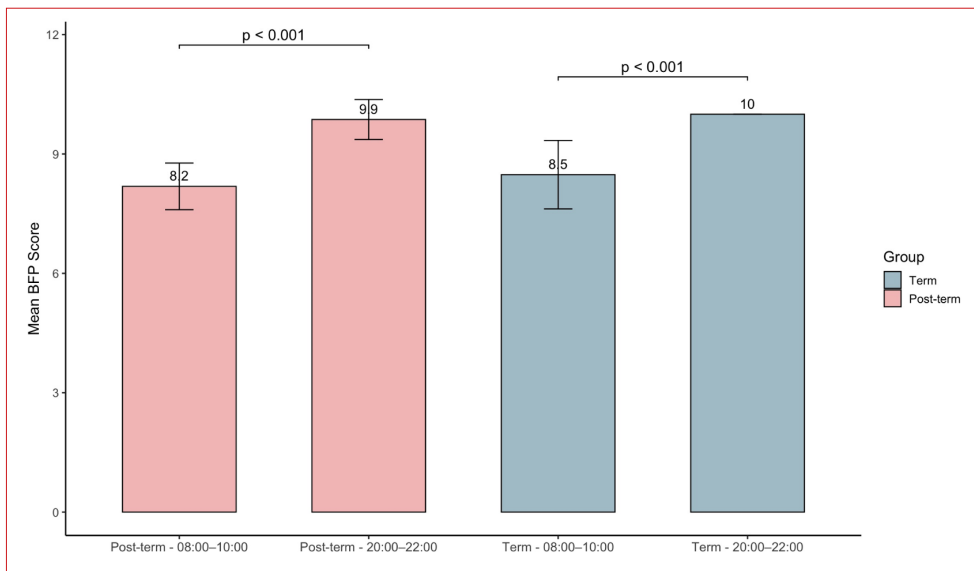


Figure 1. Comparison of Mean Biophysical Profile (BPP) Scores Between Morning (08:00-10:00) and Evening (20:00-22:00) Assessments in Term and Postterm Pregnancies.

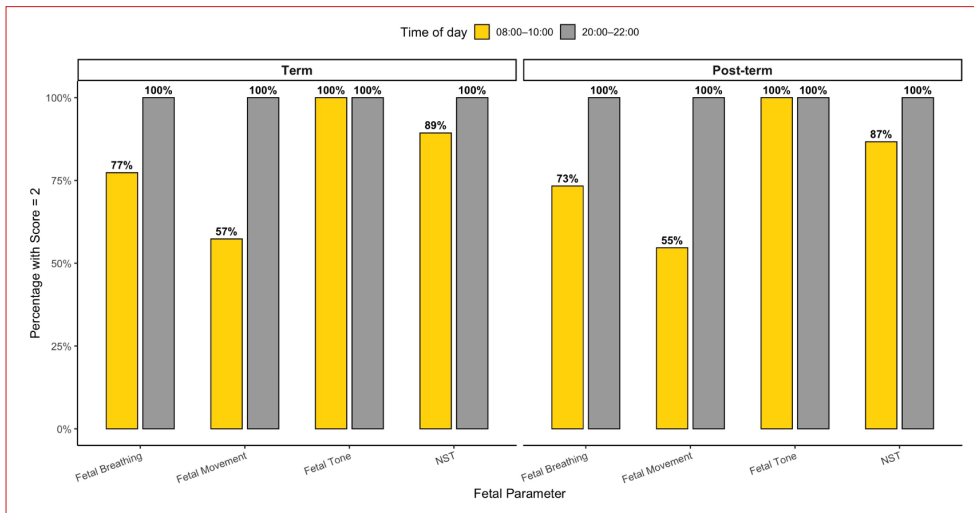


Figure 2. Comparison of the Proportion of Individual Biophysical Profile Parameters Scoring 2 Points Between Morning and Evening Assessments in Term and Postterm Pregnancies.

The proportion of individual parameters—such as fetal movement, breathing, tone, and NST—scoring 2 points varied between morning and evening evaluations. When term and postterm groups were compared, the rate of scoring 2 points in fetal movement and breathing was notably higher during the evening assessments (Figure 2).

DISCUSSION

In the morning BPP assessments, the lowest score observed in both groups was 8, and no cases had a score below 8. The mean morning BPP score across all participants was 8.3. These values are consistent with the generally accepted BPP range of 8–10, which indicates adequate fetal well-being in the absence of pathological findings. Similarly, in the evening assessments, the lowest BPP score recorded was also 8, and the mean score was calculated

as 9.9. The absence of any scores below 8 in the evening further supports the reliability of BPP evaluations performed at different times of the day in reflecting fetal well-being.

In a study conducted by Manning et al. involving 360 term and postterm pregnancies, the mean BPP score in cases without risk factors was reported to be 8.6, regardless of the time of day (16). In our study, the mean BPP score was 9.1, similarly indicating a generally good fetal condition among the participants. In another study, Zhang et al. reported that the most challenging parameters in BPP scoring were fetal tone and breathing (17). This was attributed to the greater influence of the sonographer's experience in evaluating these two parameters, as well as the relative difficulty of assessing them compared to the others. In our study, the lowest scores in the morning assessments were primarily due to reductions in fetal tone and breathing, which is consistent with the literature. In the evening assessments, however, nearly all participants had scores close to

the maximum, making it difficult to draw meaningful conclusions about differences between individual parameters.

Baskett et al., in their study investigating BPP findings associated with fetal asphyxia and adverse neonatal outcomes, reported that the worst outcomes were typically observed when fetal movement was absent on ultrasound and accompanied by at least one additional abnormal parameter (6). In that study as well, the lowest scores were assigned based on the absence of fetal movement, which aligns with the findings of our study.

Although the studies conducted by Patrick et al., which monitored fetal movement and cardiac activity throughout the day, were not conducted in the same context as ours, their findings are consistent with those of our study (18,19). These studies reported higher NST variability and more frequent accelerations during evening assessments, along with a greater number of fetal movements observed sonographically and fewer abnormal findings. These results align with our study, in which higher BPP scores were recorded in the evening.

In a study by Higuchi et al. involving 244 patients, NST was found to be reactive in nearly all cases; however, fetal tone could be observed in only 215 patients (88%) (20). This observation rate is higher than the 78.6% fetal tone visualization rate we found in the morning assessments. Their study included only pregnancies between 38 and 39 weeks of gestation, a period in which reduced spatial limitation and relatively higher amniotic fluid levels may facilitate the detection of fetal movements compared to the postterm period. In this context, a study using a similar methodology but conducted at later gestational ages would likely yield results more comparable to ours. Considering the inclusion of postterm cases in our sample, the relatively lower rate of tone assessment in our study can be explained, and when this factor is taken into account, the findings in the term group appear consistent with the existing literature.

In our study, when morning and evening measurements were compared, parameters such as fetal movement, fetal breathing, NST, and mean BPP scores were found to be significantly lower in the morning than in the evening. Although their study did not include overall BPP assessment, Petrikovsky et al. demonstrated that NST quality and fetal cardiac activity were better in the evening hours (21). This finding is consistent with our results. Similarly, Babazadeh et al., in their study involving high-risk pregnancies, reported that fetal cardiac activity exhibited more accelerations in the evening assessments (22).

De Heus et al. reported that, in patients receiving antenatal corticosteroids, NST assessments conducted in the morning

showed less suppression of fetal cardiac activity by glucocorticoids compared to those performed in the evening. Although this may initially seem contradictory to our findings, it is important to interpret their results with caution due to the heterogeneous nature of their study population, differences in timing and administration of steroid treatment, and the lack of standardization. Furthermore, their study did not evaluate maternal biochemical parameters and was limited by a relatively small sample size. Since their population focused on preterm pregnancies, it differs significantly from ours (23). According to our findings, elevated levels of catecholamines and steroid-based hormones following morning arousal may suppress fetal activity. This hypothesis is supported by the reduced fetal movements observed in morning assessments.

The exact mechanisms underlying daily fluctuations in BPP scores during pregnancy have not yet been fully elucidated. However, diurnal rhythms have been observed in fetal movements, breathing, and fetal heart rate (FHR), and it has been suggested that these rhythms may be related to either fetal or maternal adrenal activity. The hypothalamic-pituitary-adrenal (HPA) axis exhibits rhythmic activity on a daily basis, with ACTH and cortisol levels peaking in the morning and gradually declining to their lowest levels by evening (24). Melatonin, on the other hand, is a hormone secreted by the pineal gland during nighttime and plays a key role in regulating biological rhythms. During late pregnancy, maternal melatonin levels increase. Due to its lipophilic nature, melatonin easily crosses the placenta and enters the fetal circulation. According to Tamura et al., maternal melatonin transmits photoperiodic information to the fetus and contributes to the development of the fetal biological clock. The circadian regulatory effects of melatonin during pregnancy may play a role in determining fetal biophysical status (25). In obstetric practice, with the increasing integration of artificial intelligence and machine learning methods (source), incorporating maternal sleep-wake cycle patterns and vital signs, optimal fetal monitoring may be achieved in the future through virtual health tools (26).

In our study, melatonin levels were not directly measured; however, it is hypothesized that lower melatonin concentrations in the morning may be associated with the lower BPP scores observed at that time. Conversely, increased melatonin levels in the evening may have a more favorable impact on fetal status.

This study has several limitations. First, its single-center design and limited sample size may restrict the generalizability of the findings. Additionally, biochemical parameters such as cortisol and melatonin were not measured, which prevented direct evaluation of the hormonal basis of the observed diurnal differences. BPP assessments were performed only at two time points (morning and evening), excluding other periods of the day. This may limit the

ability to fully characterize the effects of diurnal rhythm throughout the entire day. Lastly, although all evaluations were performed by a single observer, observer bias cannot be completely ruled out for subjective parameters such as fetal movement and tone. These limitations could be addressed in future studies through multi-center designs with larger sample sizes and the inclusion of hormonal biomarkers.

CONCLUSION

In this study, evening assessments yielded significantly higher values in terms of fetal movement, fetal breathing, NST findings, and mean BPP scores when compared to morning evaluations. When morning measurements were considered, mean BPP scores in postterm pregnancies were significantly lower than those in term pregnancies.

In conclusion, this study is among the limited number of investigations demonstrating the impact of diurnal rhythm on fetal biophysical activity and contributes to the existing literature. Future large-scale, multicenter studies incorporating hormonal measurements are needed to better elucidate the influence of biological rhythms on fetal well-being.

Conflict to Interest : The authors declare no Conflict of Interest for this article

Funding: Our study did not receive any funding.

REFERENCES

1. Manning FA, Platt LD, Sipos L. Antepartum fetal evaluation: development of a fetal biophysical profile. *Am J Obstet Gynecol* 1980;136:787–795.
2. Biagiotti R, Marini S, Russo G, Acanfora L. [Usefulness and limits of a fetal biophysical profile in the management of pregnancy at risk]. *Minerva Ginecol* 1992;44:1–4.
3. Soufizadeh N, Farhadifar F, Tamri S, Behafarid S, Sharifi K, Aslani S, et al. Diagnostic value of rapid biophysical profile in comparison to biophysical profile in pregnant women with insulin-dependent diabetes. *J Family Reprod Health* 2019;13:209–213.
4. Manning FA, Snijders R, Harman CR, Nicolaides K, Menticoglou S, Morrison I. Fetal biophysical profile score. VI. Correlation with antepartum umbilical venous fetal pH. *Am J Obstet Gynecol* 1993;169(4):755–763.
5. Manning FA, Morrison I, Harman CR, Lange IR, Menticoglou S. Fetal assessment based on fetal biophysical profile scoring: experience in 19,221 referred high-risk pregnancies. II. An analysis of false-negative fetal deaths. *Am J Obstet Gynecol* 1987;157(4 Pt 1):880–884.
6. Magann EF, Sandlin AT, Ounpraseuth ST. Amniotic fluid and the clinical relevance of the sonographically estimated amniotic fluid volume: oligohydramnios. *J Ultrasound Med* 2011;30(11):1573–1585.
7. Petrikovsky BM, Kaplan GP. Diurnal non-stress test variations in healthy term fetuses. A call for evening appointments for fetal testing. *Early Hum Dev* 1996;44:127–130.
8. Babazadeh R, Abdali K, Lotfalizadeh M, Tabatabaie HR, Kaviani M. Diurnal nonstress test variations in the human fetus at risk. *Int J Gynecol Obstet* 2005;90:189–192.
9. Bocking AD. Observations of biophysical activities in the normal fetus. *Clin Perinatol* 1989;16:583–594.
10. Kalsbeek A, Buijs RM, Engelmann M, Wotjak CT, Landgraf R. In vivo measurement of a diurnal variation in vasopressin release in the rat suprachiasmatic nucleus. *Brain Res* 1995;682:75–82.
11. Kalsbeek A, Buijs RM, van Heerikhuizen JJ, Arts M, van der Woude TP. Vasopressin-containing neurons of the suprachiasmatic nuclei inhibit corticosterone release. *Brain Res* 1992;580:62–67.
12. Kraves S, Weitz CJ. A role for cardiotrophin-like cytokine in the circadian control of mammalian locomotor activity. *Nat Neurosci* 2006;9:212–219.
13. Cheng MY, Bullock CM, Li C, Lee AG, Bermak JC, Belluzzi J, et al. Prokineticin 2 transmits the behavioural circadian rhythm of the suprachiasmatic nucleus. *Nature* 2002;417:405–410.
14. Kramer A, Yang FC, Snodgrass P, Li X, Scammell TE, Davis FC, et al. Regulation of daily locomotor activity and sleep by hypothalamic EGF receptor signaling. *Science* 2001;294:2511–2515.
15. Ozkaya E, Baser E, Cinar M, Korkmaz V, Kucukozkan T. Does diurnal rhythm have an impact on fetal biophysical profile? *J Matern Fetal Neonatal Med* 2012;25(4):335–338.
16. Manning FA, Lange IR, Morrison I, Harman CR. Fetal biophysical profile score and the nonstress test: a comparative trial. *Obstet Gynecol* 1984;64(3):326–331.
17. Zhang DT. [Monitoring of fetal biophysical profile]. *Zhonghua Fu Chan Ke Za Zhi* 1988;23(4):240–243.
18. Patrick J, Campbell K, Carmichael L, Natale R, Richardson B. Patterns of gross fetal body movements over 24-hour observation intervals during the last 10 weeks of pregnancy. *Am J Obstet Gynecol* 1982;142(4):363–371.
19. Patrick J, Campbell K, Carmichael L, Natale R, Richardson B. Patterns of human fetal breathing during the last 10 weeks of pregnancy. *Obstet Gynecol* 1980;56(1):24–30.
20. Higuchi M, Hirano H, Takahashi H, Mochizuki O, Maki M, Hasegawa M. [Human fetal breathing movements: basic analysis and clinical relationship to fetal well-being (author's transl)]. *Acta Obstet Gynaecol Jpn* 1981;33(5):597–606.
21. Petrikovsky BM, Kaplan GP. Diurnal non-stress test variations in healthy term fetuses. A call for evening appointments for fetal testing. *Early Hum Dev* 1996;44:127–130.
22. Babazadeh R, Abdali K, Lotfalizadeh M, Tabatabaie HR, Kaviani M. Diurnal nonstress test variations in the human fetus at risk. *Int J Gynecol Obstet* 2005;90:189–192.
23. de Heus R, Mulder EJ, Derks JB, Koenen SV, Visser GH. Differential effects of betamethasone on the fetus between morning and afternoon recordings. *J Matern Fetal Neonatal Med* 2008;21:549–554.
24. Van Cauter E, Refetoff S. Multifactorial control of the 24-hour secretory profiles of pituitary hormones. *J Endocrinol Invest* 1985;8:381–391.
25. Tamura H, Nakamura Y, Terron MP, Flores LJ, Manchester LC, Tan DX, et al. Melatonin and pregnancy in the human. *Reprod Toxicol* 2008;25:291–303.
26. Zorlu U, Elmas B, Ergün GT, Sucu ST, Ozan E, Aydoğdu E, et al. Determining the risk of gestational diabetes using machine learning: A study on first-trimester PAPP-A and β -hCG data. *Int J Gynaecol Obstet* 2025 Jun 2. doi:10.1002/ijgo.70264. Epub ahead of print. PMID:40454615.

Comparison of Liver Function-Based Scoring Systems and Development of a Predictive Model for Intrahepatic Cholestasis of Pregnancy: A Retrospective Cohort Study

Karaciğer Fonksiyon Testlerine Dayalı Puanlama Sistemlerinin Karşılaştırılması ve Gebelikte İntrahepatik Kolestaz için Yeni Bir Tanı Modelinin Geliştirilmesi: Retrospektif Kohort Çalışması

İsmail BAGLAR¹, Esra KELES¹, Fatih ŞANLIKAN¹, Uğur Kemal ÖZTÜRK¹, Metin AYĞAR¹, Sahra Sultan KARA¹, Esra Buse ERGÜN¹

¹University of Health Sciences, Kartal Lütfi Kırdar City Hospital, Department of Obstetrics and Gynecology, İstanbul, Türkiye

ABSTRACT

Aim: Intrahepatic cholestasis of pregnancy (ICP) is the most prevalent pregnancy-specific liver disorder, associated with significant risks of adverse perinatal outcomes. The diagnostic gold standard, serum bile acid measurement, has limited availability, necessitating alternative diagnostic tools based on routine laboratory parameters. This study aimed to evaluate the diagnostic utility of the Albumin-Bilirubin (ALBI) score, Aspartate Aminotransferase-to-Platelet Ratio Index (APRI), Platelet-Albumin-Bilirubin (PALBI) index, and Fibrinogen-to-Albumin Ratio (FAR) in patients with ICP.

Materials and Methods: This retrospective cohort study included 65 pregnant women diagnosed with ICP and 67 healthy pregnant women as controls. Data were collected between January 2020 and December 2024 at a tertiary maternity center. The ALBI, APRI, PALBI, and FAR scores, alongside inflammatory markers such as the Neutrophil-to-Lymphocyte Ratio (NLR), Platelet-to-Lymphocyte Ratio (PLR), and Red Cell Distribution Width (RDW), were calculated from routine biochemical and hematological analyses. A novel composite score was subsequently developed using multivariate logistic regression.

Results: The ALBI, APRI, PALBI, and FAR scores were all significantly elevated in the ICP cohort compared to the control group ($p < 0.001$ for all). A newly developed composite score, integrating ALBI, NLR, PLR, and RDW, yielded superior diagnostic accuracy (AUC = 0.86), with a sensitivity of 81% and a specificity of 75%. This novel score also showed a significant correlation with adverse perinatal outcomes.

Conclusion: The novel composite score proposed herein offers a practical, cost-effective, and highly accurate method for early diagnosis and risk stratification, particularly in clinical settings where bile acid assays are not readily accessible.

Keywords: Intrahepatic cholestasis of pregnancy; ALBI score; APRI score; PALBI score; Fibrinogen-to-albumin ratio.

ÖZ

Amaç: Gebelikte intrahepatik kolestaz (ICP), gebeliğe özgü en yaygın karaciğer hastalığıdır ve perinatal sonuçlarda önemli riskler ile ilişkilidir. Tanı için altın standart olan serum safra asidi ölçümü sınırlı erişilebilirliğe sahiptir, bu da rutin laboratuvar parametrelerine dayalı alternatif tanı araçlarına ihtiyaç duyulmasına neden olmaktadır. Bu çalışma, ICP hastalarında Albümin-Bilirubin (ALBI) skoru, Aspartat Aminotransferaz-Trombosit Oranı İndeksi (APRI), Trombosit-Albümin-Bilirubin (PALBI) indeksi ve Fibrinojen-Albümin Oranı (FAR) tanı araçlarının yararını değerlendirmek amacıyla yapılmıştır.

Gereç ve Yöntemler: Bu retrospektif kohort çalışmasına, ICP tanısı konmuş 65 hamile kadın ve kontrol grubu olarak 67 sağlıklı hamile kadın dahil edildi. Veriler, Ocak 2020 ile Aralık 2024 tarihleri arasında bir üçüncü basamak doğum merkezinde toplandı. ALBI, APRI, PALBI ve FAR skorları, nötrofil-lenfosit oranı (NLR), trombosit-lenfosit oranı (PLR) ve kırmızı kan hücresi dağılım genişliği (RDW) gibi inflamatuvar belirteçlerle birlikte rutin biyokimyasal ve hematolojik analizlerden hesaplandı. Daha sonra çok değişkenli lojistik regresyon kullanılarak yeni bir bileşik skor geliştirildi.

Sonuçlar: ALBI, APRI, PALBI ve FAR skorları, kontrol grubuna kıyasla ICP kohortunda tümüyle anlamlı şekilde yükselmiştir (tümü için $p < 0,001$). ALBI, NLR, PLR ve RDW'yi birleştiren yeni geliştirilen bir bileşik skor, %81 duyarlılık ve %75 özgüllük ile üstün tanı doğruluğu (AUC = 0,86) sağladı. Bu yeni skor ayrıca, olumsuz perinatal sonuçlarla önemli bir korelasyon gösterdi.

Sonuç: Burada önerilen yeni bileşik skor, özellikle safra asidi testlerinin kolayca erişilebilir olmadığı klinik ortamlarda, erken tanı ve risk sınıflandırması için pratik, maliyet etkin ve yüksek doğrulukta bir yöntem sunmaktadır.

Anahtar Kelimeler: Gebelikte intrahepatik kolestaz; ALBI skoru; APRI skoru; PALBI skoru; Fibrinojen-albümin oranı.

Cite as: Bağlar İ, Keles E, Şanlıkan F, Öztürk UK, Ayğar M, Kara SS et al. Comparison of Liver Function-Based Scoring Systems and Development of a Predictive Model for Intrahepatic Cholestasis of Pregnancy: A Retrospective Cohort Study. Jinekoloji-Obstetrik ve Neonatoloji Tıp Dergisi 2026;23(2):154–159.

Geliş/Received: 07.07.2025 • Kabul/Accepted: 02.10.2025

Sorumlu Yazar/Corresponding Author: İsmail Bağlar, University of Health Sciences, Kartal Lütfi Kırdar City Hospital, Department of Obstetrics and Gynecology, İstanbul, Türkiye
E-mail: ismailbg@gmail.com

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

INTRODUCTION

Intrahepatic cholestasis of pregnancy (ICP) is a reversible cholestatic disorder that typically manifests in the second or third trimester. Although the exact aetiology is multifactorial, the central pathophysiology is impaired biliary excretion with accumulation of bile acids in maternal plasma [1]. ICP commonly presents with intractable pruritus, often localized to the palms and soles and worsening at night, which significantly impairs quality of life. However, the principal clinical significance of ICP lies in its association with a heightened risk of adverse fetal outcomes. These include spontaneous preterm birth, meconium staining of the amniotic fluid, low Apgar scores, and, most critically, sudden intrauterine fetal death [2].

The diagnosis of ICP relies on the combination of characteristic clinical symptoms and elevated fasting serum total bile acid concentrations ($\geq 10 \mu\text{mol/L}$) after exclusion of other causes of liver dysfunction. Elevated levels of aminotransferases, such as aspartate aminotransferase (AST) and alanine aminotransferase (ALT), as well as alkaline phosphatase (ALP) and bilirubin, are often observed but are not universally present.

In recent years, several non-invasive scoring systems originally developed to assess liver fibrosis and function in chronic liver diseases - such as Albumin-Bilirubin (ALBI) score, the AST-to-Platelet Ratio Index (APRI), the Platelet-Albumin-Bilirubin (PALBI) index, and the Fibrinogen-to-Albumin Ratio (FAR) – as well as inflammation-based indices, including Neutrophil-to-Lymphocyte Ratio (NLR), Platelet-to-Lymphocyte Ratio (PLR), Red Cell Distribution Width (RDW), and Mean Platelet Volume (MPV), have been examined for their utility in ICP [3–6]. However, a comprehensive analysis of these scores within a single cohort and integration into a combined predictive model are limited. Therefore, this study aimed to compare the diagnostic performance of the ALBI, APRI, PALBI, and FAR scores in patients with ICP. Our secondary objective was to develop a novel, clinically practical predictive model by combining these biochemical scores with inflammatory markers. Finally, we sought to evaluate the association between these scoring systems and key perinatal outcomes to determine their utility not only for diagnosis but also for prognostic risk stratification.

MATERIALS AND METHODS

Study Design and Population

This retrospective cohort study was conducted using data from pregnant women followed at a single tertiary-level maternity center from January 2020 to December 2024. The study protocol

was approved by the Institutional Ethics Committee (Approval No: 2025/010.99/15/21 Number: 30.04.2025) and was performed in accordance with the principles of the Declaration of Helsinki.

A total of 65 women with ICP and 67 healthy controls, matched for age and gestational week, were included in the final analysis.

The diagnosis of ICP was established based on the presence of clinically significant pruritus without a rash, a fasting total serum bile acid level $\geq 10 \mu\text{mol/L}$, and the exclusion of other hepatobiliary diseases. Exclusion criteria for both groups included multiple gestations, preeclampsia, HELLP (hemolysis, elevated liver enzymes, low platelet count) syndrome, active systemic infection, known autoimmune or chronic liver disease, pre-existing hematological disorders, smoking, alcohol consumption, and incomplete clinical or laboratory data.

Data Collection and Laboratory Analysis

Clinical and laboratory data were retrospectively retrieved from the electronic hospital information system. The following maternal variables were collected: age, gestational age at diagnosis, parity, gravida, body mass index (BMI), and family history of ICP. Laboratory parameters recorded included albumin, total bilirubin (TBIL), direct bilirubin, AST, ALT, ALP, fibrinogen, hemoglobin, neutrophil count, lymphocyte count, platelet count (PLT), MPV, and RDW.

Perinatal outcome data included gestational age at delivery, mode of delivery, birth weight, 1- and 5-minute Apgar scores, and the requirement for neonatal intensive care unit (NICU) admission.

Calculation of Scoring Indices

Four established liver function scores and two inflammatory ratios were calculated using the following formulas:

ALBI Score: $\text{ALBI} = (0.66 \times \log_{10}[\text{TBIL } (\mu\text{mol/L})]) - (0.085 \times \text{Alb } (\text{g/L}))$

APRI: $\text{APRI} = ([\text{AST } (\text{U/L}) / \text{Upper Limit of Normal for AST}] / \text{PLT } (10^9/\text{L})) \times 100$

PALBI Index: $\text{PALBI} = 2.02 \times \log_{10}[\text{TBIL } (\mu\text{mol/L})] - 0.37 \times (\log_{10}[\text{TBIL } (\mu\text{mol/L})])^2 - 0.04 \times \text{Alb } (\text{g/L}) - 3.48 \times \log_{10}[\text{PLT } (10^9/\text{L})] + 1.01 \times (\log_{10}[\text{PLT } (10^9/\text{L})])^2$

FAR: $\text{FAR} = \text{Fibrinogen } (\text{g/L}) / \text{Albumin } (\text{g/L})$

NLR: $\text{NLR} = \text{Absolute Neutrophil Count} / \text{Absolute Lymphocyte Count}$

PLR: $\text{PLR} = \text{Platelet Count} / \text{Absolute Lymphocyte Count}$

Note: For the ALBI and PALBI calculations, bilirubin values were first converted from mg/dL to $\mu\text{mol/L}$ by multiplying by 17.1.

Statistical Analysis

Statistical analyses were performed using SPSS version 26.0 (IBM Corp., Armonk, NY, USA). The distribution of continuous variables was assessed using the Kolmogorov-Smirnov test. Normally distributed data were presented as mean $\pm$ standard deviation (SD), while non-normally distributed data were presented as median (minimum–maximum). Intergroup comparisons were conducted using the independent samples t-test for normally distributed variables and the Mann-Whitney U test for non-normally distributed variables. Categorical variables were compared using the Chi-square test or Fisher's exact test, as appropriate.

Receiver Operating Characteristic (ROC) curve analysis was performed to evaluate the diagnostic accuracy of each score for ICP. The area under the curve (AUC), with its 95% confidence interval (CI), was calculated. Optimal cut-off values were determined using the Youden index (Sensitivity + Specificity - 1).

Parameters found to be significant in the ROC analysis were entered into a multivariate logistic regression model (forward conditional method) to identify independent predictors and develop a novel composite predictive score. The performance of this new score was then evaluated using ROC analysis, and its sensitivity, specificity,

positive predictive value (PPV), and negative predictive value (NPV) were calculated. A two-tailed p-value < 0.05 was considered statistically significant.

RESULTS

Demographic and Clinical Characteristics

The primary analysis included 65 patients with ICP and 67 healthy controls. The groups were well-matched, with no statistically significant differences in maternal age, gestational age at sampling, parity, gravida, or BMI ($p > 0.05$ for all). A family history of ICP was significantly more common in the ICP group (9.6% vs. 2.0%, $p < 0.01$). As expected, serum ALT and AST levels were significantly higher in the ICP group ($p < 0.001$). The demographic and baseline clinical characteristics are detailed in Table 1.

Comparison of Biochemical and Hematological Scores

All four primary scoring indices—ALBI, APRI, PALBI, and FAR—were significantly higher in the ICP group compared to the healthy control group ($p < 0.001$ for all). The inflammatory marker NLR was also significantly elevated in patients with ICP ($p < 0.001$). A comparison of these scores is provided in Table 2.

Table 1. Demographic and Obstetric Characteristics of the Study Participants

Characteristic	ICP Group (n=65)	Control Group (n=67)	p-value
Age (years, mean $\pm$ SD)	29.6 $\pm$ 4.3	29.2 $\pm$ 4.1	0.384
Gestational Age (weeks, mean $\pm$ SD)	35.8 $\pm$ 1.6	36.1 $\pm$ 1.5	0.092
Parity (median, min–max)	1 (0–5)	1 (0–4)	0.443
Gravida (median, min–max)	2 (1–6)	2 (1–5)	0.498
BMI (kg/m ² , mean $\pm$ SD)	28.2 $\pm$ 3.9	27.6 $\pm$ 4.1	0.172
Family History of ICP, n (%)	6 (9.6%)	1 (2.0%)	<0.01
UDCA Use, n (%)	34 (53.0%)	-	-
ALT (U/L, mean $\pm$ SD)	72.1 $\pm$ 34.6	28.4 $\pm$ 15.7	<0.001
AST (U/L, mean $\pm$ SD)	59.3 $\pm$ 28.9	24.9 $\pm$ 13.2	<0.001

ICP: Intrahepatic Cholestasis of Pregnancy; UDCA: Ursodeoxycholic acid; ALT: Alanine Aminotransferase; AST: Aspartate Aminotransferase; BMI: Body mass index, SD: Standard Deviation. Data are presented as mean $\pm$ SD for normally distributed continuous variables and median (min–max) for non-normally distributed variables. Intergroup comparisons were performed using the independent samples t-test or Mann-Whitney U test as appropriate. Categorical variables were compared using the Chi-square or Fisher's exact test.

Table 2. Comparison of Laboratory Scores Between ICP and Control Groups

Parameter	ICP Group (n=65) (Mean $\pm$ SD / Median)	Control Group (n=67) (Mean $\pm$ SD / Median)	p-value
ALBI Score	-2.13 $\pm$ 0.45	-2.42 $\pm$ 0.40	<0.001
APRI Score	0.42 (0.25–0.83)	0.28 (0.14–0.49)	<0.001
PALBI Score	-2.01 $\pm$ 0.33	-2.33 $\pm$ 0.28	<0.001
FAR	0.145 $\pm$ 0.03	0.111 $\pm$ 0.02	<0.001
NLR	3.9 $\pm$ 1.2	2.7 $\pm$ 0.9	<0.001

ALBI: Albumin-Bilirubin Score; APRI: AST-to-Platelet Ratio Index; PALBI: Platelet-Albumin-Bilirubin Index; FAR: Fibrinogen-to-Albumin Ratio; NLR: Neutrophil-to-Lymphocyte Ratio. Data are presented as mean $\pm$ SD for normally distributed continuous variables and median (min–max) for non-normally distributed variables. Intergroup comparisons were performed using the independent samples t-test or Mann-Whitney U test as appropriate. Categorical variables were compared using the Chi-square or Fisher's exact test.

Table 3. ROC Analysis of Scoring Systems for the Diagnosis of ICP

Score	AUC (95% CI)	Optimal cut-off	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
APRI	0.83 (0.76–0.91)	>0.30	76	79	77.8	77.3
PALBI	0.80 (0.72–0.88)	>–2.10	74	76	75.0	75.1
ALBI	0.75 (0.66–0.84)	>–2.45	69	72	70.5	70.6
FAR	0.72 (0.63–0.81)	>0.135	67	70	68.4	68.7
Novel composite score	0.86 (0.80–0.92)	>0.55	81	75	75.9	80.3

AUC: Area Under the Curve; CI: Confidence Interval; APRI: AST-to-Platelet Ratio Index; PALBI: Platelet-Albumin-Bilirubin Index; ALBI: Albumin-Bilirubin Score; FAR: Fibrinogen-to-Albumin Ratio.

Table 4. Comparison of Perinatal Outcomes

Outcome	ICP Group (n=65)	Control Group (n=67)	p-value
Gestational Age at Delivery (weeks)	36.0 ± 1.3	38.2 ± 1.1	<0.001
Birth Weight (grams)	2780 ± 410	3105 ± 390	<0.001
Apgar Score, 1 min (median, range)	7 (4–9)	8 (6–9)	0.002
Apgar Score, 5 min (median, range)	8 (6–10)	9 (8–10)	0.008
NICU Admission, n (%)	20 (30.8%)	5 (7.5%)	<0.001

NICU: Neonatal Intensive Care Unit.

Diagnostic Performance of Scoring Models

ROC curve analysis revealed that the APRI score demonstrated the highest diagnostic accuracy among the individual indices, with an AUC of 0.83 (95% CI: 0.76–0.91). This was followed by the PALBI score (AUC=0.80), ALBI score (AUC=0.75), and FAR (AUC=0.72).

A new composite score was developed via multivariate logistic regression, incorporating ALBI, NLR, RDW, and PLR. This score yielded the highest diagnostic performance, with an AUC of 0.86 (95% CI: 0.80–0.92). At an optimal cut-off value of >0.55, the new score had a sensitivity of 81% and a specificity of 75%. The detailed results of the ROC analysis are presented in Table 3.

Perinatal Outcomes

Patients in the ICP group delivered at a significantly earlier gestational age (36.0 ± 1.3 weeks vs. 38.2 ± 1.1 weeks, $p < 0.001$) and had infants with a lower mean birth weight (2780 ± 410 g vs. 3105 ± 390 g, $p < 0.001$). Median 1- and 5-minute Apgar scores were significantly lower in the ICP group ($p=0.002$ and $p=0.008$, respectively). Furthermore, NICU admission was significantly higher in the ICP group compared with controls (20/65 [30.8%] vs. 5/67 [7.5%], $p < 0.001$). A summary of these outcomes is presented in Table 4.

introduces a novel composite model with superior predictive accuracy. Our findings confirm that the ALBI, APRI, and PALBI scores, alongside the inflammatory marker-based FAR, are significantly elevated in pregnancies complicated by ICP. This supports their utility as accessible, cost-effective adjuncts to clinical diagnosis, corroborating the results of recent investigations [7–9].

Pregnancy is associated with physiologic changes that can influence liver-function and inflammation markers [10]. Maternal plasma albumin falls progressively due to hemodilution and altered synthesis, and fibrinogen increase during pregnancy [11]. In addition, platelet counts commonly decline in the second–third trimester, which affects platelet-dependent indices [12]. These changes may systematically influence ALBI, PALBI and FAR values. To mitigate this, we matched controls for gestational week; nevertheless, pregnancy-specific reference ranges of these indices (including gestational-age-specific cut-offs) will be required for routine obstetric use.

The ALBI score, which reflects both synthetic (albumin) and excretory (bilirubin) liver function, proved to be a reliable marker. Its significant elevation in our ICP cohort is consistent with the findings of Ozkavak et al., who reported its utility in differentiating ICP patients from healthy controls [3]. Similarly, the strong performance of the APRI and PALBI scores, which incorporate markers of hepatocellular injury (AST) and portal pressure surrogates (platelet count), suggests they capture distinct aspects of the hepatic pathophysiology in ICP. Our findings align with those of Karabay et al., who demonstrated a sensitivity exceeding 70%

DISCUSSION

This study provides a comprehensive evaluation of several non-invasive, liver function-based scores for the diagnosis of ICP and

for the PALBI score in an ICP population [4]. Notably, Sakcak et al. demonstrated that second–third trimester APRI was associated with both the development of ICP and the requirement for neonatal intensive care [13]. This is consistent with our results and supports further evaluation of APRI as a clinically useful biomarker for early risk stratification

A noteworthy finding of our study is the diagnostic potential of FAR. This ratio, which reflects the balance between a positive acute-phase reactant (fibrinogen) and a negative one (albumin), is an emerging marker of systemic inflammation. Its elevation in our ICP cohort provides further evidence for the role of an underlying inflammatory state in the pathogenesis of the disease and extends its application into the obstetric field, where it has recently been explored for predicting other pregnancy complications [14, 15]. The significant increase in NLR in our ICP group further substantiates this link between ICP and systemic inflammation, a finding consistent with multiple prior studies [16–18].

The most significant contribution of our work is the development and validation of a novel composite score integrating ALBI, NLR, RDW, and PLR. With an AUC of 0.86, this model outperformed all individual scores, demonstrating that a multi-faceted approach combining markers of liver function, inflammation, and red cell homeostasis provides a more powerful diagnostic tool. This enhanced accuracy suggests that such a model could be instrumental for early risk stratification, allowing for timely intervention and heightened surveillance, especially in resource-limited settings.

Regarding clinical use of the novel composite score (cut-off >0.55 in this cohort), we propose a cautious, pragmatic integration: patients with scores ≤ 0.55 may be considered at lower probability of ICP and managed routinely, whereas patients with scores >0.55 warrant closer evaluation — expedited bile-acid testing (when available), increased maternal/fetal surveillance, consideration of ursodeoxycholic acid according to local practice, and multidisciplinary discussion about timing of delivery guided by serial bile acids and clinical course. It must be emphasized that these recommendations are provisional and prospective studies are required before this score is used to direct management.

Our analysis of perinatal outcomes reinforces the well-established association between ICP and adverse neonatal results. The observed increases in prematurity, low birth weight, and NICU admissions in the ICP cohort are consistent with landmark studies, such as the meta-analysis by Ovadia et al., which definitively linked elevated bile acid levels to poor fetal outcomes [2, 19]. Critically, the positive correlation between our novel composite score and these adverse outcomes suggests its potential value extends beyond diagnosis to prognosis. This dual utility could empower clinicians to identify not

only which patients have ICP but also which are at the highest risk for fetal compromise, thereby guiding management decisions such as the timing of delivery [20, 21].

This study has several strengths, including a well-characterized patient cohort, the breadth of biochemical and hematological parameters analyzed, and the development of a novel, high-performing predictive model. However, we acknowledge its limitations. The retrospective design may have introduced selection bias, and reliance on electronic records may have resulted in missing data for some variables. The primary limitation is that fasting serum bile acid levels, the gold standard for diagnosis, were used for case definition but their specific quantitative levels were not uniformly available for correlation analysis across the entire cohort. Another limitation of our study is that no a priori sample size calculation was undertaken, as the study cohort was defined retrospectively. The observed effect sizes can inform future power analyses for prospective validation.

CONCLUSION

In conclusion, this study validates the diagnostic utility of the ALBI, APRI, PALBI, and FAR scores in intrahepatic cholestasis of pregnancy. We have demonstrated that a novel composite score, developed by integrating routine biochemical and hematological markers, significantly enhances diagnostic accuracy and correlates with adverse perinatal outcomes. This model represents a promising, accessible, and effective tool for clinical practice, facilitating early diagnosis and risk stratification.

Ethical Approval: This study was approved by the Ethics Committee of Kartal Dr. Lütfi Kırdar Şehir Hastanesi, Etik Kurulu (Approval Number: 2025/010.99/15/21, Date of Approval: 30.04.2025)

Authors' contributions: Concept and Design: İ.B., U.K.O, E.K., S.S.K., M.A., E.B.E.; Data Collection or Processing: İ.B., U.K.O, E.K., S.S.K., F.Ş., M.A.; Analysis or Interpretation: İ.B., U.K.O, E.K., S.S.K., E.B.E; Literature Search: İ.B., U.K.O, E.K., F.Ş., M.A., E.B.E Writing: : İ.B., E.K., S.S.K., F.Ş., M.A., E.B.E.

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

Financial Disclosure: The authors declared that this study has received no financial support.

Availability of data and material: All relevant data used and/or analyzed for the study are available in anonymized form from the corresponding author upon reasonable request.

Acknowledgements: The authors would like to thank the clinical records department for assistance in accessing patient data.

REFERENCES

1. Geenes V, Williamson C. Intrahepatic cholestasis of pregnancy. *World J Gastroenterol*. 2009;15(17):2049–2066.
2. Ovadia C, Seed PT, Geenes V, et al. Association of adverse perinatal outcomes of intrahepatic cholestasis of pregnancy with biochemical markers: results of aggregate and individual patient data meta-analyses. *Lancet*. 2019;393(10174):899–909.

3. Ozkavak OO, Tanacan A, Haksever M, et al. The utility of albumin–bilirubin score in patients with intrahepatic cholestasis of pregnancy: a retrospective comparative study. *Rev Assoc Med Bras*. 2024;70(11):e20240860.
4. Karabay G, Şeyhanlı Z, Sucu ST, et al. Evaluation of Liver Function Indices in Intrahepatic Cholestasis of Pregnancy. *Ankara Etlik City Hospital*. 2024;57(3):114–119.
5. Luo M, Wang L, Yao H, et al. Diagnostic and prognostic value of blood inflammation and biochemical indicators for intrahepatic cholestasis of pregnancy. *Sci Rep*. 2022;12:20833.
6. Ovadia C, Williamson C. Intrahepatic cholestasis of pregnancy: Recent advances. *Clin Dermatol*. 2016;34(3):327-34.
7. Cemortan M, Tulbure CI, Sagaidac I, et al. Assessment of aspartate aminotransferase to Platelet Ratio Index and Fibrosis-4 Index score on women with intrahepatic cholestasis of pregnancy. *AJOG Glob Rep*. 2024;4(2):100337.
8. Silva J, Magenta M, Sisti G, et al. Association Between Complete Blood Count Components and Intrahepatic Cholestasis of Pregnancy. *Cureus*. 2020;12(12):e12381.
9. Cemortan M, Cernetchil O. Assessment of the role of hematological inflammatory markers in the severity of intrahepatic cholestasis of pregnancy. *Moldovan Journal of Health Sciences*. 2022;28(2).
10. Soma-Pillay P, Nelson-Piercy C, Tolppanen H, Mebazaa A. Physiological changes in pregnancy. *Cardiovasc J Afr*. 2016;27(2):89-94.
11. Chandra S, Tripathi AK, Mishra S, Amzarul M, Vaish AK. Physiological changes in hematological parameters during pregnancy. *Indian J Hematol Blood Transfus*. 2012;28(3):144-6.
12. Reese JA, Peck JD, Deschamps DR, McIntosh JJ, Knudtson EJ, Terrell DR, Vesely SK, George JN. Platelet Counts during Pregnancy. *N Engl J Med*. 2018;379(1):32-43.
13. Sakcak B, Denizli R, Farisoğulları N, İpek G, Kara Ö, Tanacan A, et al. Second-Third Trimester Aspartate Aminotransferase to Platelet Ratio Index in Predicting Intrahepatic Cholestasis of Pregnancy and its Relationship with Neonatal Intensive Care Unit Requirement: A Case Control Study From a Tertiary Hospital. *JGON*. 2023;20(3):1863-6.
14. Özkavak OO, Şahin D. The Predictive Value of First Trimester Fibrinogen-Albumin Ratio for Late Onset Fetal Growth Restriction. *Osmangazi Journal of Medicine*. 2025;47(2):316-323.
15. Agaoglu Z, Tanacan A, Aktas BA, et al. Assessment of the fibrinogen-to-albumin ratio in predicting the severity of hyperemesis gravidarum. *The Journal of Gynecology-Obstetrics and Neonatology*. 2024:309-315.
16. İpek G, Tanacan A, Peker A, et al. Systemic Inflammation Response Index as a diagnostic and prognostic predictor of intrahepatic cholestasis of pregnancy: A case-control study from a tertiary center. *Int J Gynaecol Obstet*. 2024;165(2):717-722.
17. Oğlak SC, Tunç Ş, Ölmez F. First Trimester Mean Platelet Volume, Neutrophil to Lymphocyte Ratio, and Platelet to Lymphocyte Ratio Values Are Useful Markers for Predicting Preeclampsia. *Ochsner J*. 2021;21(4):364-370.
18. Luo M, Wang L, Yao H, et al. Diagnostic and prognostic value of blood inflammation and biochemical indicators for intrahepatic cholestasis of pregnancy in Chinese pregnant women. *Sci Rep*. 2022;12(1):20833.
19. Brouwers L, Koster MP, Page-Christiaens GC, et al. Intrahepatic cholestasis of pregnancy: maternal and fetal outcomes associated with elevated bile acid levels. *Am J Obstet Gynecol*. 2015;212(1):100.e1-7.
20. Lee RH, Incerpi MH, Miller DA, et al. Sudden fetal death in intrahepatic cholestasis of pregnancy. *Obstet Gynecol*. 2009;113(2 Pt 2):528-531.
21. Gonsalkorala ES, Cannon MD, Lim TY, et al. Non-Invasive Markers (ALBI and APRI) Predict Pregnancy Outcomes in Women With Chronic Liver Disease. *Am J Gastroenterol*. 2019;114(2):267-275.

Impact of COVID-19 Vaccination on Anxiety in Pregnant Women: Insights from a Cross-Sectional Study at a Tertiary Pandemic Center

COVID-19 Aşılmasının Gebelerde Anksiyete Üzerine Etkisi: Bir Üçüncü Basamak Pandemi Merkezinde Yapılan Kesitsel Çalışmadan Bulgular

 Rahime Begüm KARACUHA¹,  Mervenur KEMENT¹,  Orhan Seyfi AKSAKAL²

¹Department of Obstetrics and Gynecology, Ministry of Health, Ankara City Hospital, Ankara, Türkiye

²University of Health Sciences, Department of Obstetrics and Gynecology, Ministry of Health, Ankara City Hospital, Ankara, Türkiye

ABSTRACT

Aim: This study aimed to investigate anxiety levels among vaccinated and unvaccinated pregnant women during the COVID-19 pandemic, exploring vaccination-related concerns, psychological impacts, and factors influencing vaccine hesitancy.

Materials and Methods: A cross-sectional study was conducted at a tertiary referral hospital, involving 505 healthy pregnant women between November 2021 and January 2022. Data on demographics, vaccination status, and anxiety levels were collected using validated scales, including the Pregnancy-Related Anxiety Scale (P-RAS), Spielberger State-Trait Anxiety Inventory and Impact of Event Scale-Revised (IES-R). Statistical analyses were performed using logistic regression and nonparametric tests.

Results: Vaccinated pregnant women exhibited significantly higher anxiety scores related to concerns about motherhood and their baby compared to unvaccinated participants ($p < 0.05$). Factors such as family history of chronic disease and higher education levels were associated with increased anxiety. Vaccine hesitancy was strongly influenced by misinformation and a lack of trust in credible information sources.

Conclusion: Pregnancy-related anxiety during the pandemic is intricately linked to vaccination decisions, with misinformation and sociopsychological factors playing pivotal roles. Enhancing access to reliable information and integrating psychological support into prenatal care could mitigate anxiety and improve vaccine acceptance among pregnant women.

Keywords: Anxiety, COVID-19, maternal mental health, pregnancy, vaccination, vaccine hesitancy.

ÖZ

Amaç: Bu çalışma, COVID-19 pandemisi sırasında aşılanmış ve aşılanmamış gebeler arasındaki anksiyete düzeylerini, aşıya ilişkin endişeleri, psikolojik etkileri ve aşı tereddüdünü etkileyen faktörleri araştırmayı amaçlamaktadır.

Gereç ve Yöntemler: Kasım 2021 ile Ocak 2022 tarihleri arasında üçüncü basamak bir sevk hastanesinde yürütülen kesitsel çalışmaya, sağlıklı 505 gebe dahil edilmiştir. Katılımcıların demografik verileri, aşılama durumları ve anksiyete düzeyleri; Gebeliğe İlişkin Anksiyete Ölçeği (P-RAS), Spielberger Durumluk-Sürekli Kaygı Envanteri ve Olayın Etkisi Ölçeği-Gözden Geçirilmiş (IES-R) gibi geçerliliği kanıtlanmış ölçeklerle değerlendirilmiştir. İstatistiksel analizlerde lojistik regresyon ve parametrik olmayan testler kullanılmıştır.

Bulgular: Aşılanmış gebeler, annelik ve bebekleri ile ilgili endişeler açısından aşılanmamış katılımcılara kıyasla anlamlı derecede daha yüksek anksiyete puanlarına sahipti ($p < 0,05$). Kronik hastalık aile öyküsü ve yüksek eğitim düzeyi, artmış anksiyete ile ilişkili bulundu. Aşı tereddüdü ise büyük ölçüde yanlış bilgilendirme ve güvenilir bilgi kaynaklarına duyulan güvensizlikten etkilendi.

Sonuç: Pandemi döneminde gebeliğe ilişkin anksiyete, aşılama kararlarıyla yakından ilişkilidir ve yanlış bilgi ile sosyopsikolojik faktörler bu süreçte önemli rol oynamaktadır. Güvenilir bilgiye erişimin artırılması ve doğum öncesi bakım hizmetlerine psikolojik desteğin entegre edilmesi, anksiyeteyi azaltabilir ve gebeler arasında aşı kabulünü artırabilir.

Anahtar Kelimeler: Anksiyete, COVID-19, maternal ruh sağlığı, gebelik, aşılama, aşı tereddüdü.

Cite as: Karacuha RB, Kement M, Aksakal OS. Impact of COVID-19 Vaccination on Anxiety in Pregnant Women: Insights from a Cross-Sectional Study at a Tertiary Pandemic Center. Jinekoloji-Obstetrik ve Neonatoloji Tıp Dergisi 2026;23(2):160–167.

Geliş/Received: 19.08.2025 • **Kabul/Accepted:** 10.12.2025

Sorumlu Yazar/Corresponding Author: Mervenur Kement, Department of Obstetrics and Gynecology, Ministry of Health, Ankara City Hospital, Ankara, Türkiye

E-mail: mervenur.kement@saglik.gov.tr

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

INTRODUCTION

The COVID-19 pandemic has highlighted the importance of preparedness against public health threats and emphasized the critical role of vaccination. This is particularly relevant during pregnancy, which is a period marked by changes in the immune system that increase susceptibility to infections (1).

Pregnancy is a time of both physiological and sociological changes. Public health crises such as the COVID-19 pandemic have exacerbated these psychological challenges. For instance, a study by Saccone et al. involving 100 pregnant women revealed that two-thirds experienced heightened anxiety during the pandemic (2).

Beyond the direct impact of the pandemic, factors such as the limited availability of long-term studies on the perinatal effects of the COVID-19 vaccine and the spread of anti-vaccination propaganda have contributed to anxiety and stress among vaccinated pregnant women (3). Pregnant women often exhibit a cautious approach toward vaccines, including those recommended during pregnancy such as COVID-19, influenza, and pertussis (4). Vaccination rates among pregnant women remain lower compared to the general population, reflecting higher levels of vaccine hesitancy (5). According to a study by D'Alessandro et al., 24% of pregnant women considered vaccination dangerous for both themselves and their fetus (6). Concerns about vaccine safety and fears of potential side effects are frequently cited as the primary reasons for vaccine refusal among this group (7). These concerns have often been shown to increase anxieties related to motherhood and fears about potential harm to the baby (1, 8).

This study aims to compare the anxiety levels of vaccinated and unvaccinated pregnant women during the COVID-19 pandemic, explore the sources of negative perceptions toward vaccination, and evaluate the potential anxiety-inducing effects of both vaccination and vaccine hesitancy. The findings of this study will provide valuable insights for the development of future public health measures to mitigate similar challenges in the future effectively.

METHODS

Participants and Procedure

This study was conducted at the antenatal care clinic of Ankara Bilkent City Hospital, a tertiary referral center designated as a COVID-19 pandemic hospital. Ethical approval was obtained from the Clinical Research Ethics Committee of Ankara Bilkent City Hospital, University of Health Sciences (Approval number: E2-21-955) in October 2021. The research was planned as a cross-sectional observational study and conducted as a survey. As no directly comparable study was available in the literature, the

sample size was calculated based on the effect size. The effect size for the difference between the mean anxiety scores of vaccinated and unvaccinated groups was set at 0.25. With a significance level of 0.05 and power of 0.80, a minimum of 253 participants per group (a total of 506) was deemed adequate for the study using a two-sided Student's t-test. The study included 505 healthy pregnant women with confirmed fetal heartbeats who visited the clinic between November 1, 2021, and January 1, 2022. During this period, a total of 10,540 patients attended the clinic; however, only 505 participants met the inclusion criteria and provided informed consent. Demographic and clinical data were collected through face-to-face interviews.

The following exclusion criteria were applied:

- Declined participation,
- Known psychiatric disorders,
- Receives active depression treatment,
- Known systemic chronic diseases,
- History of COVID-19 respiratory illness during pregnancy,
- Early pregnancies (<6 weeks).
- Sociodemographic and Clinical Characteristics

The demographic and clinical characteristics of the participants were comprehensively assessed. Demographic data included age, body mass index (BMI), smoking and alcohol use, education level, and income level. Clinical data encompassed gestational age, parity, previous type of delivery, history of psychiatric disorders before pregnancy, history of COVID-19 infection prior to pregnancy, and vaccination status. Participants were also asked about their sources of information regarding COVID-19 vaccines, which included television, newspapers, radio, social media, the internet, doctors, healthcare professionals, family and friends, government institutions. To evaluate anxiety and its contributing factors, validated assessment tools were utilized, including the Pregnancy-Related Anxiety Scale (P-RAS), Impact of Event Scale-Revised (IES-R), Spielberger State-Trait Anxiety Inventory, and Visual Analog Scale (VAS).

Impact of Event Scale-Revised (IES-R):

The IES-R consisted of 22 questions scored between 0 and 4, and three subscales, including re-experiencing, avoidance, and hyperarousal. The total score ranges from 0 to 88, with individual subscale scores calculated separately (9).

Pregnancy-Related Anxiety Scale (P-RAS):

The P-RAS consisting of 33 questions scored between 1-4. It was used to assess concerns related to childbirth, body image, attitudes

toward childbirth, maternal worries, pregnancy acceptance, anxiety symptoms, attitudes toward medical staff, avoidance and concerns about the baby. The total score ranges from 33 to 132, with higher scores indicating greater pregnancy-related anxiety (10).

Spielberger State-Trait Anxiety Inventory:

This inventory included two separate scales, each with 20 items. The State Anxiety Scale measures how individuals feel at a specific moment under certain conditions, while the Trait Anxiety Scale assesses how individuals feel in general. Total scores range from 20 to 80, with higher scores indicating greater anxiety and lower scores reflecting lower anxiety. On average, scores typically range between 36 and 41 (11).

Statistical Analysis

All statistical analyses were performed using SPSS version 17.0 (SPSS Inc., Chicago, IL, USA). The normality of quantitative variables was assessed using the Kolmogorov–Smirnov or Shapiro–Wilk tests supported by graphical methods (histograms and Q-Q plots). Descriptive statistics were reported as mean $\pm$ standard deviation and 95% confidence interval for normally distributed data, and as median (minimum–maximum) or median with interquartile range (IQR) for non-normally distributed data. Categorical variables were expressed in numbers and percentages. Comparisons between two independent groups were performed using the Student's t-test for normally distributed variables and the Mann–Whitney U test for non-normally distributed variables. For comparisons involving more than two groups, one-way ANOVA was used for normally distributed data, while the Kruskal–Wallis H test was applied for non-normally distributed data. Associations between categorical variables were assessed using the chi-square or Fisher's exact tests when appropriate. To determine the risk factors associated with high pregnancy-related anxiety, univariate logistic regression analysis was initially performed. Variables with $p < 0.05$ in univariate tests were entered into a multivariate logistic regression model using the enter method. Odds ratios (OR) and 95% confidence intervals (CI) were calculated. All statistical tests were two-tailed, and a p -value < 0.05 was considered statistically significant.

RESULTS

Sources of Information and Their Credibility

Participants reported various sources of COVID-19 vaccine information. The most common information sources were television (65.3%), the internet (49.7%), social media (45.1%), healthcare professionals (38.4%), and doctors (38.2%). The most trusted sources were doctors (25.3%), healthcare professionals (18.9%),

television (17.3%), the internet (13.1%), and social media (12.0%). Less trusted sources included family (2.9%), relatives and friends (2.5%), government institutions (1.7%), and self-reported sources (1.9%). Additionally, 17 participants (3.6%) reported complete distrust in any source (Table 1).

Concerns About Motherhood and Babies

Significant differences emerged between vaccinated and unvaccinated pregnant women for the subscales "Concerns About Motherhood" and "Concerns About the Baby" ($p = 0.011$ and $p = 0.008$, respectively). Mean "Concerns About Motherhood" scores were higher among vaccinated women than unvaccinated women (5.0 vs. 4.0). Similarly, "Concerns About the Baby" scores were significantly higher in vaccinated participants.

Differences Associated with Chronic Diseases

Among vaccinated women, those with a family history of chronic diseases had significantly higher "Concerns About Motherhood" scores (5.0 vs. 4.0, $p = 0.022$) and higher "Re-experiencing" subscale scores (7.0 vs. 6.0; $p = 0.032$) (data not shown). No significant differences were found for Avoidance or total Pregnancy-Related Anxiety scores ($p > 0.05$).

Table 1. Distribution of Responses to the Questions "Where Did You Learn About the Covid-19 Vaccine and Covid-19?" and "Which of These Sources Do You Trust the Most?"

Where Did You Learn About the Covid-19 Vaccine and Covid-19?	n (%)
Television	330 (65.3)
Newspaper	40 (7.9)
Radio	19 (3.8)
Social media	228 (45.1)
Internet	251 (49.7)
Doctor	193 (38.2)
Healthcare professionals	194 (38.4)
Family	104 (20.6)
Relatives and friends	86 (17.0)
Government institutions	33 (6.5)
Other	12 (2.4)
Which of These Sources Do You Trust the Most?	
Television	82 (17.3)
Social media	57 (12.0)
Internet	62 (13.1)
Doctor	120 (25.3)
Healthcare personnel	90 (18.9)
Family	14 (2.9)
Relatives and friends	12 (2.5)
Government institutions	8 (1.7)
Other	4 (0.8)
None	17 (3.6)
Myself	9 (1.9)

*Multiple choices could be selected.

Table 2. Comparison of Pregnancy-Related Anxiety Scale Scores Based on Chronic Illness in Family and COVID-19 Vaccination Status

Subscale	Group	Value*	z	p
Fear of Childbirth	Vaccinated, Chronic Yes	14.7 ± 4.3	-1.648	0.099
	Vaccinated, Chronic No	13.7 ± 4.4		
	Non-Vaccinated, Chronic Yes	13.4 ± 4.3	-0.130	0.897
	Non-Vaccinated, Chronic No	13.6 ± 4.7		
Body Image Concerns	Vaccinated, Chronic Yes	8.6 ± 2.8	-0.787	0.431
	Vaccinated, Chronic No	8.3 ± 2.5		
	Non-Vaccinated, Chronic Yes	9.0 ± 3.2	-2.203	0.028
	Non-Vaccinated, Chronic No	8.0 ± 2.5		
Attitudes Toward Childbirth	Vaccinated, Chronic Yes	8 (3-12)	-1.670	0.095
	Vaccinated, Chronic No	8 (3-12)		
	Non-Vaccinated, Chronic Yes	8 (3-12)	-0.155	0.877
	Non-Vaccinated, Chronic No	8 (3-12)		
Concerns About Motherhood	Vaccinated, Chronic Yes	5 (3-10)	-2.286	0.022
	Vaccinated, Chronic No	4 (3-12)		
	Non-Vaccinated, Chronic Yes	4 (3-12)	-0.797	0.426
	Non-Vaccinated, Chronic No	4 (3-12)		
Acceptance of Pregnancy	Vaccinated, Chronic Yes	4 (3-12)	-0.020	0.984
	Vaccinated, Chronic No	4 (3-12)		
	Non-Vaccinated, Chronic Yes	4 (3-12)	-0.837	0.403
	Non-Vaccinated, Chronic No	4 (3-12)		
Anxiety Symptoms	Vaccinated, Chronic Yes	7.5 (4-15)	-0.121	0.904
	Vaccinated, Chronic No	7 (4-15)		
	Non-Vaccinated, Chronic Yes	7 (4-16)	-0.984	0.325
	Non-Vaccinated, Chronic No	7 (4-15)		
Attitudes Toward Healthcare Personnel	Vaccinated, Chronic Yes	6 (3-12)	-0.217	0.828
	Vaccinated, Chronic No	6 (3-12)		
	Non-Vaccinated, Chronic Yes	6 (3-12)	-1.985	0.047
	Non-Vaccinated, Chronic No	7 (3-12)		
Avoidance	Vaccinated, Chronic Yes	5 (3-11)	-1.241	0.215
	Vaccinated, Chronic No	4 (3-12)		
	Non-Vaccinated, Chronic Yes	3 (3-12)	-0.457	0.648
	Non-Vaccinated, Chronic No	4 (3-12)		
Concerns About Baby	Vaccinated, Chronic Yes	6 (3-12)	-0.559	0.576
	Vaccinated, Chronic No	6 (3-12)		
	Non-Vaccinated, Chronic Yes	5 (3-12)	-2.011	0.044
	Non-Vaccinated, Chronic No	6 (3-12)		
Total Pregnancy-Related Anxiety Score	Vaccinated, Chronic Yes	66.30 ± 11.36	-1.045	0.296
	Vaccinated, Chronic No	64.36 ± 11.79		
	Non-Vaccinated, Chronic Yes	63.73 ± 14.47	-0.407	0.684
	Non-Vaccinated, Chronic No	63.11 ± 13.02		

Notes: *Numeric variables were presented as median (minimum-maximum) or mean ± SD. Mann-Whitney U Test was used to compare groups. Statistically significant p-values (≤ 0.05) are highlighted.

In unvaccinated women, family history of chronic disease was associated with significant differences in “Body Image Concerns” ($p=0.028$), “Attitudes Toward Medical Staff” ($p=0.047$), and “Concerns About the Baby” ($p=0.048$). “Body Image Concerns” scores were higher in those with a family history (9.0 vs. 8.0), whereas “Attitudes Toward Medical Staff” and “Concerns About the Baby” were higher in those without a family history (Table 2).

Differences Based on Education Level

Across all participants, education level was significantly associated with “Concerns About Childbirth” ($p=0.001$), “Concerns About Motherhood” ($p=0.009$), and “Acceptance of Pregnancy” ($p<0.001$). “Concerns About Childbirth” scores increased with education: primary school 12.0; middle school 12.0 high school 14.0; university 14.0; postgraduate 14.0. “Concerns About Motherhood”

Table 3. Comparison of Pregnancy-Related Anxiety Scale Scores According to Education Level in Individuals with the Covid-19 Vaccinated and Non-Vaccinated

	Covid-19 Vaccinated			
Pregnancy-Related Anxiety Scale & Sub-Dimensions	Education Level	Value*	χ²	p
Attitudes Towards Childbirth	Primary School	8.0 (3-12)	χ²=10.204	0.037
	Middle School	9.0 (3-15)		
	High School	7.0 (3-12)		
	University	8.0 (3-15)		
	Postgraduate & above	8.0 (3-12)		
Concerns About Motherhood	Primary School	3.0 (2-9)	χ²=11.026	0.026
	Middle School	4.0 (2-12)		
	High School	4.0 (2-12)		
	University	6.0 (2-13)		
	Postgraduate & above	6.0 (2-13)		
Acceptance of Pregnancy	Primary School	6.0 (3-12)	χ²=15.092	0.005
	Middle School	5.0 (3-12)		
	High School	4.0 (3-12)		
	University	4.0 (2-10)		
	Postgraduate & above	3.0 (3-8)		
	Non-Vaccinated			
Pregnancy-Related Anxiety Scale & Sub-Dimensions	Education Level	Value*	χ²	p
Concerns About Childbirth	Primary School	12.0 (6-17)	χ²=15.892	0.003
	Middle School	12.0 (6-22)		
	High School	14.0 (6-24)		
	University	14.0 (6-24)		
	Covid-19 Vaccinated			
Pregnancy-Related Anxiety Scale & Sub-Dimensions	Education Level	Value*	χ²	p
	Postgraduate &above	14.0 (7-18)	χ²=12.348	0.015
Concerns About Motherhood	Primary School	4.0 (3-9)		
	Middle School	4.0 (3-12)		
	High School	4.0 (3-12)		
	University	4.0 (3-12)		
	Postgraduate & above	3.0 (3-6)	χ²=16.380	0.003
Acceptance of Pregnancy	Primary School	6.0 (3-12)		
	Middle School	5.0 (3-12)		
	High School	4.0 (2-12)		
	University	4.0 (2-12)		
	Postgraduate & above	5.0 (3-9)	χ²=10.684	0.030
Attitudes Towards Medical Personnel	Primary School	8.0 (3-12)		
	Middle School	6.0 (3-12)		
	High School	6.0 (3-12)		
	University	6.0 (3-12)		
	Postgraduate & above	9.0 (3-11)		

Notes: *Numeric variables were presented as median (minimum-maximum) or mean $\pm$ SD. χ^2 : Kruskal-Wallis Test Statistic, Different letters indicate significant differences at $p<0.05$.

were highest among university graduates and lowest among middle school graduates. Among vaccinated women, "Acceptance of Pregnancy" scores tended to decrease with higher education levels (6.0 for primary school and 3.0 for postgraduate).

Among vaccinated women, education level significantly affected "Attitudes Toward Childbirth" ($p=0.036$), "Concerns About Motherhood" ($p=0.021$), and "Acceptance of Pregnancy" ($p=0.006$). For "Attitudes Toward Childbirth," scores ranged from

8.0 (primary) to 8.0 (postgraduate). “Concerns About Motherhood” were highest in postgraduates, lowest in middle school graduates. “Acceptance of Pregnancy” ranged from 6.0 (primary) to 3.0 (postgraduate).

Among unvaccinated women, education level influenced “Concerns About Childbirth” ($p=0.003$), “Concerns About Motherhood” ($p=0.019$), “Acceptance of Pregnancy” ($p=0.004$), and “Attitudes Toward Medical Staff” ($p=0.032$). “Concerns About Childbirth” ranged from 12.0 (primary) to 14.0 (university). “Concerns About Motherhood” were highest in university graduates, lowest in postgraduates. “Acceptance of Pregnancy” scores ranged from 6.0 (primary) to 4.0 (university). “Attitudes Toward Medical Staff” were highest in postgraduates and lowest in middle school graduates (Table 3).

Univariate Analysis of Risk Factors for Pregnancy-Related Anxiety

Univariate logistic regression identified gestational age ($p=0.035$), belief that the vaccine may cause preterm birth ($p=0.026$), total IES-R score ($p<0.001$), STAI-State score ($p<0.001$) and STAI-Trait

score ($p<0.001$) as significant predictors of Pregnancy-Related Anxiety Scale (PRAS) scores.

Each one-unit increase in gestational age decreased the risk of high pregnancy-related anxiety by 0.976. Belief that the vaccine could cause preterm birth increased the risk 1.699 times. Each one-point increase in IES-R score raised the risk by 1.052 times; STAI-State score by 1.119 times; and STAI-Trait score by 1.177 times (Table 4). Higher IES-R, STAI-State, and STAI-Trait scores were independently associated with increased risk of pregnancy-related anxiety (all $p<0.01$).

Multivariate Analysis of Risk Factors for Pregnancy-Related Anxiety

Variables significant in univariate analysis—gestational age, perceived risk of vaccine-related preterm birth, total IES-R score, STAI-State, and STAI-Trait scores—were entered into multivariate logistic regression. Gestational age ($p=0.023$), total IES-R score ($p<0.001$), STAI-State score ($p=0.002$) and STAI-Trait score ($p<0.001$) remained significant predictors.

Table 4. Univariate and Multivariate Logistic Regression Analysis of Factors Affecting Pregnancy-Related Anxiety Scale

Variables (Reference)		Univariate				Multivariate			
		p value	OR	95% CI		p value	OR	95% CI	
				Lower Limit	Upper Limit			Lower Limit	Upper Limit
Age		0.252	1.027	0.981	1.074				
Gestational Week		0.035	0.976	0.954	0.998	0.023	0.970	0.944	0.996
BMI		0.313	0.974	0.925	1.025				
Education Level (primary education)	High School	0.649	1.165	0.603	2,250				
	Bachelor's or higher	0.140	1.594	0.858	2,962				
Chronic Illness in the Family (Absent)	Present	0.174	1.390	0.864	2,234				
COVID-19 Diagnosis Before Pregnancy (No)	Yes	0.877	1.036	0.658	1,632				
COVID-19 in the Family (No)	Yes	0.769	1.071	0.677	1,694				
COVID-19 Vaccination During Pregnancy (No)	Yes	0.376	1.223	0.783	1,910				
Vaccine May Harm the Body (No)	Yes	0.529	1.163	0.727	1,860				
Vaccine Causes COVID-19 (No)	Yes	0.681	1.098	0.703	1,716				
Vaccine May Cause Fetal Anomalies (No)	Yes	0.056	1.594	0.988	2,572				
Vaccine May Cause Developmental Delay in Baby (No)	Yes	0.073	1.537	0.960	2,461				
Vaccine May Cause Preterm Birth (No)	Yes	0.026	1.699	1.064	2,713				
Impact of Events Scale (IES-R) Total Score		<0.001	1.052	1.036	1.069	<0.001	1.033	1.015	1.052
Spielberger State Anxiety Inventory Score		<0.001	1.119	1.085	1.153	0.002	1.060	1.022	1.099
Spielberger Trait Anxiety Inventory Score		<0.001	1.177	1.133	1.224	<0.001	1.130	1.081	1.180

Note: β = Regression Coefficient, SE = Standard Error, OR = Odds Ratio, CI = Confidence Interval. Statistically significant p-values (≤ 0.05) are highlighted.

In the multivariate model, each one-unit increase in gestational age reduced the likelihood of high pregnancy-related anxiety by 0.970 times. Each one-point increase in IES-R score increased the risk by 1.033 times; STAI-State score by 1.060 times; and STAI-Trait score by 1.130 times (Table 4).

DISCUSSION

This study investigated the differences in anxiety levels between vaccinated and unvaccinated pregnant women during the COVID-19 pandemic, highlighting the interplay between vaccination decisions, psychological well-being, and sociocultural influences. The findings suggest that pregnancy-related anxiety levels are associated with vaccination decisions, which are influenced by information sources as well as psychological and social factors (12).

The results revealed that vaccinated pregnant women exhibited higher overall pregnancy-related anxiety scores compared to their unvaccinated counterparts. Notably, higher scores on the subscales "Concerns About Motherhood" and "Concerns About the Baby" suggest that vaccine hesitancy persists and vaccination alone does not alleviate anxiety. This aligns with the previous findings that vaccinated individuals experience heightened concerns about potential risk to their babies (13).

The study also employed the IES-R scale to assess PTSD symptoms during the pandemic. While no significant differences in total IES-R scores were observed based on vaccination status, participants with a family history of chronic diseases demonstrated higher scores on the re-experiencing subscale. This finding suggests that a family history of chronic illness may amplify the psychological impact of the pandemic, potentially exacerbating PTSD-related symptoms (14).

Education levels significantly influenced anxiety levels among pregnant women in this study. Higher education levels were associated with higher anxiety scores, particularly among vaccinated participants, aligning with the previous findings correlating education level and anxiety (15, 16). The anxiety scores among vaccinated participants with higher-level education decreased post-vaccination. Conversely, unvaccinated participants exhibited higher anxiety scores as their education levels increased.

Misinformation was identified as a major contributor to vaccine hesitancy. This finding is in line with the previous works that correlate the use of social media with anxiety (17, 18, 19). The proliferation of inaccurate information on digital platforms likely exacerbates concerns about vaccine safety, further fueling hesitancy.

The increased psychological burden experienced in pregnancy during the pandemic appears to contribute to elevated anxiety levels and increased vaccine hesitancy. Integrating psychological support programs into prenatal care may help reduce pregnancy-related anxiety and increase vaccine acceptance, ultimately improving maternal and fetal health outcomes (14, 20).

Despite important findings, the study also has some limitations. Firstly, the cross-sectional design limits its ability to establish causality. Secondly, while associations between vaccination status and anxiety levels were identified, the temporal relationship remains unclear. A longitudinal design could better clarify these dynamics. Additionally, the single-center population may restrict generalizability. The findings may not represent broader populations with different sociodemographic or healthcare access characteristics. To enhance the applicability of these findings, future research should involve multicenter studies with diverse populations.

CONCLUSION

This study highlights that differences in anxiety levels between vaccinated and unvaccinated pregnant women are influenced by factors such as family history of chronic disease and education level. Addressing vaccine hesitancy requires a multifaceted approach, including enhancing access to accurate information and implementing psychological support programs during prenatal care. Developing effective communication techniques on social media and other information resources is crucial to mitigating the negative impact of anxiety among pregnant women.

REFERENCES

1. Comparcini D, Tomietto M, Pastore F, Nichol B, Miniscalco D, Flacco ME, et al. Factors Influencing COVID-19 Vaccine Hesitancy in Pregnant and Breastfeeding/Puerperium Women: A Cross-Sectional Study. *Vaccines (Basel)*. 2024;12(7).
2. Saccone G, Florio A, Aiello F, Venturella R, De Angelis MC, Locci M, et al. Psychological impact of coronavirus disease 2019 in pregnant women. *Am J Obstet Gynecol*. 2020;223(2):293-5.
3. Dey A, Chozhavel Rajanathan TM, Chandra H, Pericherla HPR, Kumar S, Choonia HS, et al. Immunogenic potential of DNA vaccine candidate, ZyCoV-D against SARS-CoV-2 in animal models. *Vaccine*. 2021;39(30):4108-16.
4. Vilca LM, Cesari E, Tura AM, Di Stefano A, Vidiri A, Cavaliere AF, et al. Barriers and facilitators regarding influenza and pertussis maternal vaccination uptake: A multi-center survey of pregnant women in Italy. *Eur J Obstet Gynecol Reprod Biol*. 2020;247:10-5.
5. Murphy J, Vallières F, Bentall RP, Shevlin M, McBride O, Hartman TK, et al. Psychological characteristics associated with COVID-19 vaccine hesitancy and resistance in Ireland and the United Kingdom. *Nat Commun*. 2021;12(1):29.
6. D'Alessandro A, Napolitano F, D'Ambrosio A, Angelillo IF. Vaccination knowledge and acceptability among pregnant women in Italy. *Hum Vaccin Immunother*. 2018;14(7):1573-9.

7. Laenen J, Roelants M, Devlieger R, Vandermeulen C. Influenza and pertussis vaccination coverage in pregnant women. *Vaccine*. 2015;33(18):2125-31.
8. Schaal NK, Zöllkau J, Hepp P, Fehm T, Hagenbeck C. Pregnant and breastfeeding women's attitudes and fears regarding the COVID-19 vaccination. *Arch Gynecol Obstet*. 2022;306(2):365-72.
9. Şolt A, Gül DK. Pregnancy-related Anxiety Scale (The PrAS): Validity and reliability study of its Turkish version. *Celal Bayar Üniversitesi Sağlık Bilimleri Enstitüsü Dergisi*. 2020;7(4):529-37.
10. Çorapçıoğlu A, Yargic I, Geyran P, Kocabasoglu N. Validity and Reliability of Turkish Version of "Impact of Event Scale-Revised" (IES-R). *Yeni Symposium*. 2006;44:14-22.
11. Sakaoğlu HH, Orbatu D, Emiroglu M, Çakır Ö. Spielberger state and trait anxiety level in healthcare professionals during the Covid-19 outbreak: A case of Tepecik hospital. *The Journal of Tepecik Education and Research Hospital*. 2020;30(2):1-9.
12. Jamieson DJ, Rasmussen SA. Protecting Pregnant Women and Their Infants From COVID-19: Clues From Maternal Viral Loads, Antibody Responses, and Placentas. *JAMA network open*. 2020;3(12):e2030564-e.
13. Alkhalifah M, AlHusseini N, McGhee J. COVID-19 Vaccine Hesitancy Among Pregnant Women. *Cureus*. 2023;15(6):e41126.
14. Touré AA, Camara LM, Magassouba AS, Doumbouya A, Camara G, Camara AY, et al. Psychosocial impacts of COVID-19 in the Guinean population. An online cross-sectional survey. *PLoS One*. 2021;16(2):e0245751.
15. Castillo E, Patey A, MacDonald N. Vaccination in pregnancy: Challenges and evidence-based solutions. *Best Pract Res Clin Obstet Gynaecol*. 2021;76:83-95.
16. Kaplan S, Koç A, Atasoy E, Alaca C, Altun E, Öztürk Ö. Gebe Kadınlarda COVID-19 Korkusu ve Prenatal Stresin COVID-19 Aşı Kabulü Üzerine Etkisinin İncelenmesi. *Ankara Sağlık Bilimleri Dergisi*. 2024;13(1):1-13.
17. Jones E, Neely E. COVID-19 vaccination in pregnancy: ambiguity in decision-making. *Health Promot Int*. 2023;38(6).
18. Kalok A, Razak Dali W, Sharip S, Abdullah B, Kamarudin M, Dasrilsyah RA, et al. Maternal COVID-19 vaccine acceptance among Malaysian pregnant women: A multicenter cross-sectional study. *Front Public Health*. 2023;11:1092724.
19. Waring ME, Pagoto SL, Rudin LR, Ho C, Horkachuck A, Kapoor IA, et al. Factors associated with mothers' hesitancy to receive a COVID-19 vaccine. *J Behav Med*. 2023;46(1-2):179-84.
20. Badell ML, Dude CM, Rasmussen SA, Jamieson DJ. Covid-19 vaccination in pregnancy. *Bmj*. 2022;378:e069741.

Comparison of Four Cervical Ripening and Labor Induction Strategies in Term Singleton Pregnancies with an Unfavorable Cervix: A Retrospective Cohort Study

Elverişsiz Serviksi Olan Term Tekil Gebeliklerde Dört Servikal Olgunlaştırma Ve Doğum İndüksiyonu Stratejisinin Karşılaştırılması: Retrospektif Kohort Çalışma

İD Cemal ÜNLÜ¹, İD Gonca TÜRKER ERGÜN², İD Özlem MORALOĞLU TEKİN²

¹Department of Obstetrics and Gynecology, Special Clinic, Kayseri, Türkiye

²Ankara Bilkent City Hospital, Department of Obstetrics and Gynecology, Ankara, Türkiye

ABSTRACT

Aim: To compare four cervical ripening and labor induction strategies in term singleton pregnancies with an unfavorable cervix with respect to vaginal delivery rate and induction-to-delivery interval.

Materials and Methods: This retrospective exploratory comparative cohort study was conducted at the Obstetrics Clinic of Ankara Bilkent City Hospital between November 2019 and September 2023. A total of 120 women at 37+0 to 42+0 weeks of gestation with singleton vertex pregnancies, cervical dilatation between 1 and 3 cm, and a Bishop score below 7 were included. Women were classified into four groups: manual cervical stretching with concomitant membrane sweeping alone, dinoprostone alone, immediate combination of the mechanical procedure and dinoprostone, and dinoprostone followed, when clinically indicated, by oxytocin augmentation as an escalation pathway. The primary outcome was vaginal delivery rate, and the main secondary outcome was the induction-to-vaginal-delivery interval among women who achieved vaginal birth.

Results: Vaginal delivery rate differed significantly among groups (53.3%, 76.7%, 80.0%, and 90.0%, respectively; $p=0.009$). In the whole cohort, the induction-to-delivery interval also differed significantly and was longest in Group 1 and shortest in Group 4 (31.2 ± 4.5 h, 28.5 ± 7.4 h, 26.3 ± 7.2 h, and 25.0 ± 4.8 h, respectively; $p<0.001$). Among women who delivered vaginally, the induction-to-vaginal-delivery interval remained significantly different ($p=0.005$). Cesarean delivery rates decreased progressively from Group 1 to Group 4. Apgar scores and postpartum pain scores were similar across groups.

Conclusion: In term singleton pregnancies with an unfavorable cervix, dinoprostone-containing strategies were associated with higher vaginal delivery rates than the mechanical-only approach. The highest vaginal delivery rate was observed in the group managed with oxytocin augmentation after dinoprostone; however, this group represented a clinically indicated escalation pathway rather than a pre-planned independent initial strategy, and this finding should be interpreted cautiously. The mechanical-only approach was associated with the longest induction-to-delivery interval.

Keywords: Labor, Induced; Cervical Ripening; Dinoprostone; Oxytocin; Term Birth

ÖZ

Amaç: Bu çalışmada, elverişsiz serviksi olan term tekil gebeliklerde kullanılan dört servikal olgunlaştırma ve doğum indüksiyonu stratejisinin vajinal doğum oranı ve doğum indüksiyonu-doğum aralığı açısından karşılaştırılması amaçlandı.

Gereç ve Yöntemler: Bu retrospektif keşifsel karşılaştırmalı kohort çalışması, Kasım 2019-Eylül 2023 tarihleri arasında Ankara Bilkent Şehir Hastanesi Obstetri Kliniğinde yürütüldü. Çalışmaya 37+0 ile 42+0 gebelik haftaları arasında, baş geliş, servikal dilatasyonu 1 cm ile 3 cm arasında ve Bishop skoru 7'nin altında olan 120 gebe dahil edildi. Olgular belge kayıtlarına göre dört gruba ayrıldı: yalnızca manuel servikal germe ve eş zamanlı membran sıyırma, yalnızca dinoproston, mekanik işlem sonrası hemen dinoproston ve klinik gereksinim halinde dinoproston sonrası oksitosin augmentasyonu şeklindeki bir eskalasyon yolu. Primer sonlanım vajinal doğum oranıydı. Ana sekonder sonlanım, vajinal doğum yapan kadınlarda doğum indüksiyonu-vajinal doğum aralığıydı.

Bulgular: Vajinal doğum oranı gruplar arasında anlamlı olarak farklıydı (%53,3; %76,7; %80,0; %90,0; $p=0,009$). Doğum indüksiyonu ile doğum arasındaki süre tüm kohortta anlamlı farklılık gösterdi ve en uzun süre Grup 1'de, en kısa süre Grup 4'te saptandı ($31,2\pm4,5$ saat; $28,5\pm7,4$ saat; $26,3\pm7,2$ saat; $25,0\pm4,8$ saat; $p<0,001$). Vajinal doğum yapan kadınlarda indüksiyon-vajinal doğum aralığı da anlamlı farklıydı ($p=0,005$). Sezaryen oranı Grup 1'den Grup 4'e doğru azaldı. Apgar skorları ve postpartum ağrı skorları açısından gruplar arasında anlamlı fark yoktu.

Sonuç: Elverişsiz serviksi olan term tekil gebeliklerde dinoproston içeren stratejiler, yalnızca mekanik yaklaşıma göre daha yüksek vajinal doğum oranları ile ilişkililiydi. En yüksek vajinal doğum oranı, dinoproston sonrası oksitosin augmentasyonu uygulanan grupta gözlemlendi; ancak bu grup, başlangıçtan planlanmış bağımsız bir stratejiden ziyade klinik gereksinim halinde uygulanan bir eskalasyon yolunu temsil etmekteydi ve bu bulgu temkinli yorumlanmalıdır. Yalnızca mekanik yaklaşım ise en uzun doğum indüksiyonu-doğum aralığı ile ilişkililiydi.

Anahtar Kelimeler: Doğum indüksiyonu; servikal olgunlaşma; dinoproston; oksitosin; term doğum

Cite as: Ünlü C, Türker Ergün G, Moraloğlu Tekin Ö. Comparison of Four Cervical Ripening and Labor Induction Strategies in Term Singleton Pregnancies with an Unfavorable Cervix: A Retrospective Cohort Study. Jinekoloji-Obstetrik ve Neonatoloji Tıp Dergisi 2026;23(2):168–173.

Geliş/Received: 02.04.2026 • Kabul/Accepted: 14.04.2026

Sorumlu Yazar/Corresponding Author: Cemal Ünlü, Department of Obstetrics and Gynecology, Special Clinic, Kayseri, Türkiye

E-mail: cunlu06@gmail.com

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

INTRODUCTION

Induction of labor is a key obstetric intervention when the maternal or fetal benefits of delivery outweigh the risks of continuing pregnancy (1). In women with an unfavorable cervix, the method and sequence of cervical ripening may influence both vaginal delivery rates and the induction-to-delivery interval (2). This issue is particularly relevant at term, where several accepted options exist but direct comparative evidence remains limited (1,2).

Membrane sweeping is a simple bedside procedure that may promote labor onset and reduce the need for formal induction, although systematic reviews suggest its effects on delivery mode are less consistent than its effects on spontaneous labor onset and pregnancy duration (3,4). Its role as a formal induction method has been studied less than its outpatient or serial use to prevent prolonged gestation. In the randomized trial by El-Torkey and Grant, sweeping increased spontaneous labor in prolonged pregnancy, but the primary endpoint was spontaneous labor rather than vaginal delivery (5). Similarly, trials by de Miranda et al. and Yildirim et al. mainly assessed serial or term sweeping to reduce post-term pregnancy and encourage spontaneous labor before inpatient induction was required (6,7).

Dinoprostone remains a widely used pharmacologic agent for cervical ripening at term. Meta-analyses and prospective studies support the effectiveness of controlled-release dinoprostone vaginal inserts, although vaginal delivery rates and time intervals vary according to cervical status, parity, and local protocols (8-10). Evidence on combining or sequencing dinoprostone with sweeping-based procedures is limited and inconsistent. One randomized study found no significant benefit of adjunctive sweeping on delivery timing or mode, whereas another reported higher spontaneous vaginal delivery rates and a shorter induction-to-delivery interval when sweeping was performed at the start of formal induction (11,12).

We therefore compared four routine cervical ripening and induction strategies in term singleton pregnancies with an unfavorable cervix: manual cervical stretching with concomitant membrane sweeping alone, dinoprostone alone, their immediate combination, and dinoprostone followed by oxytocin augmentation when clinically indicated. The primary outcome was vaginal delivery rate, and the main secondary outcome was the induction-to-vaginal-delivery interval among women who achieved vaginal birth.

MATERIALS AND METHODS

This retrospective exploratory comparative study was conducted at the Obstetrics Clinic of Ankara Bilkent City Hospital and included

women managed between November 2019 and September 2023. Ethical approval was obtained from the Ankara Bilkent City Hospital 1st Medical Research Scientific and Ethical Evaluation Board (TABED 1/178/2024, 08 May 2024). Individual informed consent was waived because de-identified archived records were reviewed retrospectively. The study complied with the Declaration of Helsinki.

Eligible women were aged ≥ 21 years and had singleton, vertex pregnancies at 37+0 to 42+0 weeks, cervical dilatation ≥ 1 cm and < 3 cm at admission, and a Bishop score < 7 . Gestational age was based on the last menstrual period and revised by first-trimester ultrasonography when discordant. Women with previous cesarean delivery, prior uterine surgery, grand multiparity, non-vertex presentation, ruptured membranes at admission, or any contraindication to vaginal birth were excluded.

Archived obstetric records and labor charts were reviewed retrospectively. Because of practical file-review constraints and the approved study plan, the sample was assembled as an exploratory comparative cohort rather than as a consecutive all-eligible series. Screening within each analytic group continued until 30 eligible women were identified, yielding 120 women in total. Thus, the study sample represented a non-consecutive, pragmatically assembled cohort rather than a randomly selected sample from a complete eligible population. This sampling approach should be considered when interpreting between-group comparability.

The induction approach in routine practice was chosen by the treating team and was not randomized. Women were classified retrospectively into four analytic groups according to the documented intervention sequence: Group 1, manual cervical stretching with concomitant membrane sweeping alone; Group 2, controlled-release dinoprostone vaginal insert (Propess®, 10 mg dinoprostone [prostaglandin E2]) alone, without subsequent oxytocin augmentation; Group 3, manual cervical stretching with concomitant membrane sweeping followed immediately by dinoprostone during the same examination; and Group 4, dinoprostone followed by oxytocin augmentation after dinoprostone removal when adequate spontaneous uterine contractions did not develop. Group 4 was therefore a retrospectively defined escalation pathway rather than a pre-planned initial strategy. Records with other intervention sequences were excluded, including manual cervical stretching with concomitant membrane sweeping plus dinoprostone followed by oxytocin augmentation.

In Groups 1 and 3, the mechanical procedure was performed during vaginal examination as part of routine institutional practice. The examining finger was introduced into the cervical canal and gentle but firm digital pressure was applied to stretch the cervix.

When the internal os could be traversed, the inferior pole of the fetal membranes was circumferentially separated from the lower uterine segment using a circular sweeping motion. Because of the retrospective design, formal operator-level standardization could not be assessed; however, cases were classified only when the documented procedure was consistent with this institutional approach.

In Groups 2, 3, and 4, dinoprostone was administered as a controlled-release vaginal insert. In Group 3, the insert was placed immediately after the mechanical procedure. In Group 4, oxytocin augmentation was considered only after dinoprostone removal and a waiting interval of at least 30 minutes. Oxytocin was started in women who had not entered spontaneous labor and had not developed an adequate uterine contraction pattern, defined as 3–4 contractions in 10 minutes. Dinoprostone and oxytocin were not used concurrently.

Collected variables were maternal age, body mass index, gravida, parity, previous vaginal births, gestational age at admission, indication for induction, Bishop score at admission, duration of dinoprostone exposure, duration of oxytocin exposure, mode of delivery, time from induction initiation to delivery, cesarean indication, 1- and 5-minute Apgar scores, and postpartum visual analog scale pain score.

The primary outcome was vaginal delivery rate. The main secondary outcome was the interval from induction initiation to vaginal delivery among women who achieved vaginal birth. Additional secondary outcomes were the overall induction-to-delivery interval in the full cohort, cesarean delivery rate, cesarean indications, Apgar scores, postpartum pain score, and duration of dinoprostone and oxytocin exposure.

Induction initiation was defined as the time of the first cervical ripening or induction intervention. In Group 3 it was the time

of the mechanical procedure, and in Group 4 it was the time of dinoprostone insertion rather than oxytocin initiation.

Continuous variables were summarized as mean $\pm$ standard deviation and categorical variables as number and percentage. Categorical variables were compared using Pearson chi-square or Fisher's exact test, and baseline continuous variables using one-way analysis of variance. Because variance homogeneity was not present for delivery interval outcomes, Welch analysis of variance was used for induction-to-delivery comparisons. Kruskal-Wallis testing was used for Apgar and postpartum pain scores. When overall comparisons were significant, exploratory pairwise comparisons were performed with Welch t tests and Holm correction. All tests were two-sided, and $p < 0.05$ was considered statistically significant. Analyses were performed with Python 3.13 using pandas, SciPy, and statsmodels.

RESULTS

A total of 120 women met the study criteria and were analyzed, with 30 women in each group. No included record had missing data for the primary outcome or the induction-to-delivery interval. Baseline maternal and obstetric characteristics were comparable across groups, with no significant differences in age, body mass index, parity-related variables, gestational age, or admission Bishop score (Table 1). Indications for induction were also similar, and post-term pregnancy was the most common indication in all groups (Table 3).

The primary outcome, vaginal delivery rate, differed significantly among the four strategies ($p = 0.009$). Vaginal delivery occurred in 53.3% of women in Group 1, 76.7% in Group 2, 80.0% in Group 3, and 90.0% in Group 4 (Table 2). Exploratory pairwise analysis showed that the main difference was between Groups 1 and 4 and remained significant after Holm correction.

Table 1. Baseline maternal and obstetric characteristics

Characteristic	Group 1	Group 2	Group 3	Group 4	p
Age, years	30.6 $\pm$ 6.4	30.7 $\pm$ 6.5	30.4 $\pm$ 6.7	30.3 $\pm$ 6.9	0.996
Body mass index, kg/m ²	25.5 $\pm$ 4.2	24.7 $\pm$ 4.1	24.8 $\pm$ 4.1	24.3 $\pm$ 4.0	0.727
Gravida	1.2 $\pm$ 0.6	1.3 $\pm$ 0.6	1.4 $\pm$ 0.9	1.3 $\pm$ 0.7	0.793
Previous vaginal births, n	0.2 $\pm$ 0.5	0.3 $\pm$ 0.6	0.4 $\pm$ 0.9	0.3 $\pm$ 0.7	0.689
Gestational age at admission, weeks	40.1 $\pm$ 1.5	39.7 $\pm$ 1.3	39.5 $\pm$ 1.3	39.6 $\pm$ 1.2	0.325
Admission Bishop score	3.7 $\pm$ 1.1	3.3 $\pm$ 1.2	3.3 $\pm$ 1.1	3.1 $\pm$ 1.1	0.256
Nulliparous, n (%)	25 (83.3)	24 (80.0)	22 (73.3)	23 (76.7)	0.806
Previous vaginal birth, n (%)	5 (16.7)	6 (20.0)	8 (26.7)	7 (23.3)	0.806

Notes: Data are presented as mean $\pm$ standard deviation or n (%). Group comparisons were performed with one-way analysis of variance for continuous variables and the chi-square test for categorical variables.

In the full cohort, the induction-to-delivery interval differed significantly across groups (Welch $p<0.001$). The mean interval was longest in Group 1 (31.2 ± 4.5 h), intermediate in Groups 2 and 3 (28.5 ± 7.4 h and 26.3 ± 7.2 h), and shortest in Group 4 (25.0 ± 4.8 h) (Table 2). Exploratory post hoc testing suggested that this difference was mainly attributable to the longer interval in Group 1 than in Groups 3 and 4.

Among women who achieved vaginal birth, the induction-to-vaginal-delivery interval also differed significantly (Welch $p=0.005$): 31.1 ± 4.6 h in Group 1, 27.7 ± 6.6 h in Group 2, 26.8 ± 7.5 h in Group 3, and 25.3 ± 5.0 h in Group 4 (Table 2). After Holm correction, the clearest pairwise difference remained between Groups 1 and 4.

Neonatal condition at birth, Apgar scores, and postpartum pain scores were similar across groups ($p=0.732$, $p=0.870$, and $p=0.240$, respectively). Among dinoprostone-treated groups, mean dinoprostone exposure duration did not differ significantly ($p=0.105$), whereas mean oxytocin exposure duration in Group 4 was 10.3 ± 4.2 h (Table 2).

Cesarean delivery rates decreased progressively from 46.7% in Group 1 to 10.0% in Group 4 (Table 2). The most frequent cesarean indication in all groups was cephalopelvic disproportion or arrest of progress, especially in Group 1, while fetal distress accounted for a minority of cesarean deliveries (Table 4).

Table 2. Induction characteristics and study outcomes

Outcome	Group 1	Group 2	Group 3	Group 4	p
Vaginal delivery, n (%)	16 (53.3)	23 (76.7)	24 (80.0)	27 (90.0)	0.009
Cesarean delivery, n (%)	14 (46.7)	7 (23.3)	6 (20.0)	3 (10.0)	0.009
Induction-to-delivery interval, h (entire cohort)	31.2 ± 4.5	28.5 ± 7.4	26.3 ± 7.2	25.0 ± 4.8	<0.001
Induction-to-vaginal-delivery interval, h*	31.1 ± 4.6	27.7 ± 6.6	26.8 ± 7.5	25.3 ± 5.0	0.005
1-minute Apgar score	7.7 ± 1.4	7.6 ± 1.4	7.6 ± 1.4	7.4 ± 1.3	0.732
5-minute Apgar score	9.3 ± 0.8	9.3 ± 0.8	9.4 ± 0.8	9.2 ± 1.0	0.870
Postpartum VAS score	6.1 ± 2.3	4.9 ± 1.3	5.0 ± 1.3	5.2 ± 1.9	0.240
Dinoprostone exposure, h†	-	14.3 ± 3.7	12.4 ± 3.7	12.7 ± 2.5	0.105
Oxytocin exposure, h‡	-	-	-	10.3 ± 4.2	-

Notes: Data are presented as mean $\pm$ standard deviation or n (%). Delivery interval outcomes were compared using Welch analysis of variance. Apgar and postpartum VAS scores were compared using the Kruskal-Wallis test. *Calculated among women who achieved vaginal delivery. †Compared among Groups 2–4 only. ‡Available only in Group 4. VAS, visual analog scale.

Table 3. Indications for labor induction, n (%)

Indication	Group 1	Group 2	Group 3	Group 4
Post-term pregnancy	19 (63.3)	19 (63.3)	17 (56.7)	19 (63.3)
IUGR	3 (10.0)	2 (6.7)	5 (16.7)	3 (10.0)
Oligohydramnios	3 (10.0)	4 (13.3)	4 (13.3)	3 (10.0)
Hypertension	2 (6.7)	2 (6.7)	2 (6.7)	2 (6.7)
Polyhydramnios	2 (6.7)	2 (6.7)	1 (3.3)	3 (10.0)
Gestational diabetes	1 (3.3)	1 (3.3)	1 (3.3)	0 (0.0)

Notes: Values are n (%). Percentages are column percentages within each group. The overall distribution of induction indications did not differ significantly between groups (chi-square $p=0.998$). IUGR, intrauterine growth restriction.

Table 4. Indications for cesarean delivery, n (%)

Cesarean indication	Group 1	Group 2	Group 3	Group 4
Cephalopelvic disproportion / arrest of progress	13 (92.9)	5 (71.4)	4 (66.7)	1 (33.3)
Fetal distress	1 (7.1)	2 (28.6)	2 (33.3)	2 (66.7)
Total cesarean deliveries, n	14	7	6	3

Notes: Values are n (%), with percentages calculated among cesarean deliveries within each group.

DISCUSSION

In this retrospective cohort of term singleton pregnancies with an unfavorable cervix, vaginal delivery rates differed significantly across the four induction strategies, being lowest in the mechanical-only group and highest in the dinoprostone-to-oxytocin escalation pathway. Both the overall induction-to-delivery interval and the induction-to-vaginal-delivery interval were longest in the mechanical-only group, whereas neonatal Apgar scores and postpartum pain scores were similar across groups. The main observed between-group differences concerned delivery success and timing rather than short-term neonatal condition.

These findings should be interpreted in the context of the membrane sweeping literature. Systematic reviews suggest that membrane sweeping may reduce formal induction and shorten pregnancy duration, but they have not shown a consistent benefit for delivery mode outcomes (3,4). Most sweeping studies were also not designed around inpatient induction success. The trial by El-Torkey and Grant evaluated sweeping as a direct induction maneuver in prolonged pregnancy, but its primary endpoint was spontaneous labor rather than vaginal delivery (5). In contrast, the trials by de Miranda et al. and Yildirim et al. mainly assessed serial sweeping in low-risk term pregnancies and reported reductions in post-term pregnancy or prolonged gestation rather than direct comparisons of inpatient induction success (6,7). In our cohort, the mechanical-only group comprised women already admitted for formal induction with an unfavorable cervix; vaginal delivery occurred in 53.3% and the mean time to vaginal birth was 31.1 h. Differences in setting and endpoint likely explain why our findings should not be viewed as a direct contradiction of earlier sweeping trials.

The dinoprostone-containing groups showed vaginal delivery rates of 76.7% to 90.0%, broadly consistent with previous reports using controlled-release dinoprostone inserts (8-10). Our dinoprostone-alone group achieved a somewhat higher vaginal delivery rate than some previous studies, which may reflect more favorable baseline cervical status because our inclusion criteria allowed Bishop scores below 7.

The comparison between Group 2 and Group 3 is also informative. Adding the sweeping-based mechanical procedure before dinoprostone was associated with a slightly higher vaginal delivery rate and a slightly shorter time to vaginal birth than dinoprostone alone, although the difference was modest. This differs from the randomized trial by Bhatia et al., in which adjunctive sweeping with dinoprostone did not significantly improve labor duration or delivery mode (11). Our findings are more directionally aligned with Tan et

al., who reported that membrane sweeping at the start of formal induction increased spontaneous vaginal delivery and shortened the induction-to-delivery interval (12). Together, these data suggest that any benefit from adding a sweeping-based maneuver may depend on technique, timing, background ripening protocol, and study population.

Group 4 should be interpreted as a clinically indicated escalation pathway rather than a pre-planned independent initial strategy, because oxytocin was added only after dinoprostone when spontaneous labor and adequate contractions had not developed. Within this escalation pathway, the highest vaginal delivery rate was observed. These findings may be compatible with a potential benefit of stepwise escalation when initial pharmacologic ripening alone is insufficient; however, this interpretation should remain cautious because the comparison was retrospective, non-randomized, and potentially affected by confounding by indication. The absence of clearly worse short-term neonatal outcomes in this group is nevertheless reassuring, but should not be interpreted as proof of superiority. Our sequential, rather than concurrent, use of dinoprostone and oxytocin also accords with prescribing guidance.

This study has several limitations. Its retrospective single-center design limited control of confounding and precluded causal inference. In addition, the sample was a non-consecutive, pragmatically assembled exploratory cohort with 30 women per group rather than a consecutive all-eligible series; therefore, selection bias cannot be excluded. Screening stopped once 30 eligible women had been identified in each group, no random selection from a complete eligible population was performed, and the total number of potentially eligible women was unavailable. Treatment allocation reflected routine clinical practice rather than randomization. Group 4 was a retrospectively defined escalation pathway among women initially managed with dinoprostone, which may have reduced between-group comparability and introduced confounding by indication. The sweeping-based mechanical procedure was operator dependent, and the retrospective dataset did not allow formal assessment of inter-operator variability or procedural standardization, which may limit reproducibility. We also lacked analyzable data on tachysystole, epidural analgesia, serial cervical change, and the clinical reasoning underlying treatment choice and escalation. Postpartum pain scores may likewise have been influenced by delivery mode and analgesic use, variables that could not be adequately adjusted for.

The study also has strengths. It compared four explicitly defined real-world intervention pathways within the same institution and time frame, applied consistent inclusion and exclusion criteria, and

evaluated a clinically meaningful outcome often underemphasized in induction studies: time to vaginal birth among women who achieved vaginal delivery. The explicit definition of induction start time also reduced ambiguity in the combined and escalation groups. These features make the findings useful for hypothesis generation and for informing the design of future prospective studies.

CONCLUSION

In term singleton pregnancies with an unfavorable cervix, dinoprostone-containing strategies were associated with higher vaginal delivery rates than the mechanical-only approach in this retrospective cohort. The highest vaginal delivery rate was observed in the group managed with oxytocin augmentation after dinoprostone; however, this group represented a clinically indicated escalation pathway rather than a pre-planned independent initial strategy. Accordingly, this finding should be interpreted as hypothesis-generating rather than as evidence of superiority. The mechanical-only approach was associated with the longest induction-to-delivery interval. Prospective comparative studies are needed.

Author Contributions: All authors contributed to the conception and design of the study. All authors participated in data collection, data curation, investigation, and interpretation of the findings. The manuscript was drafted and critically revised by all authors. All authors read and approved the final version of the manuscript.

Funding: No external funding was received for this study.

Conflict of Interest: The authors declare that they have no conflict of interest.

REFERENCES

1. World Health Organization. WHO recommendations on induction of labour, at or beyond term. Geneva: World Health Organization; 2022.
2. National Institute for Health and Care Excellence. Inducing labour. NICE guideline NG207. London: NICE; 2021.
3. Finucane EM, Murphy DJ, Biesty LM, Gyte GML, Cotter AM, Ryan EM, et al. Membrane sweeping for induction of labour. *Cochrane Database Syst Rev*. 2020;2(2):CD000451. doi:10.1002/14651858.CD000451.pub3.
4. Boulvain M, Irion O, Marcoux S, Fraser W. Sweeping of the membranes to prevent post-term pregnancy and to induce labour: a systematic review. *Br J Obstet Gynaecol*. 1999;106(5):481-485. doi:10.1111/j.1471-0528.1999.tb08302.x.
5. El-Torkey M, Grant JM. Sweeping of the membranes is an effective method of induction of labour in prolonged pregnancy: a report of a randomized trial. *Br J Obstet Gynaecol*. 1992;99(6):455-458. doi:10.1111/j.1471-0528.1992.tb13780.x.
6. de Miranda E, van der Bom JG, Bonsel GJ, Bleker OP, Rosendaal FR. Membrane sweeping and prevention of post-term pregnancy in low-risk pregnancies: a randomised controlled trial. *BJOG*. 2006;113(4):402-408. doi:10.1111/j.1471-0528.2006.00870.x.
7. Yildirim G, Güngördük K, Karadağ OI, Aslan H, Turhan E, Ceylan Y. Membrane sweeping to induce labor in low-risk patients at term pregnancy: a randomised controlled trial. *J Matern Fetal Neonatal Med*. 2010;23(7):681-687. doi:10.3109/14767050903387078.
8. Hughes EG, Kelly AJ, Kavanagh J. Dinoprostone vaginal insert for cervical ripening and labor induction: a meta-analysis. *Obstet Gynecol*. 2001;97(5 Pt 2):847-855. doi:10.1016/S0029-7844(00)01216-3.
9. Triglia MT, Palamara F, Lojacono A, Prefumo F, Frusca T. A randomized controlled trial of 24-hour vaginal dinoprostone pessary compared to gel for induction of labor in term pregnancies with a Bishop score ≤ 4 . *Acta Obstet Gynecol Scand*. 2010;89(5):651-657. doi:10.3109/00016340903575998.
10. Anh ND, Duc TA, Ha NT, Giang DT, Dat DT, Thuong PH, et al. Dinoprostone vaginal insert for induction of labor in women with low-risk pregnancies: a prospective study. *Med Arch*. 2022;76(1):39-44. doi:10.5455/medarh.2022.76.39-44.
11. Bhatia A, Teo PL, Li M, Lee JYB, Chan MXJ, Yeo TW, et al. Dinoprostone vaginal insert (DVI) versus adjunctive sweeping of membranes and DVI for term induction of labor. *J Obstet Gynaecol Res*. 2021;47(9):3171-3178. doi:10.1111/jog.14907.
12. Tan PC, Jacob R, Omar SZ. Membrane sweeping at initiation of formal labor induction: a randomized controlled trial. *Obstet Gynecol*. 2006;107(3):569-577. doi:10.1097/01.AOG.0000200094.89388.70

Association of Antenatal Education Attendance with Early Postpartum Edinburgh Postnatal Depression Scale (EPDS) Scores: A Retrospective Observational Study

Doğum Öncesi Eğitime Katılımın Erken Edinburgh Doğum Sonrası Depresyon Ölçeği Puanlarıyla İlişkisi: Retrospektif Gözlemsel Bir Çalışma

İD Berna SEYHAN^{1*}, İD Hasan Mert BAŞBUĞA², İD Hamza Arda AÇIKGÖZ³, İD Emel ÖZALP¹, İD Çağanay SOYSAL¹

¹Etilik City Hospital, Department of Obstetrics and Gynecology, Ankara, Türkiye

²Cizre State Hospital, Department of Obstetrics and Gynecology, Şırnak, Türkiye

³Hitit University, Çorum Erol Olçok Training and Research Hospital, Department of Obstetrics and Gynecology, Çorum, Türkiye

ABSTRACT

Aim: This study aimed to evaluate the association between attendance at an institutional antenatal education program and early postpartum depressive symptom burden assessed using the Edinburgh Postnatal Depression Scale (EPDS).

Materials and Methods: This retrospective study included women who completed antenatal follow-up and delivery. Women who attended at least one theoretical antenatal education session were included in the antenatal education group. EPDS was recorded within the first 24 hours postpartum as part of routine assessment. High EPDS risk was defined as EPDS ≥ 13 .

Results: The cohort included 170 women, with 85 women in each group. Median EPDS score was lower in the antenatal education group than in the control group (7 vs 14, $p < 0.001$). High EPDS risk was recorded in 12 women (14.1%) in the antenatal education group and 70 women (82.4%) in the control group ($p < 0.001$). Vaginal delivery was more frequent among women who attended antenatal education (68.2% vs 45.9%, $p = 0.003$). After adjustment, antenatal education attendance remained independently associated with lower odds of high EPDS risk (adjusted OR, 0.034; 95% CI, 0.013-0.090; $p < 0.001$) and a lower continuous EPDS score (adjusted β , -6.654; 95% CI, -7.644 to -5.664; $p < 0.001$).

Conclusion: Antenatal education attendance was associated with lower early postpartum EPDS scores, lower high EPDS risk, and a higher vaginal delivery rate. Because EPDS was assessed within the first 24 hours postpartum and the study was non-randomized, the findings should be interpreted as an association with early postpartum depressive symptom burden rather than as proof of a causal preventive effect on clinically diagnosed postpartum depression.

Keywords: Antenatal education; Edinburgh Postnatal Depression Scale; postpartum depression risk; pregnancy school; vaginal delivery; cesarean section

ÖZ

Amaç: Bu çalışma, kurumsal bir doğum öncesi eğitim programına katılım ile Edinburgh Doğum Sonrası Depresyon Ölçeği (EPDS) kullanılarak değerlendirilen erken doğum sonrası depresif semptom yükü arasındaki ilişkiyi değerlendirmeyi amaçlamıştır.

Gereç ve Yöntemler: Bu retrospektif çalışma, doğum öncesi takibini ve doğumunu tamamlayan kadınları içermiştir. En az bir teorik doğum öncesi eğitim seansına katılan kadınlar doğum öncesi eğitim grubuna dahil edilmiştir. EPDS, rutin değerlendirmenin bir parçası olarak doğumdan sonraki ilk 24 saat içinde kaydedilmiştir. Yüksek EPDS riski, EPDS ≥ 13 olarak tanımlanmıştır.

Sonuçlar: Kohort, her grupta 85 kadın olmak üzere toplam 170 kadını içermiştir. Medyan EPDS puanı, doğum öncesi eğitim grubunda kontrol grubuna göre daha düşüktü (7'ye karşı 14, $p < 0,001$). Doğum öncesi eğitim grubunda 12 kadında (%14,1) ve kontrol grubunda 70 kadında (%82,4) yüksek EPDS riski kaydedilmiştir ($p < 0,001$). Doğum öncesi eğitim alan kadınlarda vajinal doğum daha sık görülmüştür (%68,2'ye karşı %45,9, $p = 0,003$). Düzeltme yapıldıktan sonra, doğum öncesi eğitime katılım, yüksek EPDS riski olasılığının daha düşük olmasıyla (düzeltilmiş OR, 0,034; %95 CI, 0,013-0,090; $p < 0,001$) ve sürekli EPDS skorunun daha düşük olmasıyla (düzeltilmiş β , -6,654; %95 CI, -7,644 ila -5,664; $p < 0,001$) bağımsız olarak ilişkili kalmıştır.

Sonuç: Doğum öncesi eğitime katılım, erken postpartum EPDS skorlarının daha düşük olması, yüksek EPDS riskinin daha düşük olması ve vajinal doğum oranının daha yüksek olmasıyla ilişkilidir. EPDS, doğumdan sonraki ilk 24 saat içinde değerlendirildiği ve çalışma rastgeleleştirilmediği için, bulgular klinik olarak teşhis edilmiş doğum sonrası depresyon üzerinde nedensel bir önleyici etki kanıtı olarak değil, erken doğum sonrası depresif semptom yükü ile bir ilişki olarak yorumlanmalıdır.

Anahtar Kelimeler: Doğum öncesi eğitim; Edinburgh Postpartum Depresyon Ölçeği; postpartum depresyon riski; gebelik okulu; vajinal doğum; sezaryen

Cite as: Seyhan B, Başbuğa HM, Açıkgöz HA, Özalp E, Soysal Ç. Association of Antenatal Education Attendance with Early Postpartum Edinburgh Postnatal Depression Scale (EPDS) Scores: A Retrospective Observational Study. Jinekoloji-Obstetrik ve Neonatoloji Tıp Dergisi 2026;23(2):174–181.

Geliş/Received: 10.06.2026 • Kabul/Accepted: 01.07.2026

Sorumlu Yazar/Corresponding Author: Berna Seyhan, Etilik City Hospital, Department of Obstetrics and Gynecology, Ankara, Türkiye

E-mail: dr.b3rna@gmail.com

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

INTRODUCTION

Postpartum depressive symptoms are among the most clinically relevant mental health problems of the perinatal period. They may affect maternal wellbeing, mother-infant interaction, breastfeeding, and infant developmental outcomes, particularly when symptoms remain unrecognized or untreated [1,2]. For this reason, current perinatal care increasingly emphasizes early identification of depressive symptoms during pregnancy and after birth, together with appropriate referral and follow-up pathways [3].

Antenatal education is an important component of woman-centred antenatal care. These programs aim to prepare women for pregnancy, childbirth, breastfeeding, postpartum recovery, and early parenthood, while also supporting informed decision-making and reducing uncertainty about birth [4]. Antenatal education has also been discussed as a non-clinical strategy that may contribute to reducing unnecessary cesarean deliveries by addressing childbirth-related fear, expectations, and preferences [5]. Recent systematic reviews and meta-analyses suggest that antenatal education can improve childbirth self-efficacy, reduce fear of childbirth, and support vaginal birth; however, heterogeneity in program content, duration, delivery format, and outcome assessment remains substantial [6-8].

The effect of antenatal education on postpartum depressive symptoms is less certain. Some intervention studies have reported lower depressive symptom scores after structured antenatal education or psychoeducation-based programs, whereas other studies have found no significant or only transient effects on postpartum Edinburgh Postnatal Depression Scale (EPDS) outcomes [9-14]. These inconsistent findings indicate that the relationship between antenatal education and postpartum mental health may depend on the psychological content of the program, participant characteristics, social support, timing of assessment, and local healthcare context.

The present study aimed to evaluate the association between attendance at an institutional antenatal education program and early postpartum depressive symptom burden among women who completed antenatal follow-up and delivery at a tertiary obstetric center. The primary objective was to compare EPDS scores and high EPDS risk between women who attended antenatal education and those who did not. Secondary objectives were to examine mode of delivery, selected obstetric and neonatal outcomes, and program-related factors within the antenatal education group.

MATERIALS AND METHODS

Study design and setting

This retrospective observational study was conducted at the obstetrics clinic at tertiary center. Data were obtained from routine hospital records of women who received antenatal follow-up and delivered at the study center between January 1, 2025 and December 31, 2025. The study evaluated the association between attendance at the institutional antenatal education program and early postpartum Edinburgh Postnatal Depression Scale (EPDS) outcomes. No additional intervention, examination, laboratory test, questionnaire, or patient contact was performed for the purposes of the study.

Ethical considerations

The study protocol was approved by the Local Ethics Committee (approval no: AESH-BADEK2-2026-372; approval date: May 5, 2026). The study was conducted in accordance with the principles of the Declaration of Helsinki and local regulations for retrospective clinical research. Written informed consent was not required in accordance with the retrospective design and ethics committee approval. All data were anonymized before analysis, and no directly identifying information was included in the dataset or manuscript.

Study population and sampling strategy

The study population consisted of women aged 18 years or older who completed antenatal follow-up and delivery at the study center and had an EPDS result recorded within the first 24 hours postpartum. Women were eligible if they had a singleton pregnancy, available data on antenatal education attendance, and available obstetric and neonatal outcome data. Women with major maternal or fetal pathology, chronic systemic disease, inflammatory disease, chronic medication use, multiple pregnancy, fetal congenital or chromosomal anomaly, smoking or alcohol use, or delivery outside the study center were excluded.

Women were allocated to the antenatal education group if they had attended at least one theoretical session of the institutional antenatal education program. The control group was selected using a 1:1 consecutive sampling strategy. A consecutive sample of 85 eligible antenatal education attendees was selected in chronological order during the study period. For each included attendee, the next consecutive eligible non-attendee who delivered at the same center was selected as a control.

Antenatal education program

The institutional antenatal education program was organized as a structured program for pregnant women followed at the study center. According to the institutional protocol, the program included a five-week schedule with a total of 7.5 hours of theoretical education. In

the present retrospective analysis, antenatal education attendance was defined as participation in at least one 30-minute theoretical education session. Within the antenatal education group, additional program-related variables were recorded, including gestational week at program initiation, number of attended sessions, partner participation, exercise participation, and number of exercise sessions.

Data collection

Data were extracted retrospectively from electronic medical records and standardized patient follow-up forms. Maternal variables included age, gravida, parity, abortion history, and number of living children. Obstetric and neonatal variables included gestational age at delivery, mode of delivery, cesarean section indication, birth weight, 1-minute and 5-minute Apgar scores, preterm birth status, and episiotomy among women with vaginal delivery. Program-related variables were recorded only for women in the antenatal education group.

Outcome measures

The primary outcome was the EPDS score recorded within the first 24 hours postpartum as part of routine postpartum assessment. The EPDS is a 10-item self-report screening scale developed to identify depressive symptoms in the postnatal period, with total scores ranging from 0 to 30 [15]. The EPDS is a screening instrument and should not be interpreted as a diagnostic tool for postpartum depression [16]. The Turkish version of the EPDS has been validated among postpartum women [17]. In the present study, EPDS was analyzed both as a continuous variable and as a binary high-risk outcome using a cut-off score of ≥ 13 .

Because EPDS was administered within the first 24 hours after delivery, the outcome was interpreted as early postpartum depressive symptom burden or high EPDS risk rather than clinically diagnosed postpartum depression. This distinction is important because very early postpartum EPDS scores may be influenced by acute delivery-related stress, pain, fatigue, and sleep deprivation, although early scores may still help identify women requiring closer follow-up [18].

Secondary outcomes included mode of delivery, cesarean section rate, vaginal delivery rate, episiotomy among women with vaginal delivery, and program-related associations with EPDS scores within the antenatal education group.

Sample size

An a priori sample size calculation was performed using data from Badrin et al., who evaluated the effects of a guided antenatal education support program on postnatal depression among first-time mothers [10]. Based on the reported EPDS means and

standard deviations in the intervention and control groups, the calculated effect size was Cohen's $d=0.579$. Using G*Power version 3.1.9.7, with a two-tailed independent samples t-test, $\alpha=0.05$, power=0.95, and equal group allocation, at least 79 women per group AND minimum total sample size of 158 participants were required [19]. The final study sample of 170 women, with 85 women in each group, exceeded this requirement.

Statistical analysis

Statistical analyses were performed using IBM SPSS Statistics version 27.0 (IBM Corp., Armonk, NY, USA). Continuous variables were assessed for distributional characteristics using normality tests and visual inspection. Because most continuous variables did not meet normality assumptions, between-group comparisons were performed using the Mann-Whitney U test. Continuous variables are presented as median (Q1-Q3). Categorical variables are summarized as counts and percentages and were compared using Pearson's chi-square test or Fisher's exact test, depending on expected cell counts.

The primary outcome was the EPDS score. EPDS was analyzed as a continuous outcome and as a binary high-risk outcome using a cut-off value of ≥ 13 . Because EPDS was recorded within the first 24 hours after delivery, the findings were interpreted as early postpartum depressive symptom burden and high EPDS risk rather than as a definitive clinical diagnosis of postpartum depression.

Multivariable logistic regression was used to evaluate the independent association between antenatal education attendance and high EPDS risk. The model was adjusted for maternal age, gravida, parity, gestational age at delivery, neonatal birth weight scaled per 100 g, and mode of delivery. Results are presented as adjusted odds ratios (ORs) with 95% confidence intervals (CIs). A separate multivariable linear regression model was fitted for continuous EPDS score using the same adjustment set, and results are reported as adjusted β coefficients with 95% CIs.

Program-related analyses were performed within the antenatal education group only. Gestational week at program initiation, number of attended sessions, partner participation, exercise participation, and number of exercise sessions were summarized descriptively. Associations between continuous program-related variables and EPDS score were evaluated using Spearman's rank correlation. Cesarean section indications were summarized descriptively among women who underwent cesarean delivery. No imputation was performed for missing data. All statistical tests were two-sided, and $p<0.05$ was considered statistically significant.

RESULTS

Study population and baseline characteristics

The final analytic cohort included 170 women with available Edinburgh Postnatal Depression Scale (EPDS) data, comprising 85 women in the antenatal education group and 85 women in the control group. The two groups were therefore equal in size. Baseline characteristics, obstetric variables, neonatal outcomes, delivery mode, and EPDS outcomes are summarized in Table 1.

Women who attended antenatal education were younger than controls (median age, 27 vs 30 years; $p<0.001$). Gravida, parity, and abortion history also differed between groups, with lower values in the antenatal education group (all $p\leq0.003$). Gestational age at delivery, neonatal birth weight, 5-minute Apgar score, and preterm birth frequency did not differ significantly between groups. The 1-minute Apgar score was higher in the antenatal education group (median, 8 vs 8; $p=0.003$), although the absolute values in both groups were within a clinically reassuring range.

EPDS outcomes and mode of delivery

EPDS scores were substantially lower among women who attended antenatal education. The median (Q1-Q3) EPDS score was 7 (4-10) in the antenatal education group and 14 (13-16) in the control group ($p<0.001$). High EPDS risk (EPDS ≥ 13) was recorded in 12 of

85 women (14.1%) in the antenatal education group and in 70 of 85 women (82.4%) in the control group ($p<0.001$).

Mode of delivery also differed between groups. Vaginal delivery was more frequent in the antenatal education group than in the control group (68.2% vs 45.9%), whereas cesarean delivery was less frequent (31.8% vs 54.1%; $p=0.003$). Among women with vaginal delivery and available episiotomy data, episiotomy frequency did not differ significantly between groups (93.0% vs 100.0%; $p=0.144$).

Multivariable analyses

After adjustment for maternal age, gravida, parity, gestational age at delivery, neonatal birth weight, and mode of delivery, antenatal education attendance remained independently associated with lower odds of high EPDS risk (adjusted OR, 0.034; 95% CI, 0.013-0.090; $p<0.001$) (Table 2). None of the other covariates in the model reached statistical significance.

In the multivariable linear regression model, antenatal education attendance was associated with a 6.65-point lower EPDS score (adjusted β coefficient, -6.654; 95% CI, -7.644 to -5.664; $p<0.001$) (Table 3). Gestational age at delivery was also inversely associated with EPDS score (adjusted β coefficient, -0.536; 95% CI, -1.035 to -0.037; $p=0.035$). Other covariates were not statistically significant in the adjusted linear model.

Table 1. Comparison of baseline characteristics, obstetric-neonatal variables, delivery mode, and EPDS outcomes according to antenatal education attendance

Variable	Antenatal education (n=85)	Control (n=85)	p value
Age, years	27 (22-30)	30 (26-35)	<0.001
Gravida	1 (1-2)	2 (1-3)	<0.001
Parity	0 (0-1)	0 (0-1)	0.003
Abortions	0 (0-0)	1 (0-1)	<0.001
Living children	0 (0-0)	0 (0-1)	0.416
Gestational age at delivery, weeks	39 (39-40)	40 (39-40)	0.161
Birth weight, g	3330 (3090-3620)	3480 (3160-3760)	0.135
1-minute Apgar score	8 (8-9)	8 (8-8)	0.003
5-minute Apgar score	10 (9-10)	10 (9-10)	0.087
Preterm birth (<37 weeks)	3 (3.5%)	0 (0.0%)	0.246
Mode of delivery, vaginal / cesarean	58 (68.2%) / 27 (31.8%)	39 (45.9%) / 46 (54.1%)	0.003
Episiotomy among vaginal deliveries	53/57 (93.0%)	39/39 (100.0%)	0.144
EPDS score	7 (4-10)	14 (13-16)	<0.001
High EPDS risk (EPDS ≥ 13)	12 (14.1%)	70 (82.4%)	<0.001

Note. Values are presented as median (Q1-Q3) or n (%), as appropriate. Continuous variables were compared using the Mann-Whitney U test. Categorical variables were compared using the Pearson chi-square test or Fisher exact test, as appropriate. For mode of delivery, the p value refers to the overall comparison of vaginal versus cesarean delivery. Episiotomy percentages are calculated among vaginal deliveries with available episiotomy data. EPDS, Edinburgh Postnatal Depression Scale; Q1, first quartile; Q3, third quartile.

Table 2. Multivariable logistic regression for high EPDS risk (EPDS ≥ 13)

Variable	Adjusted OR	95% CI	p value
Antenatal education attendance (yes vs no)	0.034	0.013-0.090	<0.001
Age, years	1.040	0.955-1.131	0.370
Gravida	1.193	0.603-2.360	0.613
Parity	1.037	0.449-2.398	0.932
Gestational age at delivery, weeks	0.798	0.535-1.190	0.269
Birth weight, per 100 g	0.999	0.879-1.135	0.985
Cesarean vs vaginal delivery	0.592	0.233-1.500	0.269

Note. The dependent variable was high EPDS risk, defined as EPDS ≥ 13 . The model was fitted using multivariable logistic regression and adjusted for all variables listed in the table. OR, odds ratio; CI, confidence interval; EPDS, Edinburgh Postnatal Depression Scale.

Table 3. Multivariable linear regression for continuous EPDS score.

Variable	Adjusted β coefficient	95% CI	p value
Antenatal education attendance (yes vs no)	-6.654	-7.644 to -5.664	<0.001
Age, years	0.098	-0.004 to 0.201	0.061
Gravida	0.335	-0.237 to 0.907	0.252
Parity	0.110	-0.553 to 0.772	0.745
Gestational age at delivery, weeks	-0.536	-1.035 to -0.037	0.035
Birth weight, per 100 g	-0.012	-0.139 to 0.114	0.849
Cesarean vs vaginal delivery	-0.044	-1.003 to 0.916	0.929

Note. The dependent variable was continuous EPDS score. The model was fitted using multivariable linear regression and adjusted for all variables listed in the table. Adjusted β coefficients are reported. CI, confidence interval; EPDS, Edinburgh Postnatal Depression Scale.

Program-related analyses within the antenatal education group

Within the antenatal education group, the median (Q1-Q3) gestational week at program initiation was 28 weeks (24-30), and the median number of attended sessions was 3 (2-4). Partner participation was recorded in 36 of 85 women (42.4%), and exercise participation was recorded in 62 of 85 women (72.9%). No statistically significant correlations were observed between EPDS score and gestational week at program initiation, number of attended sessions, or number of exercise sessions (Table 4).

Cesarean section indications

The most common cesarean section indications in the antenatal education group were previous cesarean section (25.9%), fetal distress (22.2%), and suspected macrosomia (18.5%). In the

Table 4. Correlation analyses between program-related variables and EPDS score within the antenatal education group

Program-related variable	Spearman rho	p value
Gestational week at program initiation (n=85)	-0.010	0.926
Number of attended sessions (n=85)	0.098	0.374
Number of exercise sessions (n=85)	0.011	0.917

Note. Spearman rank correlation was used to assess associations between continuous program-related variables and EPDS score. These analyses were exploratory and restricted to women who attended antenatal education. EPDS, Edinburgh Postnatal Depression Scale.

control group, the most common indications were fetal distress (23.9%), failure to progress/arrest of labor (21.7%), and previous cesarean section (19.6%) (Table 5).

Table 5. Cesarean section indications

Cesarean indication	Antenatal education CS (n=27)	Control CS (n=46)
Cephalopelvic disproportion	1 (3.7%)	8 (17.4%)
Previous cesarean section	7 (25.9%)	9 (19.6%)
Fetal distress	6 (22.2%)	11 (23.9%)
Breech presentation	4 (14.8%)	3 (6.5%)
Suspected macrosomia	5 (18.5%)	3 (6.5%)
Maternal anxiety	1 (3.7%)	1 (2.2%)
Transverse lie	0 (0.0%)	1 (2.2%)
Failure to progress/arrest of labor	3 (11.1%)	10 (21.7%)

Note. Percentages are calculated within cesarean deliveries in each group. CS, cesarean section.

DISCUSSION

In this retrospective observational study, attendance at the institutional antenatal education program was associated with lower early postpartum Edinburgh Postnatal Depression Scale (EPDS) scores and a lower proportion of women classified as high EPDS risk. The median EPDS score was 7 in the antenatal education group and 14 in the control group, and high EPDS risk was observed in 14.1% and 82.4% of women, respectively. This association remained statistically significant after adjustment for maternal age, gravida, parity, gestational age at delivery, neonatal birth weight, and mode of delivery. Antenatal education attendance was also associated with a higher vaginal delivery rate.

The lower EPDS scores observed among women who attended antenatal education are biologically and clinically plausible. Antenatal education may reduce uncertainty about labor, increase perceived preparedness, improve childbirth self-efficacy, and provide basic coping strategies for the transition to motherhood. These mechanisms are consistent with randomized and quasi-experimental studies showing that structured antenatal education can reduce fear of birth, depressive symptoms, anxiety, and stress, while improving childbirth self-efficacy [9]. Similarly, Badrin et al. reported that guided antenatal education support reduced postnatal depression scores and improved social support and life satisfaction among first-time mothers [10]. In a cluster-randomized trial, prenatal group-based psychoeducation delivered in primary healthcare settings was also associated with a reduction in postpartum depression at follow-up [11].

The present findings are also partly consistent with recent synthesis-level evidence. Meta-analytic data suggest that antenatal education may reduce fear of childbirth and pain intensity during labor, improve childbirth self-efficacy, and support vaginal birth [6-8]. Hooper et al. reported that antenatal education improved some labor and birth outcomes, although the included studies varied substantially in intervention content and outcome definitions [6]. Zaman et al. similarly concluded that antenatal education improved maternal psychological outcomes and promoted vaginal delivery, while emphasizing high heterogeneity and potential bias [7]. In this context, the higher vaginal delivery rate in the antenatal education group in the present study supports the role of antenatal education in birth preparedness and informed decision-making.

Nevertheless, the magnitude of the EPDS difference in this study was larger than that reported in much of the previous literature and should be interpreted carefully. Several studies have not found a significant postpartum mental health benefit of antenatal education. Can Gürkan and Ekşi reported no significant difference in EPDS

scores between antenatal education and control groups at either the sixth postpartum week or sixth postpartum month [12]. In a recent Turkish retrospective analysis, Koç Tiske et al. found that antenatal education was associated with a higher vaginal delivery rate but did not significantly reduce EPDS scores or high postpartum depression risk [13]. In a large Italian perinatal sample, Camoni et al. showed that crude associations suggested lower anxiety and depressive symptoms among women attending antenatal classes, but these associations weakened after adjustment and did not persist into the postpartum period [14]. These findings suggest that the apparent effect of antenatal education on postpartum depressive symptoms may be influenced by self-selection, baseline psychosocial differences, timing of assessment, and program content.

The very high rate of high EPDS risk in the control group is one of the most important issues in interpreting the present results. An EPDS ≥ 13 rate of 82.4% is substantially higher than expected for clinically diagnosed postpartum depression in general postpartum populations. This value should therefore not be interpreted as the true prevalence of postpartum depression in the control group. The timing of EPDS assessment is particularly relevant. In the present study, EPDS was administered within the first 24 hours postpartum, when pain, fatigue, sleep disruption, acute stress, surgical recovery, or anxiety related to the newborn may influence responses. Although early postpartum EPDS assessment may help identify women who require closer follow-up, it is more appropriate to describe the outcome as early postpartum depressive symptom burden or high EPDS risk rather than confirmed postpartum depression [15,16,18].

Another possible explanation for the strong association is selection bias. Participation in antenatal education was voluntary, and women who attended the program may have differed from non-attendees in health literacy, motivation, planned pregnancy status, family support, socioeconomic status, and engagement with healthcare services. In the present cohort, women in the antenatal education group were younger and had lower gravida, parity, and abortion history than controls. Although the control group was selected using a consecutive sampling strategy to reduce investigator-driven selection, this approach does not replace randomization. The multivariable models adjusted for several demographic and obstetric variables, but residual confounding remains possible because the dataset did not include educational level, income, employment status, planned pregnancy, previous psychiatric history, previous postpartum depression, marital relationship quality, perceived social support, breastfeeding status, sleep quality, or birth satisfaction.

The association between antenatal education and mode of delivery is clinically meaningful. Women who attended antenatal education had a higher vaginal delivery rate than controls. This finding is

consistent with the broader literature suggesting that childbirth education may reduce fear, increase confidence, and support women in making informed decisions about delivery mode [6,7]. It is also supported by a recent Turkish retrospective study by Atalay Mert et al., which evaluated term deliveries in women who attended pregnancy school education and exercises and reported lower cesarean section, episiotomy, and oxytocin augmentation rates among attendees compared with controls [20]. In the present cohort, episiotomy frequency among women with vaginal delivery and available episiotomy data did not differ significantly between groups. Moreover, mode of delivery was not independently associated with EPDS score or high EPDS risk in the adjusted models. This suggests that the lower EPDS scores observed in the antenatal education group were not explained solely by the higher vaginal delivery rate.

Within the antenatal education group, no statistically significant correlations were observed between EPDS score and gestational week at program initiation, number of attended sessions, or number of exercise sessions. This finding does not support a clear dose-response pattern for these continuous program-related variables in the present dataset. However, the result should be interpreted cautiously because the analysis was exploratory, the sample size within the antenatal education group was limited, and antenatal education attendance was defined broadly as participation in at least one theoretical session. Partner participation and exercise participation were recorded descriptively; therefore, the present data do not allow firm conclusions regarding their independent effects on early postpartum EPDS outcomes.

In the linear regression model, gestational age at delivery showed a small inverse association with continuous EPDS score. However, this finding should be interpreted cautiously because gestational age distributions were clinically similar between groups and only three women in the analytic cohort delivered before 37 weeks. Therefore, this secondary association should be considered hypothesis-generating rather than a central finding of the study.

The study also has important limitations. First, its retrospective and non-randomized design prevents causal inference. Second, antenatal education attendance was voluntary, making self-selection bias likely. Third, EPDS was measured within the first 24 hours postpartum, which limits comparability with studies assessing postpartum depression at 4-8 weeks or later. Fourth, no antenatal baseline EPDS score was available, so it was not possible to determine whether the groups differed in depressive symptoms before delivery. Fifth, important psychosocial variables were not available for adjustment. Sixth, the study was conducted at a single center and included women without major maternal or

fetal pathology, which may limit generalizability. Finally, the broad definition of antenatal education attendance may have introduced heterogeneity within the intervention group.

These findings support the potential value of antenatal education as part of perinatal mental health promotion, but they should not be interpreted as evidence that antenatal education alone prevents postpartum depression. Antenatal education may be most useful when integrated with structured psychosocial screening, mental health literacy, referral pathways, partner involvement, and postpartum follow-up. Current perinatal mental health guidance emphasizes that screening should be linked to systems that ensure further assessment, treatment, and follow-up when needed [3]. Future prospective studies should include baseline antenatal EPDS assessment, standardized education content, detailed attendance data, psychosocial covariates, and repeated postpartum EPDS measurements to clarify whether antenatal education has a sustained effect on clinically relevant postpartum depressive symptoms.

CONCLUSION

In conclusion, antenatal education attendance was independently associated with lower early postpartum EPDS scores and lower high EPDS risk in this retrospective cohort. Attendance was also associated with a higher vaginal delivery rate. Because EPDS was administered within the first 24 hours postpartum and the study was non-randomized, the findings should be interpreted as an association with early postpartum depressive symptom burden rather than proof of a causal preventive effect on postpartum depression. Nevertheless, the results support strengthening antenatal education programs within broader perinatal psychosocial care models.

Ethical approval: This study was approved by the Local Ethics Committee (approval no: AEŞH-BADEK2-2026-372; approval date: May 5, 2026).

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

Funding: This research received no external funding.

Data Availability: The datasets generated and/or analyzed during the current study are not publicly available because of institutional privacy restrictions but may be available from the corresponding author upon reasonable request.

REFERENCES

1. Shorey S, Chee CYI, Ng ED, Chan YH, Tam WWS, Chong YS. Prevalence and incidence of postpartum depression among healthy mothers: A systematic review and meta-analysis. *J Psychiatr Res*. 2018;104:235-248. doi:10.1016/j.jpsychires.2018.08.001.
2. Slomian J, Honvo G, Emonts P, Reginster JY, Bruyère O. Consequences of maternal postpartum depression: A systematic review of maternal and infant outcomes. *Womens Health (Lond)*. 2019;15:1745506519844044. doi:10.1177/1745506519844044.

3. American College of Obstetricians and Gynecologists. Screening and diagnosis of mental health conditions during pregnancy and postpartum: ACOG Clinical Practice Guideline No. 4. *Obstet Gynecol.* 2023;141(6):1232-1261. doi:10.1097/AOG.0000000000005200.
4. World Health Organization. WHO Recommendations on Antenatal Care for a Positive Pregnancy Experience. Geneva: World Health Organization; 2016.
5. World Health Organization. WHO Recommendations: Non-Clinical Interventions to Reduce Unnecessary Caesarean Sections. Geneva: World Health Organization; 2018.
6. Hooper E, Mechkaroff O, Upitis A, Schofield E, Carland JE, Henry A. The effectiveness of antenatal education on improving labour and birth outcomes: A systematic review and meta-analysis. *Women Birth.* 2025;38(1):101843. doi:10.1016/j.wombi.2024.101843.
7. Zaman A, Fadlalmola HA, Ibrahim SE, Ismail FH, Abedelwahed HH, Ali AM, et al. The role of antenatal education on maternal self-efficacy, fear of childbirth, and birth outcomes: A systematic review and meta-analysis. *Eur J Midwifery.* 2025;9:13. doi:10.18332/ejm/200747.
8. Alizadeh-Dibazari Z, Abdolalipour S, Mirghafourvand M. The effect of prenatal education on fear of childbirth, pain intensity during labour and childbirth experience: A scoping review using systematic approach and meta-analysis. *BMC Pregnancy Childbirth.* 2023;23(1):541. doi:10.1186/s12884-023-05867-0.
9. Çankaya S, Şimşek B. Effects of antenatal education on fear of birth, depression, anxiety, childbirth self-efficacy, and mode of delivery in primiparous pregnant women: A prospective randomized controlled study. *Clin Nurs Res.* 2021;30(6):818-829. doi:10.1177/1054773820916984.
10. Badrin S, Badrin S, Raja Gopal RL, Johan Noor SR. Effects of guided antenatal education support programs on postnatal depression, social support, and life satisfaction among first-time mothers in Kelantan, Malaysia. *Nurse Media J Nurs.* 2021;11(2):233-243. doi:10.14710/nmjn.v11i2.37123.
11. Tessema M, Abera M, Birhanu Z. Effectiveness of group-based psycho-education on preventing postpartum depression among pregnant women by primary healthcare provider in primary healthcare institution: A cluster-randomized controlled trial. *Front Psychiatry.* 2024;15:1433942. doi:10.3389/fpsy.2024.1433942.
12. Can Gürkan Ö, Ekşi Z. Effects of antenatal education program on postpartum functional status and depression. *Clin Exp Health Sci.* 2017;7(4):133-138. doi:10.5152/clinexphealthsci.2017.284.
13. Koç Tiske P, Topcu Akduman A, Alparslan Çetin S, Türkçapar AF, Özdemir Ö. The impact of antenatal education on mode of delivery and postpartum depression: A retrospective analysis. *Gulhane Med J.* 2026;68(1):7-15. doi:10.4274/gulhane.galenos.2025.06777.
14. Camoni L, Mirabella F, Gigantesco A, Calamandrei G, Stefana A; Perinatal Mental Health Network group. Effects of antenatal education on maternal anxiety and depression in pregnancy and postpartum period in Italy: Modest and transient symptom reductions. *Front Psychol.* 2026;16:1724202. doi:10.3389/fpsyg.2025.1724202.
15. Cox JL, Holden JM, Sagovsky R. Detection of postnatal depression: Development of the 10-item Edinburgh Postnatal Depression Scale. *Br J Psychiatry.* 1987;150:782-786. doi:10.1192/bjp.150.6.782.
16. Levis B, Negeri Z, Sun Y, Benedetti A, Thombs BD; DEPRESSion Screening Data EPDS Collaboration. Accuracy of the Edinburgh Postnatal Depression Scale for screening to detect major depression among pregnant and postpartum women: Systematic review and meta-analysis of individual participant data. *BMJ.* 2020;371:m4022. doi:10.1136/bmj.m4022.
17. Aydin N, Inandi T, Yigit A, Hodoglugil NNS. Validation of the Turkish version of the Edinburgh Postnatal Depression Scale among women within their first postpartum year. *Soc Psychiatry Psychiatr Epidemiol.* 2004;39(6):483-486. doi:10.1007/s00127-004-0770-4.
18. Jardri R, Pelta J, Maron M, Thomas P, Delion P, Codaccioni X, Goudemand M. Predictive validation study of the Edinburgh Postnatal Depression Scale in the first week after delivery and risk analysis for postnatal depression. *J Affect Disord.* 2006;93(1-3):169-176. doi:10.1016/j.jad.2006.03.009.
19. Faul F, Erdfelder E, Buchner A, Lang AG. Statistical power analyses using G*Power 3.1: Tests for correlation and regression analyses. *Behav Res Methods.* 2009;41(4):1149-1160. doi:10.3758/BRM.41.4.1149.
20. Atalay Mert Ş, Kınay T, Kurt A, Özgürlük İ, Keskin HL. The effect of antenatal education and pregnancy exercises on delivery outcomes. *Akdeniz Tıp Dergisi.* 2024;10(3):558-563. doi:10.53394/akd.1402416.

Expression of Endothelial and Inducible Nitric Oxide Synthases in Tubal Ectopic Pregnancy: An Immunohistochemical Evaluation

Tubal Ektopik Gebelikte Endotelial ve İndüklenebilir Nitrik Oksit Sentazların İfadesi: Immunohistokimyasal Bir Değerlendirme

¹ Fatma ESKİCIOĞLU¹, ² Tuna ONAL^{2,4}, ³ Melis Aylin UNER AKMAN⁴, ⁴ Semih TASKENT³, ⁵ Tulay GOKMEN⁵, ⁶ Kemal OZBİLGİN⁴

¹Eskicioglu Clinic, Clinic of Obstetrics and Gynecology, Türkiye

²Bandırma Onyedi Eylül University, Faculty of Medicine, Department of Histology and Embryology, Bandırma, Türkiye

³Manisa City Hospital, Clinic of Obstetrics and Gynecology, Manisa, Türkiye

⁴Manisa Celal Bayar University, Faculty of Medicine, Department of Histology and Embryology, Manisa, Türkiye

⁵Manisa City Hospital, Clinic of Pathology, Manisa, Türkiye

ABSTRACT

Aim: The aim of the study was to investigate the expression of endothelial Nitric Oxide Synthase (eNOS) and inducible Nitric Oxide Synthase (iNOS) in fallopian tubes on Ectopic Pregnancy (EP).

Material and Methods: The study was conducted on non-pregnant women (n=10), women with healthy pregnancy (n=7) and ectopic pregnancy (n=10). eNOS and iNOS levels in tubal tissues were examined immunohistochemically in all groups. Immunostaining was evaluated by H-SCORE analysis in epithelium, subepithelium, muscle and vessel tissues. Statistical analysis was performed using SPSS.

Results: This study showed that eNOS and iNOS were expressed in the epithelium, muscle and blood vessels of the fallopian tube. The EP group showed a higher eNOS expression in both the epithelium and subepithelium of fallopian tubes, while it showed a higher iNOS expression in the epithelium of fallopian tubes. The expressions of these two NOS isoforms were not significantly different in the muscular and vascular regions of the fallopian tubes. The expressions of eNOS and iNOS are increased in tubal epithelium of EP.

Conclusion: This information may indicate that these two Nitric Oxide Synthase (NOS) isoforms induce facilitatory effects for implantation in ciliated and secretory cells of luminal epithelium that can lead to the formation of a suitable microenvironment for EP.

Keywords: Ectopic pregnancy, fallopian tubes, endothelial nitric oxide synthase, inducible nitric oxide synthase, nitric oxide synthase, immunohistochemistry

ÖZ

Amaç: Çalışmanın amacı, ektopik gebelikte (EP) fallop tüplerinde endotel nitrik oksit sentaz (eNOS) ve indüklenebilir nitrik oksit sentaz (iNOS) ekspresyonunu araştırmaktır.

Gereç ve Yöntemler: Çalışma, hamile olmayan kadınlar (n=10), sağlıklı gebelikleri olan kadınlar (n=7) ve ektopik gebelikleri olan kadınlar (n=10) üzerinde gerçekleştirilmiştir. Tüm gruplarda tüp dokularındaki eNOS ve iNOS düzeyleri immünohistokimyasal olarak incelenmiştir. İmmunboyama, epitel, subepitel, kas ve damar dokularında H-SKOR analizi ile değerlendirilmiştir. İstatistiksel analiz SPSS kullanılarak yapılmıştır.

Sonuçlar: Bu çalışma, eNOS ve iNOS'un fallop tüpünün epitelinde, kasında ve kan damarlarında eksprese olduğunu göstermiştir. EP grubu, fallop tüpünün hem epitelinde hem de subepitelinde daha yüksek eNOS ekspresyonu gösterirken, fallop tüpünün epitelinde daha yüksek iNOS ekspresyonu göstermiştir. Bu iki NOS izoformunun ekspresyonları, fallop tüpünün kas ve damar bölgelerinde anlamlı bir fark göstermemiştir. EP'nin tüp epitelinde eNOS ve iNOS ekspresyonları artmıştır.

Sonuç: Bu bilgi, bu iki Nitrik Oksit Sentez Enzimi (NOS) izoformunun, EP için uygun bir mikroortam oluşumuna yol açabilecek, lümen epitelinin siliyer ve salgı hücrelerinde implantasyonu kolaylaştırıcı etkiler indüklediğini gösterebilir.

Anahtar Kelimeler: Ektopik gebelik, fallop tüpleri, endotel nitrik oksit sentez enzimi, indüklenebilir nitrik oksit sentez enzimi, nitrik oksit sentez enzimi, immünohistokimya

Cite as: Eskicioglu F, Onal T, Uner Akmen MA, Taskent S, Gokmen T, Ozbilgin K. Expression of Endothelial and Inducible Nitric Oxide Synthases in Tubal Ectopic Pregnancy: An Immunohistochemical Evaluation. Jinekoloji-Obstetrik ve Neonatoloji Tıp Dergisi 2026;23(2):182–189.

Geliş/Received: 24.06.2025 • **Kabul/Accepted:** 29.09.2025

Sorumlu Yazar/Corresponding Author: Tuna Onal, Bandırma Onyedi Eylül Üniversitesi, Tıp Fakültesi, Temel Tıp Bilimleri Bölümü, Histoloji Ve Embriyoloji

Anabilim Dalı, Türkiye

E-mail: tonal@bandirma.edu.tr

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

INTRODUCTION

Ectopic pregnancy (EP) refers to the localization of a fertilized ovum anywhere but the uterine cavity. Fallopian tubes are the site of implantation in 98% of EP cases. EP continues to cause a significant maternal morbidity and mortality worldwide even though important medical advances have been recently witnessed in the management of this condition (1). Latest studies have implicated defective embryo-tubal transport as well as pathological changes in tubal milieu for the implantation of fertilized ovum in the fallopian tubes (2).

Fertilization and embryonic development preeminently occur in the fallopian tubes owing to the latter providing favorable medium for both carriage and maturation of gametes and embryos (3). Smooth muscle contractions, ciliary activity, and secretory functions of fallopian tubes operate as parts of a complex, ill-understood mechanism working for the transport of gamete and embryo (4). Although it is a common knowledge that walls of fallopian tubes are densely equipped with smooth muscle cells with phasic and tonic contractions, the contribution of these muscles and their contractions to embryo transport remains largely unknown (5).

Nitric oxide (NO) is regarded as one of the important biological and physiological regulatory molecules for the reproductive system as it reportedly modulated several functions including ovulation, cilia beats, contractility, relaxation, and the transport of gametes and embryos (3,4,6,7). Furthermore, it also has smooth muscle relaxing effects so that its deficiency leads to vasospasm and vascular infarction (8). This property suggests that it also plays a role in placental circulation during a healthy pregnancy (9). NO synthase (NOS) family containing several isoenzymes with the ability to catalyze the oxidation of L-arginine to NO and citrulline are responsible for the production of NO. The isoforms of the enzyme are the calcium-independent inducible NOS (iNOS) and the calcium-dependent endothelial NOS (eNOS) and neural NOS (nNOS) (10).

Currently the limited studies focused on the role of the NOSs for EP in human. These studies showed that especially changes of eNOS and iNOS expressions were effective in EP. However, the results of these studies were contradictory (11,12). In a study Fath-Bayati (2014) evaluated only eNOS and found that expression of eNOS in luminal epithelium for women with EP was increased compared to non-pregnant women at luteal phase and healthy labour (11). Subsequently, In another study Hu (2014) claimed that only iNOS isoform between three NOSs was increased in fallopian tubes with EP comparing between non-pregnant women and women with EP (12).

Thus, in this study we aimed to investigate the expression of eNOS and iNOS in the fallopian tubes for women with EP in the first trimester intrauterine pregnancy and for non-pregnant women by using immunohistochemical technique. To our best knowledge, this is the first study comparing these two NOS isoforms' expression changes in fallopian tubes between these three groups.

MATERIALS AND METHODS

This study was conducted in the Department of Obstetrics and Gynecology by the Principles of the Declaration of Helsinki. Ethical approval was acquired from Celal Bayar University Faculty of Medicine Ethics Committee, with approval number 26/03/2014/20478486/26. In the experiments, new sections were taken from the tubal tissue samples obtained in our previously published study (13). Briefly, tubal tissues were obtained from 10 non-pregnant women (NonP), 7 with intrauterine healthy pregnancy (HP: isthmus, ampulla, fimbriae), and 10 with ectopic pregnancy (EP). Participants were 25–35 years old, had at least one live birth, and gave informed consent. Exclusion criteria were pelvic disease, prior EP or tubal surgery, smoking, recent hormonal therapy, or unwanted pregnancy. In HP cases, CRL was <10 weeks and fetal heart activity was confirmed by ultrasound.

Immunohistochemistry

Tissue samples fixed in 10% formalin and histological tissue process was performed. Immunohistochemistry was performed on sections taken from different parts of the fallopian tube. To break protein cross links, 2% trypsin solution was used for 15 minutes. To inhibit endogenous peroxidase activity, a 3% H₂O₂ solution was used for 15 minutes. Sections were then blocked with ready-to-use serum blocking solution for 10 minutes and kept overnight with eNOS (1:100, 25078 ABBOTEC, San Diego, CA) and iNOS primary antibodies (1:100, 25078 ABBOTEC, San Diego, CA). The following day, the morning was treated with biotinylated secondary antibody and enzyme conjugate for 10 minutes. The nuclei were stained with Mayer's haematoxylin (ScyTek Laboratories, Logan, Utah, USA) following DAB (DAB Kit, Invitrogen, UK) chromogenylation. The sections were then dehydrated and covered with entellan (01730 Surgipath, Cambridge, UK).

Immunostaining for eNOS and iNOS expressions were evaluated with H-SCORE. Five different area randomized selected of each group were evaluated at 200x magnification. The immunostaining intensities were categorized by the following scores: 0 (no staining), 1 (weak), 2 (moderate), and 3 (strong). A H-SCORE value was derived for each specimen by calculating the sum of the percentage of cells for epithelium, subepithelium, vessel and

muscle of fallopian tube that stained at each intensity category, multiplied by its respective score, using the formula $H\text{-SCORE} = \sum P_i (i+1)$, where i is the intensity of staining with a value of 1, 2 or 3 corresponding to weak, moderate or strong staining, respectively, and P_i is the percentage of stained cells for each intensity, varying from 0 to 100%. H-SCORE evaluation was performed independently by blinded three investigators (13).

Statistical Analysis

Statistics analyzed SPSS (15.0). The Kruskal-Wallis test was used for comparisons. Post hoc comparisons were performed with Mann-Whitney U test. For immunostaining evaluation, $p < 0.005$ (0.05/10) are considered statistically significant. For demographic data, $p < 0.016$ (0.05/3) is regarded as statistically significant.

RESULTS

Among the study groups, NonP and EP groups had different mean age ($p=0.016$) and no difference was evident between the mean

numbers of abortions of the groups ($p=0.63$). EP and HP groups were different regarding term delivery ($p=0.005$) (Table 1).

Evaluation of eNOS

EP group had a higher expression in epithelium and subepithelium compared to the HP groups (Figure 1 and Table 2). There was no difference for epithelium between the HP groups (Figure 1A₂-1D₂). The higher subepithelial expression was observed in HP-fim group (Figure 1D₁-1D₂) than the HP-ist group (Figure 1B₁-1B₂). HP-fim group (Figure 1D₁-1D₂) had a higher expression in the muscle region compared to HP-ist (Figure 1B₁-1B₂) and EP (Figure 1E₁-1E₂) groups. No differences were found between the groups in the vascular region.

Evaluation of iNOS

EP group showed the highest expression in epithelium (Figure 2 and Table 3). For subepithelium, NonP (Figure 2A₁-2A₂) and EP (Figure 2E₁-2E₂) groups were higher than other groups. NonP group (Figure 2A₁-2A₂) showed a higher expression than the HP-ist (Figure 2B₁-2B₂) and HP-amp (Figure 2C₁-2C₂) groups. HP-fim group (Figure

Table 1. Demographic data for groups.

	NonP (n=10)	HP (n=7)	EP (n=10)	p*
Age (mean±SD)	35,30 ± 2,75	34,00 ± 7,04	28,10 ± 4,84	0.016**
Term parity (median (min-max))	3 (1-4)	3 (2-5)	2 (1-3)	0.009**
Abortion (median (min-max))	1 (0-2)	0 (0-2)	0 (0-1)	0.063
Ectopic pregnancy (median (min-max))	0	0	1 (1-2)	

Data are expressed as mean ± SD.

** Among the study groups, NonP and EP groups had different mean age ($p=0.016$) and no difference was evident between the mean numbers of abortions of the groups ($p=0.63$). EP and HP groups were different with regard to term delivery ($p=0.005$).

Table 2. The comparison of immunohistochemical staining H-Score values for eNOS in epithelium, subepithelium, muscle and vessel region of fallopian tubes.

eNOS	NonP (a)	HP-ist (b)	HP-amp (c)	HP-fim(d)	EP(e)
Epithelium	232,00 ± 12,78	237,80 ± 11,65	232,70 ± 19,72	229,70 ± 7,49	272,90 ± 11,76*
Subepithelium	203,50 ± 4,88	195,30 ± 7,97	198,40 ± 8,09	205,50 ± 4,64*	226,90 ± 4,33*
Muscle	226,50 ± 6,90	215,70 ± 9,49	228,00 ± 13,15	233,50 ± 6,18**	214,80 ± 8,77
Vessel	251.10 ± 14.60	250.90 ± 17.03	235.30 ± 20.22	243.90 ± 14.64	244.10 ± 13.34

Data are expressed as mean ± SD. The Kruskal-Wallis test was used for comparisons of more than 2 groups' comparisons. For post hoc comparisons, Mann-Whitney U test is used. Statistical comparisons with a p-value below (0.05/10=0.005) are assumed as statistically significant for the immunostaining evaluation.

*p= 0,005 EP group (epithelium and subepithelium) statistically significant than other groups. *p= 0,005 HP-fim group (subepithelium) statistically significant than HP-ist group. ** p= 0,005 HP-fim (muscle) statistically significant than Hp-ist and EP groups.

Table 3. The comparison of immunohistochemical staining H-Score values for iNOS in epithelium, subepithelium, muscle and vessel region of fallopian tubes.

iNOS	NonP (a)	HP-ist (b)	HP-amp (c)	HP-fim(d)	EP(e)
Epithelium	254,90 ± 21,46	238,70 ± 28,88	242,50 ± 11,48	223,50 ± 2,91	284,10 ± 22,99*
Subepithelium	226,10 ± 3,47*	200,80 ± 10,40	209,00 ± 15,29	210,50 ± 14,08	223,50 ± 8,44*
Muscle	238,60 ± 24,24**	212,70 ± 8,26	218,20 ± 7,51	225,90 ± 8,38**	224,50 ± 8,61
Vessel	243,00 ± 17,61	248,80 ± 16,30	239,30 ± 6,37*	230,80 ± 4,56	236,30 ± 14,50

Data are expressed as mean ± SD.

*p= 0,005 EP group (epithelium) statistically significant than other groups. # p= 0,005 EP group and NonP group (subepithelium) statistically significant than HP-ist and HP-fim groups. **p= 0,005 NonP group (muscle) statistically significant than HP-ist and HP-amp groups. **p= 0,005 Hp-fim group (muscle) statistically significant than HP-ist group.

*p= 0,017 Hp-fim group (vessel) statistically significant than HP-amp group.

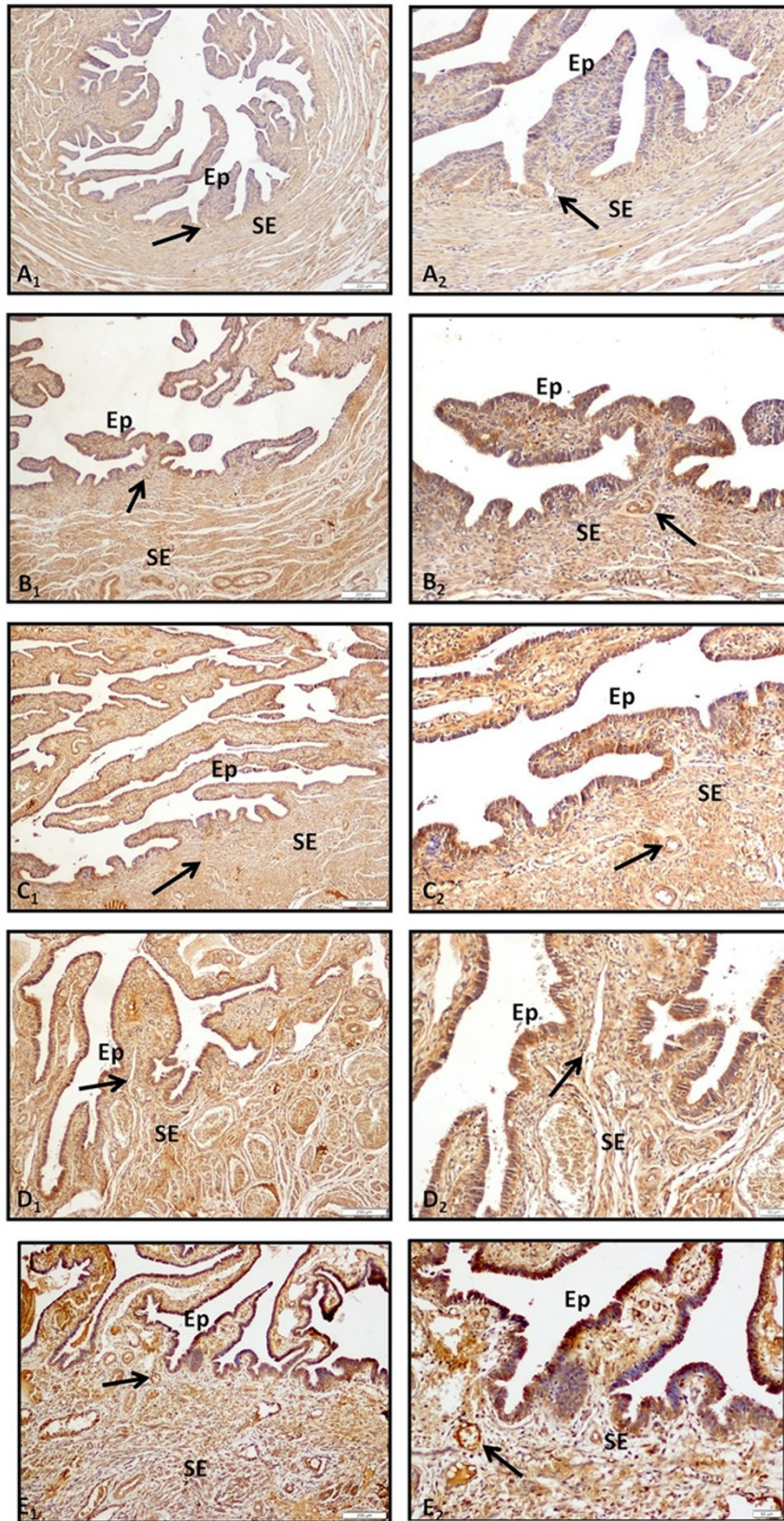


Figure 1. Immunohistochemical analysis of eNOS. The eNOS immunoreactivity of epithelium (Ep) and subepithelium (SE) in fallopian tube in nonpregnant (A) and isthmus (B), ampulla (C) and fimbria (D) of normal pregnancy group were observed weak than the ectopic pregnancy group (E). There were no differences among the vessels (arrow) of the all groups (Scale Bar: A₁-E₁: 200 µm; A₂-E₂: 50 µm).

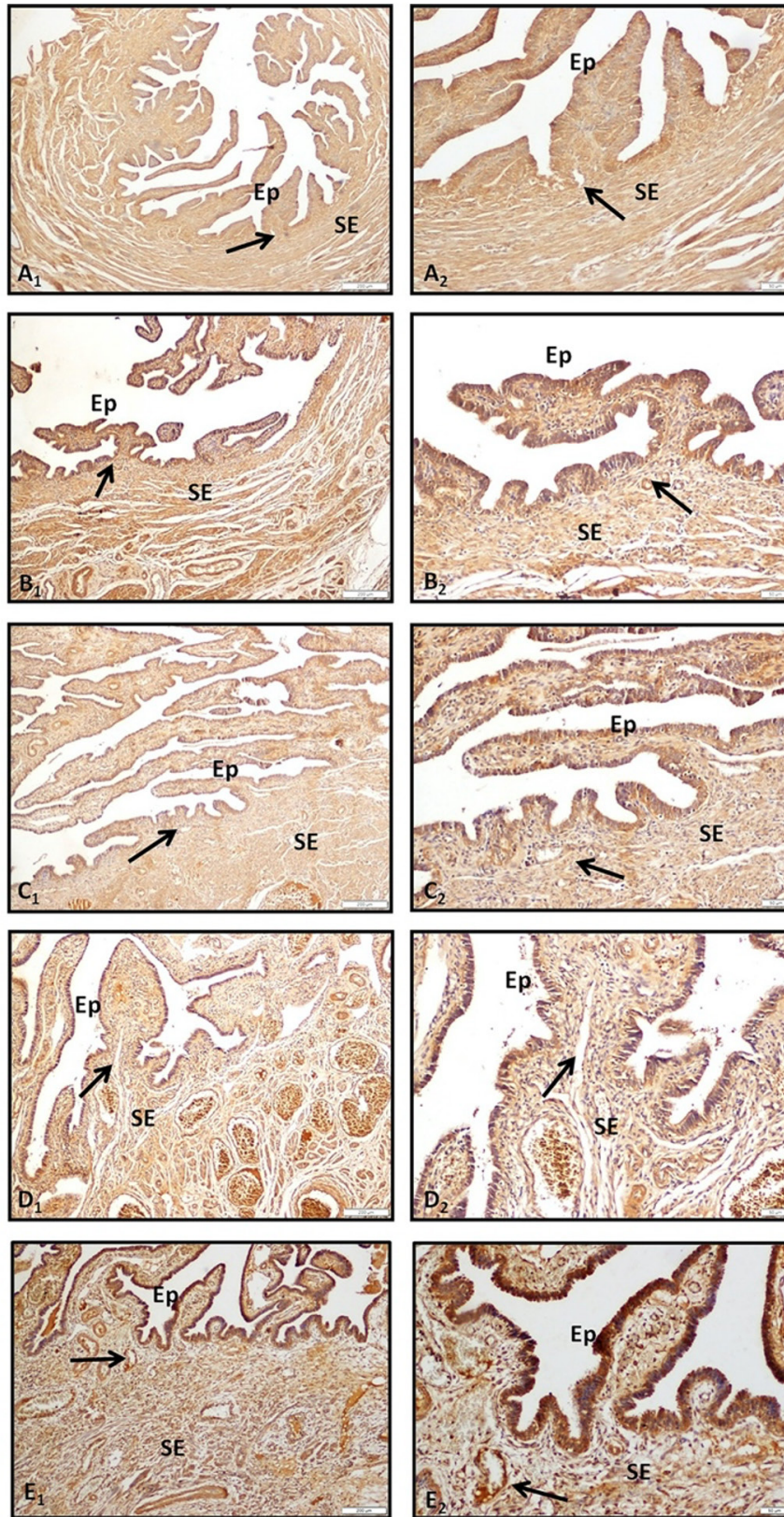


Figure 2. Immunohistochemical analysis of iNOS. The iNOS immunoreactivity of epithelium (Ep) in fallopian tube in nonpregnant (A) and isthmus (B), ampulla (C) and fimbria (D) of normal pregnancy group were observed weak than the ectopic pregnancy group (E). There were no differences among subepithelium (SE) and the vessels (arrow) of the all groups (Scale Bar: A₁-E₁: 200 µm; A₂-E₂: 50 µm).

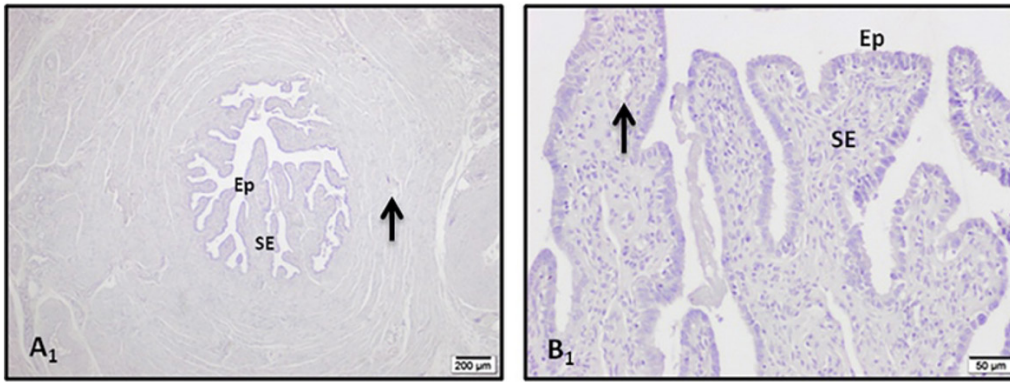


Figure 3. Immunohistochemical analysis of negative control. The negative control of epithelium (Ep), subepithelium (SE) and the vessels (arrow) in fallopian tube in isthmus (A) of normal pregnancy group (Scale Bar: A₁: 200 µm; A₂: 50 µm).

2D₁-2D₂) had a higher expression compared to the HP-ist group (Figure 2B₁-2B₂). In the vascular region, HP-fim group (Figure 2D₁-2D₂) was associated with a lower expression than the HP-amp group. (Figure 2C₁-2C₂).

Specific staining was negative in negative controls of immunohistochemical analyses of tubal tissue samples (Figure 3).

DISCUSSION

In this study, eNOS and iNOS expressions were determined in the fallopian tubes of all-human with NonP, HP, and EP cases. The results of the study demonstrated that, as compared to the NonP and HP groups, the EP group showed a higher eNOS expression in both the epithelium and subepithelium of the fallopian tubes, while it showed a higher iNOS expression in the epithelium of the fallopian tubes. The expressions of these two smooth muscle relaxants (8) were not significantly different in the muscular and vascular regions of fallopian tubes. These results may indicate that these NOS isoforms may induce some alterations facilitating implantation in ciliated and secretory cells of luminal epithelium and subepithelium.

Each isoform of the enzyme family is coded by certain loci on different chromosomes. eNOS is primarily found in cytosol and responsible for short-term NO generation. These enzymes generate NO that functions as a transduction mechanism on which several separate physiological responses are constructed (14, 15). NOS play an important role in signal transduction associated with ciliary functions (16). The activation of macrophages and the stimulatory effects of cytokines like interleukin (IL)-1, IL-2, and IL-12, tumor necrosis factor alpha, and the endotoxin lipopolysaccharide can induce the function of iNOS in endothelial cells and in some various other cell types. iNOS expression ends up with the production of huge amounts of calcium in a calcium-dependent fashion over long periods of time (14, 15).

As Fath-Bayati et al. in 2014 said that was designed a study to investigate the existence and distribution of eNOS in the ampullary sections from fallopian tubes samples of three groups of women: women with EP, women at luteal phase of menstrual cycle and pregnant women at term. Expression of eNOS in luminal epithelium of women with EP compared to the other two groups showed statistically significant increase. It was claimed that increases in expression of eNOS in luminal epithelium of fallopian tube might lead to development of EP. However, various factors are reportedly responsible for the expression of NOS isoforms, fallopian tube variants of these isoforms fluctuate parallelly with hormonal alterations in humans (12). Therefore, our study was not superior to that of Fath-Bayati et al. in 2014 by studying both NOS isoforms simultaneously but by studying fallopian tubes of the first trimester HP that were like fallopian tubes in EP weeks but not those in term pregnancies. It is suggested that we were able to study fallopian tubes under the influence of similar hormone levels by this method (11).

A subsequent study by Hu et al. in 2014 suggested that human fallopian tube epithelium expressed both eNOS and iNOS whereas only iNOS was expressed in muscle cells. They interpreted that the physiological functions such as contractility of the fallopian tube may be dependent on NOS-induced NO production. However, in this study it was demonstrated that both NOS isoforms were expressed in both epithelium and muscle. Muscular expression of iNOS isoform was not different in EP than the other groups. eNOS, on the other hand, showed a higher expression only in the muscles of intrauterine pregnancy fimbriae (12).

A sufficient amount of placental circulation and fetal vascular maturity are prerequisites for a healthy gestation. A complex interplay and cooperation between various cell types and growth factors during fertilized ovum implantation, embryonic development, and placentation are central for the emergence of a vascular network with normal functions (17,18). A number of pregnancy complications ranging from intrauterine growth retardation and

preeclampsia to intrauterine fetal demise and pregnancy loss may emerge as a consequence of abnormally generated and functioning placental vessels (18). NO is a known vascular smooth muscle relaxant and the deficiency of which is known to cause vasospasm and vascular infraction (8). In our study, however, we found no significant differences in eNOS and iNOS of the fallopian tube vessels of the EP group compared to the other groups.

EP is a result of the interplay of a multitude of different factors, some of which can be named as pelvic inflammatory diseases, infections, increased age at conception, smoking, and in vitro fertilization. Chlamydia infection in particular, and other conditions, that induce inflammatory reactions in genitalia are a primary culprit for EP in humans (2). Chlamydia infection favors fallopian tubes as the primary site of invasion (19), and these structures regulate innate and adaptive immune responses to function as the initial defensive site against this infection (20). Such that, early abnormalities of the motility of tubal cells elicited by infection lead to defective ciliary activity, epithelial secretory function, and weakened contractility, which may end up with ectopic pregnancy. Fallopian tubes witness the attack and invasion of epithelial cells and macrophages by Chlamydia Trachomatis (CT) as the microorganism's primary cellular targets (21). An interesting aspect of this study was to find the presence of specific iNOS and eNOS expression in epithelial cells, a site for the regulation of NO production by NO synthases via autocrine and paracrine effects. However, it is not entirely clear how CT infection, eNOS, iNOS, and tubal tissue/cell destruction are interconnected with each other. It has been suggested by some robust evidence that long-term and severe inflammation results in tissue remodeling and scarring of fallopian tubes that leads to the risk of tubal ectopic gestation (22,23).

Tubal NO production induced by CT infection can be both beneficial and harmful. NO can be part of immune responses against certain microorganisms in these structures, although excessive reactions may cause tubal scarring and EP (24). Despite the multifactorial origin of ectopic pregnancy, eNOS and iNOS are probably important factors in the occurrence of this pathological condition, as suggested by increased levels of these isoforms in the epithelium of the fallopian tubes of women with tubal EP (11,12).

Recent advancements in understanding the role of nitric oxide (NO) and its synthases (NOS) in reproductive health continue to shed light on conditions like ectopic pregnancy (EP) and endometriosis. A narrative review by Yeo et al. (2025) highlights the dual role of NO in the pathogenesis of endometriosis, emphasizing the involvement of eNOS and iNOS. While their focus is on endometriosis, the shared inflammatory and physiological pathways with EP suggest that these findings are highly relevant (25). The review indicates that

increased NO levels are often associated with the pathogenesis of endometriosis, mediated by various factors including inflammatory molecules and hormonal actions. This aligns with our findings of increased eNOS and iNOS expression in EP, suggesting a similar underlying mechanism where NO contributes to pathological changes in the fallopian tube microenvironment.

Further research by Refaat et al. (2025) specifically investigates the role of inducible nitric oxide synthase (iNOS) in ectopic implantation within the fallopian tubes, reinforcing the significance of iNOS in the context of EP (26). This supports our observation of higher iNOS expression in the epithelium of fallopian tubes in EP cases. The intricate balance of NO production, influenced by both eNOS and iNOS, appears crucial for normal tubal function and embryo transport. Disruptions in this balance, as seen in increased expression of these enzymes, could create a microenvironment conducive to ectopic implantation.

Moreover, a scoping review by Jackuliak et al. (2025) on infertility in diabetic women mentions increased expression of eNOS in the diabetic uterus, linking it to uterine tube infertility (27). While not directly about EP, this further underscores the sensitivity of the reproductive tract to changes in NOS expression and the potential for systemic conditions to impact tubal health and fertility outcomes. These recent studies collectively emphasize the ongoing importance of understanding NOS isoforms in reproductive disorders and provide contemporary context for our findings regarding eNOS and iNOS in tubal ectopic pregnancy.

The limitation of our study was the inability to study NOS expression in all tubal regions of the two groups other than the HP group. For the sake of the operative procedures, EP group samples belonged to the ampullar region, the most common location of EP, NonP group samples were from the tubal isthmus region. We noted higher expressions of both eNOS and iNOS in the fimbria muscle region than the isthmic muscle region in the HP group. This may indicate that an increase in these two NOS isomers in the muscular region of tubal fimbriae may in fact be necessary for the transport of the oocyte to the ampulla in human fallopian tubes. Lapointe et al. in 2006 also suggested a possible role of iNOS in the tubal transport of oocytes in the fallopian tubes of bovine oviducts (28).

CONCLUSION

The expression of eNOS and iNOS is increased in the tubal epithelium of ectopic pregnancy. This finding suggests that these two NOS isoforms may have facilitatory effects on implantation within the ciliated and secretory cells of the luminal epithelium and

subepithelium, potentially creating a favorable microenvironment for EP. However, further research is required to determine whether this alteration acts as a pathological factor promoting EP development or serves as a protective mechanism against it.

Funding: The author(s) received no financial support for the research, authorship and/or publication of this article.

Author Contributions: Conceptualization: F.E, Data Curation: T.O., M.A.U.A., S.T., T.G, Formal Analysis: T.O., M.A.U.A, Investigation: F.E., K.O, Methodology: T.O, M.A.U.A, Project Administration: F.E, Supervision: F.E, Writing – Original Draft: F.E., T.O., K.O, Writing – Review & Editing: T.O,

Conflict of interests: The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

REFERENCES

- Varma R, Gupta J. Tubal ectopic pregnancy. *BMJ Clin Evid*. 2012;2012:1406.
- Shaw JL, Dey SK, Critchley HO, Horne AW. Current knowledge of the aetiology of human tubal ectopic pregnancy. *Hum Reprod Update* 2010;16(4):432-44.
- Ekerhovd E, Brännström M, Alexandersson M, Norström A. Evidence for nitric oxide mediation of contractile activity in isolated strips of the human Fallopian tube. *Hum Reprod*. 1997;12(2):301-5.
- Rosselli M, Keller PJ, Dubey RK. Role of nitric oxide in the biology, physiology and pathophysiology of reproduction. *Hum Reprod Update*. 1998;4(1):3-24.
- Perez Martinez S, Viggiano M, Franchi AM, Herrero MB, Ortiz ME, Gimeno MF, et al. Effect of nitric oxide synthase inhibitors on ovum transport and oviductal smooth muscle activity in the rat oviduct. *J Reprod Fertil*. 2000;118(1):111-7.
- Szóstek AZ, Siemieniuch MJ, Deptula K, Woclawek-Potocka I, Majewska M, Okuda K, et al. Ovarian steroids modulate tumor necrosis factor- α and nitric oxide-regulated prostaglandin secretion by cultured bovine oviductal epithelial cells. *Domest Anim Endocrinol*. 2011;41(1):14-23.
- Kim BH, Kim CH, Jung KY, Jeon BH, Ju EJ, Choo YK. Involvement of nitric oxide during in vitro fertilization and early embryonic development in mice. *Arch Pharm Res*. 2004;27(1):86-93.
- Cauwels A, Brouckaert P. Nitrite regulation of shock. *Cardiovasc Res*. 2011;15;89(3):553-9.
- Khankin EV, Royle C, Karumanchi SA. Placental vasculature in health and disease. *Semin Thromb Hemost*. 2010;36(3):309-20.
- Moncada S, Palmer RM, Higgs EA. Nitric oxide: physiology, pathophysiology, and pharmacology. *Pharmacol Rev*. 1991;43(2):109-42.
- Fath Bayati L, Ghaffari Novin M, Fadaei Fathabadi F, Piryaee A, Heidari MH, Bandehpour M, et al. Association between increased expression of endothelial isoform of nitric oxide synthase in the human fallopian tube and tubal ectopic pregnancy. *Iran J Reprod Med*. 2014;12(1):19-28.
- Hu J, Ma S, Zou S, Li X, Cui P, Weijdegård B, et al. The regulation of nitric oxide synthase isoform expression in mouse and human fallopian tubes: potential insights for ectopic pregnancy. *Int J Mol Sci*. 2014;16(1):49-67.
- Ozbilgin MK, Eskicioğlu F, Birinci H, Turkoz Uluer E, Karanlık B, Gökmen T. Vasoactive intestinal Peptide/Pituitary Adenylate Cyclase activating polypeptide and their receptors in tubal ectopic pregnancy and missed abortion. *International Journal of Sciences & Applied Research*. 2018;5(10):01-12.
- Bryan NS, Bian K, Murad F. Discovery of the nitric oxide signaling pathway and targets for drug development. *Front Biosci (Landmark Ed)*. 2009;14:1-18.
- Maul H, Longo M, Saade GR, Garfield RE. Nitric oxide and its role during pregnancy: from ovulation to delivery. *Curr Pharm Des*. 2003;9(5):359-80.
- Zhan X, Li D, Johns RA. Expression of endothelial nitric oxide synthase in ciliated epithelia of rats. *J Histochem Cytochem*. 2003;51(1):81-7.
- Reynolds LP, Redmer DA. Angiogenesis in the placenta. *Biol Reprod*. 2001;64(4):1033-40.
- Reynolds LP, Borowicz PP, Caton JS, Vonnahme KA, Luther JS, Buchanan DS, et al. Uteroplacental vascular development and placental function: an update. *Int J Dev Biol*. 2010;54(2-3):355-66.
- Shao R, Hu J, Billig H. Toward understanding Chlamydia infection-induced infertility caused by dysfunctional oviducts. *J Infect Dis*. 2013;208(4):707-9.
- Wira CR, Fahey JV, Sentman CL, Pioli PA, Shen L. Innate and adaptive immunity in female genital tract: cellular responses and interactions. *Immunol Rev*. 2005;206:306-35.
- Igiertseme JU, Perry LL, Ananaba GA, Uriri IM, Ojior OO, Kumar SN, et al. Chlamydial infection in inducible nitric oxide synthase knockout mice. *Infect Immun*. 1998;66(4):1282-6.
- Stephens RS. The cellular paradigm of chlamydial pathogenesis. *Trends Microbiol*. 2003;11(1):44-51.
- Entrican G, Wattedegera S, Rocchi M, Fleming DC, Kelly RW, Wathne G, et al. Induction of inflammatory host immune responses by organisms belonging to the genera *Chlamydia*/*Chlamydia*. *Vet Immunol Immunopathol*. 2004;100(3-4):179-86.
- Refaat B, Al-Azemi M, Geary I, Eley A, Ledger W. Role of activins and inducible nitric oxide in the pathogenesis of ectopic pregnancy in patients with or without *Chlamydia trachomatis* infection. *Clin Vaccine Immunol*. 2009;16(10):1493-503.
- Yeo SG, Oh YJ, Lee JM, Kim SS, Park DC. A Narrative Review of the Expression and Role of Nitric Oxide in Endometriosis. *Antioxidants (Basel)*. 2025;14(3):247.
- Refaat B, Simpson H, Britton E, Biswas J, Wells M, Aplin JD, Ledger W. Why does the fallopian tube fail in ectopic pregnancy? The role of activins, inducible nitric oxide synthase, and MUC1 in ectopic implantation. *Fertil Steril*. 2012;97(5):1115-23.
- Jackuliak P, Jankovský M, Kovářová M, Voller J, Feitscherová C, Varga I. Impact of hyperglycaemia on cellular microenvironment and function of endometrium and uterine tube: scoping review focused on infertility in diabetic women. *Front Cell Dev Biol*. 2025;13:1582039.
- Lapointe J, Roy M, St-Pierre I, Kimmins S, Gauvreau D, MacLaren LA, et al. Hormonal and spatial regulation of nitric oxide synthases (NOS) (neuronal NOS, inducible NOS, and endothelial NOS) in the oviducts. *Endocrinology*. 2006;147(12):5600-10.

Menstrual Hassasiyet İndeksi: Türkçe Geçerlik ve Güvenirlik Çalışması

Menstrual Sensitivity Index: Turkish Validity and Reliability Study

 Ebru İNAN KIRMIZIGÜL¹,  Didem ŞİMŞEK KÜÇÜKKELEPÇE²

¹Sağlık Bilimleri Üniversitesi Gülhane Sağlık Bilimleri Fakültesi Ebelik Bölümü, Ankara, Türkiye

²Lokman Hekim Üniversitesi Sağlık Bilimleri Fakültesi Ebelik Bölümü, Ankara, Türkiye

ÖZ

Amaç: Bu araştırma, Menstrual Hassasiyet İndeksi (Menstrual Sensivity Index/MSI)'nin Türk toplumuna uyarlanması, geçerlik güvenirliğinin yapılması amacıyla gerçekleştirilmiştir.

Gereç ve Yöntemler: Metodolojik tipteki bu araştırmanın örneklemini doğurganlık çağındaki 393 kadın oluşturmuştur. Verilerin toplanmasında, "Tanıtıcı Bilgi Formu", "Visual Analog Skala (VAS)", "Menstrual Hassasiyet İndeksi (MHI)" ve "Menstrüasyon Semptom Ölçeği (MSÖ)" kullanılmıştır. İstatistiksel analizde SPSS 22 ve AMOS 25 paket programı kullanılmıştır. Ölçeğin geçerliliği, dil, kapsam, yapı ve ölçüt bağıntılı geçerlik ile; güvenirliliği ise Cronbach alfa katsayısı ve madde analizleri ile değerlendirilmiştir. Madde toplam korelasyon ve %27'lik alt grup üst grup karşılaştırması yapılmıştır.

Bulgular: Ölçeğin kapsam geçerlik indeksi 0,94 olarak belirlenmiştir. Madde-toplam puan korelasyonu 0,41 ile 0,72 değerleri arasında değişmektedir. Ölçeğin 4. Maddesinin faktör yükü 0,45 olup, diğer tüm maddelerin faktör yükleri 0,60'ın üzerinde bulunmuştur. MHI Türkçe formunun Cronbach alfa değeri 0,84 olarak tespit edilmiştir. MHI'nin üç faktörlü yapısının doğrulanarak ($p < 0,01$; $\chi^2/df=3,69$; RMSEA=0,080; CFI=0,96; GFI=0,96), modelin veriyle iyi düzeyde uyum sağladığı belirlenmiştir.

Sonuç: MHI'nin Türkçe versiyonunun doğurganlık çağındaki kadınlarda menstrual hassasiyeti belirlemede kullanılabilecek geçerli ve güvenilir bir ölçüm aracı olduğu belirlenmiştir.

Anahtar Kelimeler: Geçerlik, güvenirlik, hassasiyet, hemşirelik, menstrual.

ABSTRACT

Aim: The aim of this study was to adapt the Menstrual Sensitivity Index (MSI) into Turkish.

Materials and Methods: The sample of this methodological study consisted of 393 women of childbearing age. "Descriptive Information Form", "Visual Analog Scale (VAS)", "Menstrual Sensitivity Index (MSI)" and "Menstrual Symptom Scale (MSQ)" were used for data collection. SPSS 22 and AMOS 25 package programs were used for statistical analysis. The validity of the scale was assessed by language, content, construct and criterion-related validity; reliability was assessed by Cronbach's alpha coefficient and item analysis. Item-total correlations and 27% subgroup-superior group comparisons were made.

Results: The content validity index of the scale was determined as 0.94. The item-total score correlation ranged between 0.41 and 0.72. The factor loading of the 4th item of the scale was 0.45, and the factor loadings of all other items were found to be above 0.60. The Cronbach's alpha value of the Turkish version of the MSI was found to be 0.84. The three-factor structure of the MSI was confirmed ($p < 0,01$; $\chi^2/df=3,69$; RMSEA=0,080; CFI=0,96; GFI=0,96) and the model was found to fit the data well.

Conclusion: It was determined that the Turkish version of the MSI is a valid and reliable measurement tool that can be used to determine menstrual sensitivity in women of childbearing age.

Keywords: Validity, reliability, sensitivity, nursing, menstrual.

Cite as: İnan Kırmızıgül E ve Şimşek Küçükkelepçe D. Menstrual Hassasiyet İndeksi: Türkçe Geçerlik ve Güvenirlik Çalışması. Jinekoloji-Obstetrik ve Neonatoloji Tıp Dergisi 2026;23(2):190–197.

Geliş/Received: 24.07.2025 • **Kabul/Accepted:** 15.11.2025

Sorumlu Yazar/Corresponding Author: Ebru İnan Kırmızıgül, Sağlık Bilimleri Üniversitesi Gülhane Sağlık Bilimleri Fakültesi Ebelik Bölümü, Türkiye

E-mail: inanebruli@gmail.com

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

GİRİŞ

Menstruasyon; menarşla başlayıp periyotlarla devam eden kadın yaşamında önemli dönemlerden biridir. Bu dönemde kadınların menstrüasyonla ilgili yoğun kanama, ağrı, yorgunluk ve ruh hali değişiklikleri ile fiziksel, sosyal ve duygusal açıdan etkilendikleri bilinmektedir (1). Tüm dünyada menstrual sorunlar jinekolojik ziyaretlerin en yaygın nedenidir ve kadınların %50-90'ını etkilemektedir (2). Yapılan toplum tabanlı bir araştırmada, kadınların yarısından fazlası (%59) menstrüasyon semptomları nedeniyle sosyal aktivitesini kısıtladığını ve %45'inin yılda birkaç kez okula gidemediğini bildirmiştir (3). Bu etkilenmenin en önemlisi kadınların yaşam kalitesini düşürmesidir (4). Buna rağmen ağrının kadınlar için menstrüasyonun bir parçası olduğuna dair yaygın inanış, tıbbi yardıma başvurmalarında en büyük engel olarak görülmektedir (2). Menstrual semptomların deneyimi ve etkisi her kadın için farklı olduğundan, menstrüel ağrı ve semptomlara karşı daha hassas olanları belirleme ve bu hassasiyete katkıda bulunan faktörleri tanımlama konusunda karşılanmamış bir ihtiyaç vardır (5-7).

Menstrual semptomlara yönelik hassasiyetin fizyolojik ve psikolojik boyutları bulunmaktadır. Yapılan bir meta analiz çalışmasında; orta ve şiddetli menstrual ağrıya sahip kadınların kronik pelvik ağrı yaşama durumlarının daha yüksek olduğu belirlenmiştir (8). Bu durumun ağrı hassasiyetini artıran nörofizyolojik ve biyokimyasal faktörler olduğunu göstermektedir (9). Üreme çağındaki 760 kadınla yapılan kesitsel çalışmada; menstrüasyon boyunca ağrı yaşadığını ifade edenlerin ağrı şiddeti daha yüksek bulunmuştur (10). Psikolojik açıdan incelendiğinde; ağrıya yönelik negatif duyguların ve anksiyetenin ağrı hassasiyetini artırdığı bilinmektedir. Aynı zamanda anksiyete düzeyi arttıkça menstrual ağrı şiddetinin de arttığı belirlenmiştir (7,11). Bu veriler, bireyin ağrıyı nasıl algıladığı ve ağrıyla nasıl başa çıktığı gibi bilişsel süreçlerin, gerçek ağrı deneyimi üzerinde belirleyici olabileceğini göstermektedir (12). Bu nedenle, menstrüel semptomlara yönelik hassasiyetin, ağrının şiddetlenmesi ve devam etmesine neden olabileceği olası bir sonuç olarak görülmektedir.

Semptom duyarlılığı; mevcut sorunların derinleşmesine ve kötüye gitmesine neden olabilmektedir. Literatürde anksiyete duyarlılığı akut ve kronik ağrı ile ilişkilendirilmiştir (13). Menstrual semptomlarla ilgili anksiyete çift yönlü değerlendirilmektedir. Menstrual döngüde, gastrointestinal belirtileri ve bedensel duyuları yoğun yaşayanların anksiyete hassasiyeti yüksek iken, anksiyete hassasiyeti yüksek olanların ise bedensel duyuları algılama eşiği düşük gösterilmiştir. (5,11). Kronik pelvik ağrısı olan kadınlardan oluşan bir popülasyonda elde edilen sonuçlar ise, kronik pelvik ağrıya sahip kadınların geriye dönük incelemesinde dismenoreye ilişkin olumsuz düşüncelerin artışı ve anksiyete öyküsüne sahip

oldukları belirlenmiştir (6,10). Menstrual duyarlılık, özellikle adet kanamasının bir sonucu olarak ortaya çıkan fiziksel semptomlarla ilgili korku ve endişedir (14). Menstrüel duyarlılığın tanımlanması ve ölçülmesi, kadınların menstrüel ağrı deneyimindeki daha iyi aydınlatılmasına yardımcı olabilir ve terapötik müdahaleler için olası bir çözüm sağlayabilir. Literatürde menstrual semptomları değerlendiren ölçek bulunmaktadır ancak menstrual duyarlılığı önceden saptayan ölçeğe rastlanmamıştır. Bu nedenle, bu çalışma Handy ve arkadaşları tarafından geliştirilen menstrüel duyarlılığı değerlendiren Menstrual Hassasiyet İndeksi'nin Türkçe geçerlik ve güvenilirliğinin yapılması amacıyla yapılmıştır.

GEREÇ VE YÖNTEMLER

Araştırmanın Tipi

Bu çalışma metodolojik tipte epidemiyolojik bir araştırma olarak gerçekleştirilmiştir.

Araştırmanın Evren ve Örneklemi

Araştırmanın evreni 1 Eylül 2024- 30 Ocak 2025 tarihleri arasında sosyal medya platformları (Whatsapp, Instagram) aracılığıyla ulaşılan, doğurgan çağıdaki kadınlardan oluşmaktadır. Araştırmaya 18-55 yaş arasında olan, son 12 ay içerisinde düzenli menstrual döngüsü olduğunu bildiren ve son 3 ayda en az bir kez menstrual döngü yaşamış, çevrim içi anketi doldurabilecek telefon ve internet erişimi olan kadınlar dahil edilmiştir. Okuryazar olmayan, gebe olan kadınlar çalışma dışında tutulmuştur. Ölçek çalışmalarında, ölçeğin psikometrik özelliklerinin belirlenmesine ilişkin literatüre göre en az 300-400 kişilik örneklemin yeterli olduğu belirtilmektedir (15). Başka bir kaynakta ölçek uyarlama çalışmaları için 300 kişinin "iyi", 500 kişinin çok iyi olduğu ifade edilmektedir (16). MHI ölçeğinde 8 madde bulunmaktadır. Araştırmaya 393 kadın katılmıştır.

Veri Toplama Araçları

Araştırmada veriler; "Tanıtıcı Bilgi Formu" ve "Visual Analog Skala", "Menstrual Hassasiyet İndeksi" ve "Menstrüasyon Semptom Ölçeği" kullanılarak toplanmıştır. MHI'nin ölçüt bağıntılı geçerliliğinin değerlendirilmesinde VAS ve MSÖ kullanılmıştır.

Tanıtıcı Bilgi Formu: Katılımcıların yaş, eğitim, gelir, çalışma durumu, menstrüasyon özelliklerini inceleyen 6 sorudan oluşmaktadır.

Visual Analog Skala: Ağrı şiddetini ölçmekte ve ağrı takibinde kullanılmaktadır. Bu skala ağrının şiddetini ölçen basit (10 cm yatay ölçekten oluşan skalada, '0' ağrının olmadığını ve '10' ise ağrının en şiddetli düzeyde olduğunu ifade etmektedir) bir yöntemdir. Katılımcıların son adetinde hissettiği ağrı şiddeti seviyesini 0-10 puan arasında derecelendirmesi istenmiştir (17).

Menstrual Hassasiyet İndeksi (Ek): Ölçek Handy ve arkadaşları tarafından (2024) geliştirilmiştir. MHI menstrual semptomlara karşı hassasiyeti ve korkuyu değerlendirmeyi amaçlayan kısa bir ölçüm aracıdır. İndeks 8 maddeli üç alt boyuttan oluşmaktadır. Madde 1, 2, 3 ve 4 “somatik kaygı” (menstrüasyonla ilişkili fiziksel duyumların sonuçları hakkında endişe), madde 5 ve 6 “korku-tehlike” (menstrüasyonla ilişkili fiziksel duymalardan korku), madde 7 ve 8 “ilaca bağlı kaygı” (menstrüasyona bağlı ağrıyı hafifletme yeteneğiyle ilgili kaygı) alt boyutunu temsil etmektedir. Her madde 1: kesinlikle katılıyorum, 6: kesinlikle katılmıyorum şeklinde 6’lı likert tipinde oluşturulmuştur. Maddeler ters puanlanmaktadır (örn; 1 yanıtı 5 puan, 6 yanıtı 0 puan şeklinde girilir). Böylece tüm maddeler 0-5 arasında puan alır ve 0-40 arasında değişen nihai puanı oluşturmak için toplanır. Daha yüksek puanlar, daha fazla menstrual ağrı hassasiyetini göstermektedir. Ölçeğin orijinal formunda Cronbach alfa 0,80 olarak bulunmuştur (14). Bizim çalışmamızda Cronbach alfa değeri 0,84’tür.

Menstrüasyon Semptom Ölçeği: Ölçek, 1975’de Chesney ve Tasto tarafından menstrüasyon ağrısı ve semptomlarını değerlendirmek amacıyla geliştirilmiş, Türkçe geçerlik güvenirliği Güvenç ve ark. (2014) tarafından yapılmıştır. Yirmi iki maddeden oluşan 5’li likert tipte (1=hiç bir zaman, 5=her zaman) bir ölçektir. MSÖ puanı, ölçekteki maddelerin toplam puan ortalaması alınarak hesaplanmaktadır. Ölçekten alınabilecek en düşük puan 22, en yüksek puan 110’dur. Puan ortalamasının yükselmesi menstrual semptomların şiddetinin arttığını göstermektedir. Ölçeğin Cronbach alfası 0,92 olarak bulunmuştur (18). Bizim çalışmamızda Cronbach alfa değeri 0,85’tir.

Verilen Toplanması: Araştırmada kullanılan veri toplama formları Google Forms olarak online ortama yüklenmiştir. Sosyal medya (WhatsApp, Instagram) platformlarında paylaşılarak katılımcılar araştırmaya davet edilmiştir. Formların doldurulması yaklaşık 10 dakika sürmüştür.

Verilerin Analizi: Araştırmadan elde edilen verilerin analizinde SPSS (Statistical Package for the Social Sciences) 22 ve AMOS 25 paket programı kullanılmıştır. Tanımlayıcı istatistikler kapsamında, sürekli değişkenler için aritmetik ortalama, standart sapma, minimum ve maksimum değerler, kategorik değişkenler için ise frekans ve yüzde dağılımları hesaplanmıştır. Ölçeğin kapsam geçerliliği için I-CVI ve S-CVI değerleri incelenmiş, yapı geçerliliği doğrulayıcı faktör analizi (DFA) ile test edilmiştir. Ölçüt geçerliliğini belirlemek amacıyla Pearson korelasyon analizi, ayırt edicilik düzeyini değerlendirmek için ise alt ve üst %27’lik gruplar arasında bağımsız gruplar t-testi uygulanmıştır. Ölçeğin güvenirliği Cronbach’s Alpha iç tutarlılık katsayısı ve madde analizleri ile değerlendirilmiştir. Analizlerde anlamlılık düzeyi $p < 0.05$ olarak kabul edilmiştir.

Etik Yönü: MHI orijinal ölçeği geliştiren yazarlardan ölçeğin Türkçe’ye uyarlanmasında mail aracılığıyla izin alınmıştır. Lokman Hekim Üniversitesi Bilimsel Araştırmalar Etik Kurulu’ndan onay alınmış (31 Temmuz 2024, Karar No: 2024/172) ve ölçek yazarlarından kullanım izni alınmıştır. Araştırma süreci boyunca araştırma ve yayın ettiği ilkelerine uyulmuş ve araştırma Helsinki Bildirgesi’ne uygun olarak yürütülmüştür.

BULGULAR

Araştırma grubundaki kadınların %35,4’ü 18-25 yaş, %28’i 26-30 yaş, %17,3’ü 31-34 yaş, %14,2’si 36-40 yaş ve %5,1’i 41 yaş ve üzeri aralıkta olduğu belirlenmiştir. Kadınların %62,1’inin lisansüstü mezunu olduğu, %47,6’sının bekar olduğu, %51,7’sinin gelir getiren bir işte çalıştığı ve %51,9’unun gelir giderine eşit olduğu belirlenmiştir.

Dil Geçerliliği

MHI’nin orijinal formu olan Menstrual Sensivity Index-MSI’nin dil geçerliliğini değerlendirmek için Türkçe ve İngilizce’yi iyi bilen kadın sağlığı alanında çalışan yedi uzman tarafından çevirisi yapılmıştır. Çeviri sonrası ölçekte yer alan maddeler araştırmacılar tarafından değerlendirilerek Türkçe çevirisine son hali verilmiştir. Sonrasında Türkçe metin orijinal ölçeği bilmeyen bağımsız bir dil uzmanı tarafından İngilizce’ye çevrilmiştir. Bu çeviri formunun, ölçeğin orijinal hali ile tutarlı olduğu saptanmıştır.

Kapsam Geçerliliği

MHI’nin kapsam geçerliliği, alanında uzman yedi kişiden elde edilen değerlendirme puanları doğrultusunda hesaplanan Madde Düzeyi Kapsam Geçerlilik İndeksi (I-CVI) ve Ölçek Düzeyi Kapsam Geçerlilik İndeksi (S-CVI) ile değerlendirilmiştir. Uzmanlar, her bir maddeyi 4’lü dereceli bir uygunluk ölçeğinde (1 = uygun değil, 4 = tamamen uygun) puanlamıştır. Davis tekniğine dayalı analiz sonucunda, maddelerin I-CVI değerleri 0,857 ile 1,000 arasında değişmektedir. Tüm maddelerin I-CVI değeri 0,857 ve üzerindedir. Tüm maddeler için genel uyumu gösteren S-CVI değeri 0,946 olarak hesaplanmıştır. Tüm maddeler için genel uyumu gösteren S-CVI 0,946 olarak hesaplanmıştır. Alt boyutlara göre incelendiğinde; somatik kaygı için 0,929, korku-tehlike için 1,000 ve ilaca bağlı kaygı için 0,929 değerleri elde edilmiştir.

Yapı Geçerliliği

MHI’nin yapı geçerliliğini belirlemek amacıyla doğrulayıcı faktör analizi yapılmıştır. Faktör analizine geçmeden önce yapılan KMO ve Bartlett testi sonuçlarına göre, KMO değeri 0,803 ile örneklemin yeterli olduğunu göstermektedir. Bartlett’s Test sonucu anlamlıdır ($\chi^2 = 1403,512$; $sd = 28$; $p < 0,001$) ve değişkenler arasında yeterli korelasyon bulunduğunu ortaya koymaktadır. Bu bulgular, verilerin faktör analizine uygun olduğunu göstermektedir.

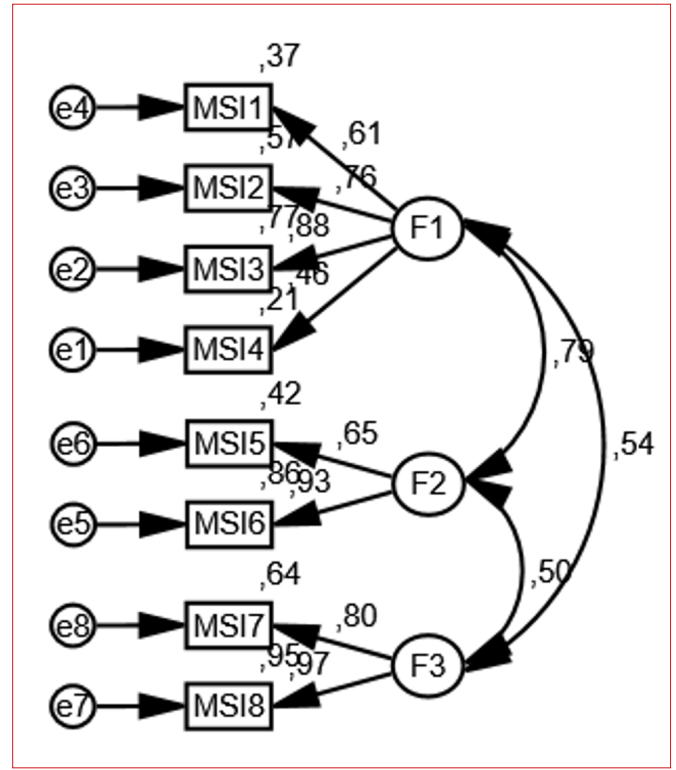
Tablo 1. Doğrulayıcı Faktör Analizi İndeks Değerleri

Uyum İndeksleri	MHi Uyum Değerleri	Normal Değer*	Kabul Edilebilir Değer**
χ^2	62,883	—	—
df	17	—	—
χ^2/df (CMIN/DF)	3,699	≤ 3	≤ 5
CFI	0,967	$\geq 0,95$	$\geq 0,90$
GFI	0,962	$\geq 0,95$	$\geq 0,90$
AGFI	0,920	$\geq 0,95$	$\geq 0,90$
NFI	0,956	$\geq 0,95$	$\geq 0,90$
TLI	0,946	$\geq 0,95$	$\geq 0,90$
IFI	0,967	$\geq 0,95$	$\geq 0,90$
RMSEA	0,080	$\leq 0,05-0,06$	$\leq 0,08$
RMR	0,079	$\leq 0,05$	$\leq 0,08$
SRMR	0,078	$\leq 0,05$	$\leq 0,08$

* Normal Değer: İdeal uyum aralıkları (Kaynak 29,30)

** Kabul Edilebilir Değer: Literatürde pratikte yeterli kabul edilen aralıklar (Kaynak 31,32)

CMIN/DF: Göreceli Ki-kare İndeksi; CFI: Karşılaştırmalı Uyum İndeksi; GFI: Uyum İyiliği İndeksi; AGFI: Düzeltilmiş Uyum İyiliği İndeksi; NFI: Normlaştırılmış Uyum İndeksi; TLI: Tucker Lewis İndeksi; IFI: Fazlalık Uyum İndeksi; RMSEA: Yaklaşık Hataların Ortalama Karekökü; RMR: Standartlaştırılmış Ortalama Hataların Karekökü; SRMR: Standartlaştırılmış Ortalama Hataların Karekökü

**Şekil 1.** Doğrulayıcı Faktör Analizi Diyagramı

Doğrulayıcı Faktör Analizi

MHi'nin yapı geçerliğini test etmek amacıyla doğrulayıcı faktör analizi (DFA) gerçekleştirilmiştir. Ölçek, kuramsal temele dayalı olarak üç faktörlü bir yapı üzerinden modellenmiş ve analiz sonucunda bu yapının veri ile uyum düzeyi değerlendirilmiştir. Modelin genel uyumuna ilişkin bulgular Şekil 1'de görselleştirilmiş, çeşitli uyum indeksleri ise Tablo 1'de sunulmuştur.

Modelin uyum iyiliğini değerlendirmek amacıyla çeşitli uyum indeksleri incelenmiştir. Elde edilen uyum değerleri, kabul edilebilir sınır aralıkları ile Tablo 2'de sunulmuştur.

Modelin uyum iyiliği indeksleri genel olarak kabul edilebilir ve iyi düzeyde uyum göstermektedir. MHi için ki karenin serbestlik derecesine bölünmesiyle elde edilen değer 3,699 bulunmuştur. Özellikle CFI, GFI, NFI ve TLI değerlerinin 0,90'ın üzerinde olması, modelin gözlenen verilerle güçlü bir şekilde örtüştüğünü göstermektedir. RMSEA değeri 0,080 ve RMR değeri 0,079 olarak bulunmuştur. Bu sonuçlar, ölçeğin varsayılan faktör yapısının doğrulandığını göstermektedir. Ayrıca, her bir maddenin ait olduğu faktöre olan yükü, standartlaştırılmış katsayılar (Std. β), standart hata (S.Hata), kritik oran (C.R) ve anlamlılık düzeyi (p) ile birlikte analiz edilmiştir. Sonuçlar Tablo 2'de verilmiştir.

Tablo 2. Menstrual Hassasiyet İndeksi Faktör Yükleri

Maddeler ve Faktörler			β	Std. β	S.Hata	C.R	p	R²
MHi4	<---	F1	1,000	,455				,642
MHi3	<---	F1	2,731	,876	,307	8,906	p<0,001	,948
MHi2	<---	F1	2,248	,757	,262	8,567	p<0,001	,423
MHi1	<---	F1	1,641	,610	,210	7,824	p<0,001	,857
MHi6	<---	F2	1,000	,926				,372
MHi5	<---	F2	,601	,650	,051	11,889	p<0,001	,573
MHi8	<---	F3	1,000	,973				,768
MHi7	<---	F3	,748	,801	,056	13,397	p<0,001	,207

MHi: Menstrual Hassasiyet İndeksi, β : Standardize edilmemiş regresyon katsayısı, Std. β : Standardize edilmiş regresyon katsayısı, S.Hata: Standart hata, C.R: Kritik oran, p: Anlamlılık düzeyi, R²: Açıklanan varyans oranı, F1-F2-F3: Ölçek alt boyutları (faktör)

Tablo 3. MHİ ile MSÖ ve VAS Ağrı Puanları Arasında Korelasyon Analizi

		MSÖ Toplam	Ağrı Şiddeti
MHİ Toplam	r	0,440**	0,520**
	p	0,000	0,000
Somatik Kaygı	r	0,457**	0,482**
	p	0,000	0,000
Korku Tehlike	r	0,208**	0,306**
	p	0,000	0,000
İlaça Bağlı Kaygı	r	0,352**	0,450**
	p	0,000	0,000

MHİ: Menstrual Hassasiyet İndeksi, MSÖ: Menstrüasyon Semptom Ölçeği, VAS: Visual Analog Skala,
 **<0,01; Pearson Korelasyon Analizi

Tüm maddelerin faktör yüklerinin istatistiksel olarak anlamlı olduğu ($p < 0,001$) ve ,60'ın üzerinde standartlaştırılmış katsayılara sahip olduğu görülmektedir. Bu sonuçlar, MHİ'nin üç faktörlü yapısının doğrulandığı, modelin veriyi iyi düzeyde uyum sağladığı ve ölçeğin yapı geçerliğine sahip olduğu sonucuna ulaşılmıştır.

Ölçüt Geçerliği

MHİ toplam ve alt boyut puanlarının VAS ile ölçülen ağrı şiddeti ve MSÖ toplam puanı arasındaki ilişki korelasyon analiziyle incelenmiştir. Yapılan analiz sonucunda, MHİ toplam puanı ile MSÖ toplam puanı arasında $r = 0,440$, ağrı şiddeti ile $r = 0,520$ düzeyinde anlamlı ve pozitif yönlü ilişkiler bulunmuştur ($p < 0,01$). Benzer şekilde, somatik kaygı alt boyutu hem MSÖ ($r = 0,457$) hem de ağrı şiddeti ($r = 0,482$) ile anlamlı şekilde ilişkili bulunmuştur. Korku/tehlike alt boyutu ile MSÖ ($r = 0,208$) ve ağrı şiddeti ($r = 0,306$) arasında zayıf fakat anlamlı ilişkiler saptanmıştır. İlaça bağlı kaygı alt boyutunun ise MSÖ ($r = 0,352$) ve ağrı şiddeti ($r = 0,450$) ile orta düzeyde pozitif ilişkili olduğu belirlenmiştir ($p < 0,01$) (Tablo 3).

Ölçek Güvenirlik ve Madde Analizi

MHİ'nin güvenilirlik düzeyini değerlendirmek amacıyla Cronbach's Alpha değeri ve madde analizlerine bakılmıştır. Ölçeğin tümüne ait iç tutarlılık katsayısı 0,849 olup, alt boyutlara ait Cronbach's Alpha

Tablo 4. Madde Analizi

	Düzeltilmiş Madde Toplam Korelasyonu	Madde Silindiğinde Cronbach Alfa Değeri
MHİ1	,518	,839
MHİ2	,662	,822
MHİ3	,723	,813
MHİ4	,414	,849
MHİ5	,540	,837
MHİ6	,702	,817
MHİ7	,531	,839
MHİ8	,613	,829

MHİ: Menstrual Hassasiyet İndeksi

değerleri de sırasıyla somatik kaygı için 0,836, korku/tehlike için 0,812 ve ilaca bağlı kaygı için 0,839 olarak bulunmuştur. Madde analizi sonuçlarına göre, düzeltilmiş madde-toplam korelasyonları 0,414 (MHİ4) ile 0,723 (MHİ3) arasında değişmektedir. Ölçek maddeleri silindiğinde yeni oluşan Cronbach's Alfa değerleri Tablo 4'de yer almaktadır.

Ayırt Edicilik

MHİ'nin ayırt edici gücünü belirlemek amacıyla ölçek puanlarının alt ve üst %27'lik gruplar arasında farklılaşıp farklılaşmadığı incelenmiştir. MHİ toplam puanı hem de tüm alt boyutlar (somatik kaygı, korku/tehlike ve ilaca bağlı kaygı) alt ve üst gruplar arasında anlamlı düzeyde farklılık göstermektedir ($p < 0,001$). Üst %27'lik grubun ortalama puanları, tüm boyutlarda alt gruba kıyasla belirgin biçimde daha yüksek bulunmuştur (Tablo 5).

TARTIŞMA

Ölçek geliştirme ve uyarlama çalışmalarında ölçeğin geçerlik ve güvenilirliğinin sağlanması iki önemli kriterdir (19). Araştırmamızda elde edilen bulgular, MHİ'nin Türk toplumuna uygun ve doğurgan çağıdaki kadınların menstrual hassasiyetini önceden belirleyen çok boyutlu, geçerli ve güvenilir bir ölçüm aracı olduğu bulunmuştur.

Tablo 5. Ölçek Puanlarının Alt-üst %27 Gruplarına Göre Farklılaşma Durumu

Gruplar	Alt %27 (n=106)		Üst %27 (n=106)		t	sd	p
	Ort	SS	Ort	SS			
MHİ Toplam	6,934	2,935	28,274	4,628	-40,090	210	0,000
Somatik Kaygı	5,745	2,626	15,991	2,580	-28,652	210	0,000
Korku Tehlike	0,849	1,128	5,708	2,457	-18,501	210	0,000
İlaça Bağlı Kaygı	0,340	0,850	6,576	2,963	-20,828	210	0,000

MHİ: Menstrual Hassasiyet İndeksi, Ort: Ortalama, SS: Standart Sapma, t: Bağımsız Gruplar T-Testi, p: Anlamlılık, sd: Serbestlik Derecesi

Kültürler arası ölçek uyarlamalarında doğru adımların takip edilmesi önemlidir. Literatürde, dil ve kültürel farklılıkların azaltılmasında çeviri-geri çeviri adımlarının uygulanması istenmektedir (20). Bu çalışmada MHI'nin dil geçerliği için yedi uzmandan görüş alınmış ve küçük farklılıklar için fikir birliği sağlanmıştır. Türkçe formun orijinal dile tekrar çevirisi ile iki ülke arasındaki dilbilimsel ve kültürel eşitlik sağlanmaya çalışılmıştır.

Kapsam geçerliği, bir aracın ölçülen yapı için uygun bir madde örneğine sahip olma derecesidir ve ölçek geliştirmede önemli bir adımdır (21). Bu özellik ölçüm aracının ölçülmek istenen özellik ile tutarlı olması esasına dayanır (19). Literatürde kapsam geçerliği için yeterli sayıda alan uzmanından (en az 3 en fazla 20) görüş alınması bildirilmiştir (20, 22). Çalışmamızda kadın sağlığı alanında uzman 7 kişiden görüş alınmıştır. Uzmanların görüşleri doğrultusunda MHI orijinal formunda yer alan "menstrual/menstruasyon" kelimesi Türk kültüründe yaygın olarak kullanılan "adet" olarak ifade edilmiştir. Literatürde kapsam geçerliği için I-CVI değerinin $\geq 0,80$ sınırının üzerinde olması beklenmektedir (23). Çalışmamızda I-CVI değeri 0,857 ve tüm maddeler için genel uyumu gösteren S-CVI değeri 0,946'dır. Bu sonuçlar, ilgili maddelerin uzmanlar tarafından büyük ölçüde uygun bulunduğunu ve ölçeğin kapsam geçerliliğinin yüksek düzeyde olduğunu göstermektedir. Elde edilen bulgular, ölçek maddelerinin hedeflenen yapı kapsamında yeterli düzeyde temsiliyet sağladığını ortaya koymaktadır.

Ölçeğin doğrulayıcı faktör analizi öncesinde örneklem büyüklüğünün yeterli düzeyde olduğu KMO değeri ve Barlett's testi ile değerlendirilmelidir. KMO değerinin 0,80-0,90 aralığında olması örneklem sayısının çok iyi olduğunu gösterir (24). Çalışmamızda KMO değeri (0.803) ile Barlett's test sonucunun anlamlı ($\chi^2=1403,512$; $sd = 28$; $p<0,001$) olması verilerin faktör analizine uygun olduğunu göstermektedir.

Literatürde faktör yapısının değerlendirilmesinde 0.45 veya daha büyük faktör yükü, ölçekler için istenen bir değerdir (25). Faktör yük değeri için kesin bir sınır bulunmazken, faktör yükü 0.40 ve üzerinde olan maddeler kabul edilmekte, 0.30-0.59 arası değerler orta, 0.60 ve üzerindeki değerler ise yüksek olduğu bildirilmiştir (26). MHI faktör yüklerinin bir madde hariç ($MS4=0.455$) 0.60'ın üzerinde olduğu görülmektedir. Bu durum, madde ile faktör arasındaki ilişkinin güçlü olduğunu ve yapının homojenliğini desteklediğini göstermektedir.

MHI'nin Doğrulayıcı Faktör Analizi (DFA), üç faktörlü yapı üzerinden modellenerek yapının veri ile uyum düzeyleri değerlendirilmiştir (27). Literatürde, χ^2/df değerinin beş veya daha az olması, test edilen modelin kabul edilebilir ve iyi düzeyde uyum iyiliğine sahip olduğunu göstermektedir (28). CFI, GFI ve TLI değerlerinin

0.90'a eşit veya büyük olması kabul edilebilir değerlerdir (29, 30). Çalışmamızda özellikle CFI, GFI, NFI ve TLI değerlerinin 0,90'ın üzerinde olması, modelin gözlenen verilerle güçlü bir şekilde örtüştüğünü göstermektedir. RMSEA ve RMR değerleri de literatürde kabul edilen eşik değerlerin altında veya sınırında yer almaktadır (31,32). Bu sonuçlar, ölçeğin varsayılan faktör yapısının doğrulandığını göstermektedir. Elde edilen bulgular doğrultusunda, MHI'nin üç faktörlü yapısının doğrulandığı, modelin veriyle iyi düzeyde uyum sağladığı ve ölçeğin yapı geçerliğine sahip olduğu sonucuna ulaşılmıştır.

Ölçüt geçerliği, ölçme aracından elde edilen puanların aynı yapıyı ölçen bir veya birkaç dış ölçütlerle ilişkisini değerlendirmektir (33). MHI'nin eş zamanlı geçerliği, VAS ve MSÖ ile yapılan korelasyon analizleriyle desteklenmiştir ($r \geq 0,30$). MHI'nin toplam ve alt boyut puanlarının hem semptom şiddeti hem de algılanan ağrı puanlarıyla ilişkili olduğu ve bu bağlamda ölçüt geçerliliğinin güçlü olduğu gösterilmiştir. Bu sonuçlar, MHI'nin benzer yapıları ölçme konusunda geçerli olduğunu göstermektedir (22,34). İlerleyen çalışmalarda yordama geçerliği için uzunlamasına veri toplanması önerilmektedir.

Bir ölçüm aracının güvenilirlik (iç tutarlılık) düzeyini değerlendirmede yaygın olarak Cronbach alfa değeri kullanılmaktadır. İç tutarlılık, ölçekteki tüm maddelerin aynı yapıyı homojen şekilde ölçüp ölçmediğinin göstergesidir (20). Cronbach's Alpha katsayısının değerlendirme kriterlerine göre; 1,00-0,80 katsayılı ölçekler yüksek, 0,60-0,79 katsayılı ölçekler oldukça güvenilir, 0,40-0,59 katsayılı ölçekler düşük güvenilirliğe sahiptir (35). MHI'nin orijinal formunda iç tutarlılık katsayısı 0,80 bulunmuştur (14). Bu çalışmada iç tutarlılık katsayısı 0,849 olup, bu değer ölçeğin yüksek düzeyde güvenilirliğe sahip olduğunu göstermektedir. Alt boyutlara ilişkin iç tutarlılık katsayısı 0,80 değerinin üzerinde bulunduğundan ölçek alt boyutlarında da yüksek iç tutarlılığın sağlandığı görülmektedir.

Likert tipi ölçeklerde yer alan maddelerin, düzeltilmiş madde-toplam puan korelasyon değerleri 0,30 ile 0,70 arasında olmalıdır (36). Çalışmamızda düzeltilmiş madde-toplam korelasyonları 0,414 ile 0,723 arasında değişmektedir. Tüm maddelerin korelasyon değerleri 0,30'un üzerinde olduğu için ölçek yapısına anlamlı katkı sağladığı belirlenmiştir. Ayrıca, herhangi bir madde ölçekten çıkarıldığında Cronbach's Alpha katsayısında belirgin bir artış gözlenmemektedir. Bu durum, ölçeğin maddelerinin homojen bir yapıya sahip olduğunu ve ölçeğin bütünlüğünü bozacak zayıf madde bulunmadığını göstermektedir.

Bir ölçüm aracının ayırt edici gücünü belirlemek amacıyla alt %27 ve üst %27'lik gruplar arasında farklılaşma durumu değerlendirilir. Dar bir aralıkta ölçüm yapan ölçeğin farklılıkları ayırt etmediği sayılır (37). Çalışmamızda Üst %27'lik grubun ortalama puanları,

tüm boyutlarda alt gruba kıyasla belirgin biçimde daha yüksek bulunmuştur. Gözlemlenen büyük farklar, ölçeğin yüksek duyarlılığa sahip bireyleri etkili şekilde ayırt ettiğini göstermektedir.

Sonuç olarak, MHİ kadınların menstrual semptomlara uyumunu ve bu semptomlardan korkusunu yansıtan bir öz bildirim aracıdır. MHİ'nin Türk toplumu için menstrüasyona özgü hassasiyeti belirlemede kullanılabilecek geçerli ve güvenli bir ölçüm aracı olduğu saptanmıştır. Ayrıca bu çalışma çevrim içi platform aracılığıyla yürütüldüğünden, yalnızca telefon ve internet erişimi olan kadınlar çalışmaya dahil edilebilmiştir. Bu durum bulguların ülkemizdeki tüm kadınlara genellenebilirliğini sınırlamaktadır. Gelecek araştırmalarda ölçeğin farklı sosyo-demografik gruplarda, yüz yüze veri toplama yöntemleriyle ve test-tekrar test uygulamalarıyla değerlendirilmesinin alana önemli katkılar sağlayacağı düşünülmektedir.

Yazar Katkıları: Kavramsallaştırma: EİK, DSK; Veri düzenleme: EİK; Araştırma: EİK, DSK; Metodoloji: EİK, DSK; Proje yönetimi: EİK, DSK; Kaynaklar: EİK, DSK; Yazılım: EİK; Süpervizyon: DSK; Görselleştirme: EİK; Roller/Yazım: orijinal taslak: EİK; Yazım-Gözden geçirme ve düzenleme: EİK, DSK.

Çıkar Çatışması Beyanı: Çalışma kapsamında herhangi bir kurum veya kişi ile çıkar çatışması bulunmamaktadır.

Destek Beyanı: Çalışma herhangi bir destek almamıştır.

KAYNAKLAR

- Matteson KA, Zaluski KM. Menstrual health as a part of preventive health care. *Obstet Gynecol Clin North Am* 2019 Sep; 46(3):441-53.
- Kho KA, Shields JK. Diagnosis and management of primary dysmenorrhea. *JAMA* 2020; 323(3):268-9.
- Söderman L, Edlund M, Marions L. Prevalence and impact of dysmenorrhea in Swedish adolescents. *Acta Obstet Gynecol Scand* 2019 Feb; 98(2):215-21.
- De Sanctis V, Soliman A, Bernasconi S, Bianchin L, Bona G, Bozzola M, et al. Primary dysmenorrhea in adolescents: Prevalence, impact and recent knowledge. *Pediatr Endocrinol Rev* 2015 Dec; 13(2):512-20.
- Sigmon ST, Dorhofer DM, Rohan KJ, Boulard NE. The impact of anxiety sensitivity, bodily expectations, and cultural beliefs on menstrual symptom reporting: a test of the menstrual reactivity hypothesis. *J Anxiety Disord* 2000 Nov-Dec; 14(6):615-33.
- Iacovides S, Avidon I, Baker FC. What we know about primary dysmenorrhea today: a critical review. *Hum Reprod Update* 2015 Nov-Dec; 21(6):762-78.
- Payne LA, Seidman LC, Sim MS, Rapkin AJ, Naliboff BD, Zeltzer LK. Experimental evaluation of central pain processes in young women with primary dysmenorrhea. *Pain* 2019 Jun; 160(6):1421-30.
- Li R, Li B, Kreher DA, Benjamin AR, Gubbels A, Smith SM. Association between dysmenorrhea and chronic pain: a systematic review and meta-analysis of population-based studies. *Am J Obstet Gynecol* 2020 Sep; 223(3):350-71.
- Slater H, Paananen M, Smith AJ, O'Sullivan P, Briggs AM, Hickey M, et al. Heightened cold pain and pressure pain sensitivity in young female adults with moderate-to-severe menstrual pain. *Pain* 2015 Dec; 156(12):2468-78.
- Ceran İG, Mızrak Şahin B. Türkiye'de kadınlarda dismenore ve ilişkili faktörlerin belirlenmesi: Kesitsel bir araştırma. İnönü Üniversitesi Sağlık Hizmetleri Meslek Yüksekokulu Dergisi 2024; 12(3):886-89.
- Lamont JM. Trait body shame predicts menstrual-related symptoms: Evidence for extending the menstrual reactivity hypothesis. *Women's Reproductive Health* 2023; 10(1):24-42.
- Carpenter JK, Bragdon L, Pineles SL. Conditioned physiological reactivity and PTSD symptoms across the menstrual cycle: Anxiety sensitivity as a moderator. *Psychological Trauma: Theory, Research, Practice, and Policy* 2022; 14(3):453-61.
- Gentile E, Fitzcharles MA, Correia V, Martel MO, Roy M. Exploring the neuropsychological profile of patients with fibromyalgia with insights from pain, psychological, and clinical predictors. *Neuropsychology* 2025; 39(4):359-74.
- Handy AB, Seidman LC, Payne LA. Development and initial validation of the menstrual sensitivity index. *Pain Med* 2024 Jan 4; 25(1):78-85.
- Çokluk Ö, Şekercioğlu G, Büyükoztürk Ş. Sosyal bilimler için çok değişkenli istatistik SPSS ve Lisrel uygulamaları. Üçüncü Baskı. Ankara: Pegem Akademi, 2014:177-246.
- Karagöz, Y. SPSS ve AMOS uygulamalı nitel-nicel-karma bilimsel araştırma yöntemleri ve yayın etiği. Birinci Baskı. Ankara: Nobel Yayınları, 2017.
- Johnson EW. Visual analog scale (VAS). *Am J Phys Med Rehabil* 2001 October; 80(10):717.
- Güvenç G, Seven M, Akşay A. Menstrüasyon Semptom Ölçeği'nin Türkçe'ye uyarlanması. *TAF Preventive Medicine Bulletin* 2014; 13(5):367-74.
- Karakoç FY, Dönmez L. Ölçek geliştirme çalışmalarında temel ilkeler. *Tıp Eğitimi Dünyası* 2014 Mayıs; 40:39-49.
- Çapık C, Gözüm S, Aksayan S. Kültürlerarası ölçek uyarlama aşamaları, dil ve kültür uyarlaması: Güncellenmiş rehber. *FNJN* 2018; 26(3):199-210.
- Shi J, Mo X, Sun Z. Content validity index in scale development. *Zhong Nan Da Xue Xue Bao Yi Xue Ban* 2012 Feb; 37(2):152-5.
- Gökdemir F, Yılmaz T. Processes of using, modifying, adapting and developing likert type scales. *J Nursology* 2023; 26(2):148-60.
- Karasar N. Scientific research method concepts principles techniques with scientific will perception framework. Ankara: Nobel Academy, 2020.
- Akgül A, Çevik Ç. İstatistiksel Analiz Teknikleri. Emek Ofset Baskı, 2003, s.104.
- Alavi M, Visentin DC, Thapa DK, Hunt GE, Watson R, Cleary M. Exploratory factor analysis and principal component analysis in clinical studies: Which one should you use? *Jan* 2020; 76:1886-89.
- Karagöz Y, Bardakçı S. Bilimsel araştırmalarda kullanılan ölçme araçları ve ölçek geliştirme. Ankara: Nobel Akademik Yayıncılık, 2020.
- Çapık C. Geçerlik ve güvenilirlik çalışmalarında doğrulayıcı faktör analizinin kullanımı. *Anadolu Hemşirelik ve Sağlık Bilimleri Dergisi* 2014; 17(3):196-205.
- Erkorkmaz Ü, Etikan İ, Demir O, Özdamar K, Sanisoğlu SY. Doğrulayıcı Faktör Analizi ve Uyum İndeksleri. *Türkiye Klinikleri J Med Sci* 2013; 33(1):210-23.
- Hu LT, Bentler PM. Cutoff criteria for fit indexes in covariance structure analysis: Conventional criteria versus new alternatives. *Structural Equation Modeling: A Multidisciplinary Journal* 1999; 6(1):1-55.
- Kline RB. Principles and practice of structural equation modeling. 4th ed. The Guilford Press, 2015.
- Byrne BM. Structural equation modeling with AMOS: Basic concepts, applications, and programming. 2nd ed. Routledge, 2010.
- Schumacker RE, Lomax RG. A beginner's guide to structural equation modeling. 4th ed. Routledge, 2016.
- Mohajan HK. Two criteria for good measurements in research: validity and reliability. *ASHU- ES* 2017; 17(4):59-82.
- Akoglu H. User's guide to correlation coefficients. *Turk J Emerg Med* 2018; 18(3):91-93.
- Bujang MA, Omar ED, Baharum NA. A review on sample size determination for cronbach's alpha test: A simple guide for researchers. *MJMS* 2018; 25(6):85-99.
- Büyükoztürk Ş. Sosyal Bilimler İçin Veri Analizi El Kitabı. İstatistik, Araştırma Deseni SPSS Uygulamaları ve Yorum. 27. Baskı. Ankara: Pegem Akademi Yayıncılık, 2020.
- Schreiber JB, Stage FK, King J, Amaury N, Barlow EA. Reporting structural equation modeling and confirmatory factor analysis results: A review. *J Educ Res* 2006; 99(6):323-37.

EK: MENSTRUAL HASSASIYET İNDEKSİ (MHI)

Aşağıda insanların regl ağrısı ve rahatsızlığına nasıl tepki verdiklerini tanımlayan ifadeler bulunmaktadır. Bu ifadelere KENDİNİZLE İLGİLİ OLARAK ne kadar katıldığınızı veya katılmadığınızı belirtiniz. Tüm ifadeleri mümkün olduğunca dürüst ve dikkatli bir şekilde yanıtlayınız.

Madde	Kesinlikle katılıyorum	Katılıyorum	Biraz katılıyorum	Biraz katılmıyorum	Katılmıyorum	Kesinlikle katılmıyorum
1. Adet dönemimle ilgili vücudumda oluşan problemlerden sıklıkla endişelenirim.	1	2	3	4	5	6
2. Adet ağrısı/rahatsızlığını aklımdan çıkaramadığım için eğlenmekte zorlanırım.	1	2	3	4	5	6
3. Adet ağrısı/rahatsızlığı hissettiğim anda endişelenmeye ve kaygılanmaya başlarım.	1	2	3	4	5	6
4. Adet olduğumda, vücudumdaki hislerin sürekli farkında olurum.	1	2	3	4	5	6
5. Adet ağrısı/rahatsızlığının ciddi bir hastalığın belirtisi olabileceğini sıklıkla düşünürüm.	1	2	3	4	5	6
6. Adet ağrısını/rahatsızlığını hissettiğimde korkarım.	1	2	3	4	5	6
7. Adetimin başlayacağını düşündüğümde ilaç alırım.	1	2	3	4	5	6
8. Adetimin başlayacağını hissettiğimde, ilacım yoksa kaygılanırım.	1	2	3	4	5	6

Comparative Clinical Outcomes of V-NOTES and Total Laparoscopic Hysterectomy: A One-Year Retrospective Cohort Study at a Tertiary Center

V-NOTES ve Total Laparoskopik Histerektominin Klinik Sonuçları: Üçüncü Basamak Bir Merkezde Bir Yıllık Retrospektif Kohort Çalışması

Alaattin KARABULUT¹, Sercan KANTARCI¹, Uğurcan DAĞLI¹, Fatih YILDIRIM¹, Serhat SARIKAYA¹, Abdurrahman Hamdi İNAN¹, Adnan BUDAK¹, Alper İLERİ¹

¹Department of Obstetrics and Gynecology, University of Health Sciences Tepecik Training and Research Hospital, İzmir, Türkiye

ABSTRACT

Aim: To compare the perioperative and postoperative clinical outcomes of transvaginal natural orifice transluminal endoscopic surgery (V-NOTES) and total laparoscopic hysterectomy (TLH) in patients undergoing surgery for benign gynecological indications.

Materials and Methods: This retrospective cohort study included patients who underwent hysterectomy at a tertiary referral center between October 1, 2024, and October 1, 2025. Patients with histopathologically confirmed malignancy, emergency procedures, and incomplete clinical data were excluded. A total of 711 patients were analyzed, including 38 in the V-NOTES group and 673 in the TLH group. Demographic, perioperative, and postoperative data were obtained from medical records and compared between groups.

Results: Baseline characteristics were similar between the groups. Operative time was significantly longer in the V-NOTES group than in the TLH group (101.47±17.89 vs. 82.46±12.86 minutes, $p<0.001$). Hemoglobin decline and hospital stay were comparable between the groups ($p=0.646$ and $p=0.279$, respectively). Uterine weight was significantly lower in the V-NOTES group (187.87±36.63 vs. 212.26±61.66 g, $p<0.001$). Postoperative pain scores at 6 and 24 hours were significantly lower in the V-NOTES group ($p=0.003$ and $p=0.012$, respectively). Intraoperative and postoperative complication rates did not differ significantly between the groups.

Conclusion: V-NOTES may be a feasible minimally invasive alternative to TLH in selected patients with benign gynecological conditions, with lower postoperative pain scores in this cohort. However, the findings should be interpreted cautiously given the marked imbalance between groups.

Keywords: V-NOTES; total laparoscopic hysterectomy; minimally invasive surgery; postoperative pain; hysterectomy

ÖZ

Amaç: Bu çalışmanın amacı, benign jinekolojik endikasyonlarla opere edilen hastalarda vajinal doğal orifis transluminal endoskopik cerrahi (V-NOTES) ile total laparoskopik histerektominin (TLH) perioperatif ve postoperatif klinik sonuçlarını karşılaştırmaktır.

Gereç ve Yöntemler: Bu retrospektif kohort çalışmaya, 1 Ekim 2024 ile 1 Ekim 2025 tarihleri arasında üçüncü basamak bir merkezde histerektomi uygulanan hastalar dahil edildi. Histopatolojik olarak malignite saptanan hastalar, acil cerrahi uygulananlar ve klinik verileri eksik olan olgular çalışma dışı bırakıldı. Toplam 711 hasta analiz edildi; bunların 38'i V-NOTES, 673'ü TLH grubundaydı. Demografik, perioperatif ve postoperatif veriler tıbbi kayıtlardan elde edilerek gruplar arasında karşılaştırıldı.

Bulgular: Gruplar arasında başlangıç özellikleri açısından anlamlı fark yoktu. Operasyon süresi V-NOTES grubunda TLH grubuna göre anlamlı olarak daha uzundu (101.47±17.89 vs. 82.46±12.86 dakika, $p<0.001$). Hemoglobin düşüşü ve hastanede kalış süresi açısından gruplar arasında anlamlı fark saptanmadı (sırasıyla $p=0.646$ ve $p=0.279$). Uterus ağırlığı V-NOTES grubunda anlamlı olarak daha düşüktü (187.87±36.63 vs. 212.26±61.66 g, $p<0.001$). Postoperatif 6. ve 24. saat ağrı skorları V-NOTES grubunda anlamlı olarak daha düşüktü (sırasıyla $p=0.003$ ve $p=0.012$). İntraoperatif ve postoperatif komplikasyon oranları açısından gruplar arasında anlamlı fark yoktu.

Sonuç: V-NOTES, benign jinekolojik hastalıklarda TLH'ye uygulanabilir minimal invaziv bir alternatif olabilir ve bu grupta ameliyat sonrası ağrı skorları daha düşüktür. Bununla birlikte, gruplar arasındaki belirgin dengesizlik göz önüne alındığında, bulgular ihtiyatlı bir şekilde yorumlanmalıdır.

Anahtar Kelimeler: V-NOTES; total laparoskopik histerektomi; minimal invaziv cerrahi; postoperatif ağrı; histerektomi

Cite as: Karabulut A, Kantarcı S, Dağlı U, Yıldırım F, Sarıkaya S, İnan AH, et al. Comparative Clinical Outcomes of V-NOTES and Total Laparoscopic Hysterectomy: A One-Year Retrospective Cohort Study at a Tertiary Center. Jinekoloji-Obstetrik ve Neonatoloji Tıp Dergisi 2026;23(2):198–202.

Geliş/Received: 24.03.2026 • **Kabul/Accepted:** 03.05.2026

Sorumlu Yazar/Corresponding Author: Alaattin Karabulut, Department of Obstetrics and Gynecology, University of Health Sciences Tepecik Training and Research Hospital, İzmir, Türkiye

E-mail: alaattin_karabulut@hotmail.com

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

INTRODUCTION

Hysterectomy is one of the most commonly performed surgical procedures in gynecology worldwide and is frequently indicated for benign conditions such as uterine fibroids, abnormal uterine bleeding, and adenomyosis (1,2). Minimally invasive surgical approaches have increasingly replaced open techniques due to their association with reduced postoperative pain, shorter hospital stay, and faster recovery (3,4).

Total laparoscopic hysterectomy (TLH) is widely utilized because it allows adequate visualization of pelvic anatomy and facilitates surgical management of adnexal structures (5). However, laparoscopic approaches still require abdominal incisions, which may contribute to postoperative discomfort and delayed recovery compared to vaginal approaches (1,6).

Transvaginal natural orifice transluminal endoscopic surgery (V-NOTES) has emerged as a minimally invasive alternative that combines vaginal access with endoscopic visualization. This technique eliminates abdominal incisions and has been associated with favorable cosmetic outcomes and reduced postoperative pain (1,7). Comparative studies have demonstrated that V-NOTES may result in lower postoperative pain scores compared to laparoscopic hysterectomy (1,7,8).

In addition to pain outcomes, V-NOTES has been associated with improved recovery parameters. Prospective data indicate shorter time to recovery of bowel function and earlier return to work following V-NOTES compared with laparoscopic approaches (9). Similarly, retrospective analyses have shown shorter hospitalization and improved postoperative recovery profiles in patients undergoing V-NOTES (2,8).

Despite these advantages, some studies have reported longer operative times and greater hemoglobin decline associated with V-NOTES procedures (7,8). These findings have been attributed to the technical complexity of the procedure and the learning curve required for its adoption (10,11).

Moreover, the current literature remains heterogeneous regarding perioperative outcomes and complication rates. While several studies have demonstrated comparable safety profiles between V-NOTES and laparoscopic hysterectomy, differences in study design, patient selection, and surgeon experience limit direct comparisons (6,12).

Furthermore, although the vaginal route is considered one of the least invasive approaches, it remains underutilized in clinical practice. V-NOTES has been proposed as a technique that may

increase the utilization of the vaginal approach by overcoming visualization limitations associated with conventional vaginal hysterectomy (13).

Importantly, most available studies are based on relatively small sample sizes or single-center experiences. Large-scale and multicenter studies evaluating postoperative recovery and safety outcomes are still limited (14,15).

Therefore, the present study aimed to compare the perioperative and postoperative clinical outcomes of V-NOTES and total laparoscopic hysterectomy in patients undergoing surgery for benign gynecological indications over a one-year period at a tertiary care center.

MATERIALS AND METHODS

This retrospective cohort study was conducted at a tertiary referral center. Medical records of patients who underwent hysterectomy between October 1, 2024, and October 1, 2025, were reviewed.

All patients who underwent hysterectomy during the study period were initially screened. Patients who underwent surgery for benign gynecological indications and were treated with either transvaginal natural orifice transluminal endoscopic surgery (V-NOTES) or total laparoscopic hysterectomy (TLH) were included in the study. Patients with histopathologically confirmed malignancy ($n=11$), those who underwent emergency surgery, and those with incomplete clinical data were excluded from the analysis.

Patient data were obtained from the hospital electronic medical record system, operative reports, and postoperative follow-up records. Demographic variables included age, body mass index (BMI), parity, smoking status, history of previous abdominal surgery, and presence of comorbidities. Surgical parameters included operative time, intraoperative complications, and uterine weight. Postoperative variables included hemoglobin decline, postoperative pain scores assessed using the visual analog scale (VAS) at the 6th and 24th hours, and length of hospital stay.

The primary outcomes of the study were perioperative and postoperative clinical parameters, including operative time, hemoglobin decline, postoperative pain scores, and hospital stay. Secondary outcomes included intraoperative complications and postoperative complications requiring hospitalization. Postoperative complications were defined as complications requiring hospital admission.

Statistical analyses were performed using SPSS software (version 22, IBM Corp., Armonk, NY, USA). Continuous variables were expressed as

mean $\pm$ standard deviation, and categorical variables were presented as frequencies and percentages. Comparisons between groups were performed using the independent samples t-test or Mann–Whitney U test for continuous variables, and the chi-square test or Fisher's exact test for categorical variables, as appropriate. A p-value of <0.05 was considered statistically significant.

The study was conducted in accordance with the principles of the Declaration of Helsinki and was approved by the University of Health Sciences Tepecik Training and Research Hospital Ethics Committee (approval no: 2025/10-11, date: November 3, 2025).

RESULTS

A total of 722 patients were initially screened during the study period. After excluding 11 patients with histopathologically confirmed malignancy and those who did not meet the inclusion criteria, 711 patients were included in the final analysis. Of these, 38 patients underwent V-NOTES and 673 underwent TLH.

The baseline characteristics of the patients are presented in Table 1. There were no statistically significant differences between the

groups in terms of age, parity, body mass index (BMI), smoking status, history of previous abdominal surgery, or presence of comorbidities ($p>0.05$ for all).

Perioperative and postoperative outcomes are summarized in Table 2. The mean operative time was significantly longer in the V-NOTES group compared to the TLH group (101.47 ± 17.89 vs. 82.46 ± 12.86 minutes, $p<0.001$). Hemoglobin decline was similar between the two groups (1.51 ± 0.56 vs. 1.55 ± 1.22 g/dL, $p=0.646$). There was no significant difference in hospital stay between the groups (31.07 ± 10.51 vs. 29.19 ± 5.83 hours, $p=0.279$).

The mean uterine weight was significantly lower in the V-NOTES group compared to the TLH group (187.87 ± 36.63 vs. 212.26 ± 61.66 g, $p<0.001$). Postoperative pain scores were significantly lower in the V-NOTES group at both the 6th and 24th hours (VAS 6 hours: 3.15 ± 1.15 vs. 3.79 ± 1.78 , $p=0.003$; VAS 24 hours: 1.86 ± 0.99 vs. 2.30 ± 1.30 , $p=0.012$).

Intraoperative complications occurred in 2 patients (5.3%) in the V-NOTES group and 11 patients (1.6%) in the TLH group, with no statistically significant difference between the groups ($p=0.150$). In the V-NOTES group, all intraoperative complications were bladder

Table 1. Baseline demographic and clinical characteristics of the study groups

	V-NOTES (n=38)	TLH (n=673)	p Value
Age (years)	51.86 ± 5.47	51.33 ± 8.02	0.574
Parity	2.92 ± 1.38	2.57 ± 1.16	0.142
BMI (kg/m ²)	27.48 ± 1.96	28.03 ± 1.53	0.098
Smokers	14 (36.8%)	223 (33.1%)	0.637
Previous abdominal surgery	Yes:21(55.3%) No:17(44.7%)	Yes:329 (48.9%) No:344 (51.1%)	0.444
Comorbidity	Yes:25 (65.8%) No:13 (34.2%)	Yes: 471 (70.0%) No: 202 (30.0%)	0.584

BMI: Body mass index

Table 2. Perioperative and postoperative outcomes of the study groups

	V-NOTES (n=38)	TLH (n=673)	p Value
Operation time (min)	101.47 ± 17.89	82.46 ± 12.86	<0.001
Hemoglobin decline (g/dL)	1.51 ± 0.56	1.55 ± 1.22	0.646
Hospital stay (hours)	31.07 ± 10.51	29.19 ± 5.83	0.279
Uterine weight (g)	187.87 ± 36.63	212.26 ± 61.66	<0.001
VAS 6 hours	3.15 ± 1.15	3.79 ± 1.78	0.003
VAS 24 hours	1.86 ± 0.99	2.30 ± 1.30	0.012
Intraoperative complication	2(5.3%)	11(1.6%)	0.150
No complication	36	662	
Bladder injury	2	8	
Bowel injury	0	1	
Ureter injury	0	2	
Postoperative complication requiring hospitalization	3(7.9%)	14(2.1%)	0.057

VAS: Visual analogue scale

injuries, whereas in the TLH group, complications included bladder injury (n=8), bowel injury (n=1), and ureteral injury (n=2).

Postoperative complications requiring hospitalization were observed in 3 patients (7.9%) in the V-NOTES group and 14 patients (2.1%) in the TLH group, without a statistically significant difference ($p=0.057$). In the V-NOTES group, complications were limited to vaginal cuff hematoma (n=2) and fistula (n=1). In contrast, the TLH group demonstrated a broader spectrum of complications, including vaginal cuff hematoma (n=5), trocar site hernia (n=1), wound infection (n=2), acute urinary retention requiring catheterization (n=1), pelvic abscess (n=2), delayed ureteral injury (n=1), urinary tract infection (n=1), and fistula (n=1).

DISCUSSION

In this retrospective cohort study, we compared perioperative and postoperative outcomes of V-NOTES and total laparoscopic hysterectomy and found that V-NOTES was associated with significantly lower postoperative pain, while most other clinical outcomes were comparable between the two techniques.

Reduced postoperative pain following V-NOTES has been consistently reported in the literature. Several comparative studies have shown that patients undergoing V-NOTES experience lower postoperative pain scores compared to laparoscopic hysterectomy (1,7,8). This finding is generally attributed to the absence of abdominal incisions, which reduces abdominal wall trauma and may decrease postoperative analgesic requirements.

In addition to pain outcomes, previous studies have suggested that V-NOTES may be associated with favorable recovery profiles. Earlier mobilization, shorter hospitalization, and faster return to daily activities have been reported in both prospective and retrospective analyses (2,9,12). Although we did not observe a statistically significant difference in hospital stay, our findings are consistent with the overall trend reported in the literature.

Operative time was significantly longer in the V-NOTES group in our study. This observation is in line with previous reports indicating that V-NOTES may be associated with longer operative times, particularly during the early phases of adoption (7,8). The technical complexity of the transvaginal approach and the learning curve are commonly cited as contributing factors (10,11,16). Previous studies have also indicated that operative time tends to decrease with increasing surgical experience.

With regard to hemoglobin decline, no significant difference was observed between the groups in our cohort. Similar findings have

been reported in systematic reviews and comparative studies, suggesting that blood loss and hemoglobin changes are generally comparable between V-NOTES and laparoscopic hysterectomy (3,4).

The rates of intraoperative and postoperative complications were comparable between the groups. Previous studies have demonstrated that V-NOTES is a safe and feasible approach with complication rates similar to those of laparoscopic hysterectomy (6,12). However, variability in complication rates across studies has been noted and is often related to differences in patient selection and surgical expertise.

Although postoperative complications requiring hospitalization were numerically higher in the V-NOTES group, this difference was not statistically significant. Importantly, the distribution of complications differed between the groups, suggesting that the evaluation of surgical techniques should consider not only the frequency but also the type of complications.

Another important factor is the learning curve associated with V-NOTES. Several studies have emphasized that surgical outcomes may vary during the early experience period, which can influence operative time and perioperative results (10,11). This highlights the importance of surgical training and experience in achieving optimal outcomes.

From a broader perspective, V-NOTES may contribute to increasing the utilization of the vaginal route in gynecologic surgery. Despite being considered a minimally invasive approach, the vaginal route has historically been underused, and V-NOTES has been proposed as a technique that may help overcome some of its limitations (13).

The strengths of this study include its real-world design and relatively large sample size. However, several limitations should be acknowledged. First, the study had a retrospective design, which introduces an inherent risk of selection bias. Second, the marked imbalance in group size, with a substantially smaller V-NOTES cohort than the TLH cohort, may have reduced the statistical power of comparisons, particularly for relatively infrequent outcomes such as intraoperative and postoperative complications. Third, the significantly lower uterine weight in the V-NOTES group suggests that the two groups may not have been fully comparable in terms of surgical complexity, which may have influenced perioperative outcomes. In addition, although the longer operative time observed in the V-NOTES group may reflect the learning curve associated with the adoption of this technique, we did not evaluate surgeon-specific experience, temporal distribution of cases, or case selection over time. Therefore, this interpretation should be considered cautious rather than definitive.

CONCLUSION

V-NOTES may represent a feasible minimally invasive alternative to total laparoscopic hysterectomy for selected patients with benign gynecological conditions. In the present study, V-NOTES was associated with lower postoperative pain scores, while other perioperative outcomes were broadly comparable between the groups. However, the marked imbalance in group size, the lower uterine weight in the V-NOTES group, and the limited number of complications require cautious interpretation of these findings. Further prospective studies with more balanced groups are needed to better define the comparative safety and effectiveness of V-NOTES.

Author Contributions: AK and SK: Concept and design; AK, SK, UD, SS and FY: Data collection and processing; AK, AHİ, AB and Aİ: Analysis or interpretation; UD, AHİ, and AB: Literature search; AK, Aİ, SS and FY: Writing the manuscript. All authors approved the final version of the manuscript.

Funding: None.

Conflict of Interest: The authors declare that there is no conflict of interest.

REFERENCES

1. Yang CY, Shen TC, Lin CL, Chang YY, Huang CC, Lin WC. Surgical outcomes of hysterectomy by transvaginal natural orifice transluminal endoscopic surgery (vNOTES) compared with laparoscopic total hysterectomy (LTH) in women with non-prolapsed and benign uterine diseases. *Taiwan J Obstet Gynecol.* 2020;59(4):565-569. doi:10.1016/j.tjog.2020.05.016
2. Mollahüseyinoğlu Küllaç F, Özdemir AZ, Yıldız Ç. A single center retrospective study of vNOTES hysterectomy, laparoscopic hysterectomy and vaginal hysterectomy operations. *Medicine (Baltimore).* 2024;103(50):e40881. doi:10.1097/MD.00000000000040881
3. Housmans S, Noori N, Kapurubandara S, Bosteels JJA, Cattani L, Alkatout I, et al. Systematic Review and Meta-Analysis on Hysterectomy by Vaginal Natural Orifice Transluminal Endoscopic Surgery (vNOTES) Compared to Laparoscopic Hysterectomy for Benign Indications. *J Clin Med.* 2020;9(12):3959. doi:10.3390/jcm9123959
4. Baekelandt J, De Mulder PA, Le Roy I, Mathieu C, Laenen A, Enzlin P, et al. Postoperative outcomes and quality of life following hysterectomy by natural orifice transluminal endoscopic surgery (NOTES) compared to laparoscopy in women with a non-prolapsed uterus and benign gynaecological disease: a systematic review and meta-analysis. *Eur J Obstet Gynecol Reprod Biol.* 2017;208:6-15. doi:10.1016/j.ejogrb.2016.10.044
5. Kaya C, Alay I, Cengiz H, Yıldız GO, Baghaki HS, Yasar L. Comparison of hysterectomy cases performed via conventional laparoscopy or vaginally assisted natural orifice transluminal endoscopic surgery: a paired sample cross-sectional study. *J Obstet Gynaecol.* 2021;41(3):434-438. doi:10.1080/01443615.2020.1741523
6. Badiglian-Filho L, Chaves Faloppa C, Narciso de Oliveira Menezes A, Mantoan H, Kumagai LY, Baiocchi G. Vaginally assisted NOTES hysterectomy with adnexectomy (vNOTES) compared with conventional laparoscopy. A retrospective observational cohort study. *Int J Gynaecol Obstet.* 2021;153(2):351-356. doi:10.1002/ijgo.13483
7. Sarıkaya S, Taskin MI, Bozhuyuk Sahin T, Guney G, Kececioğlu M, Afsar S, et al. Comparison of Perioperative Outcomes Between V-NOTES and Total Laparoscopic Hysterectomy: A Retrospective Analysis. *J Invest Surg.* 2025;38(1):2488131. doi:10.1080/08941939.2025.2488131
8. Qian P, Chen W, Su B, Chen Y, Shan W, Tang H, et al. Feasibility and safety of transvaginal natural orifice transluminal endoscopic surgery (V-NOTES) panhysterectomy: a multicentric retrospective study. *Eur J Med Res.* 2024;29(1):605. doi:10.1186/s40001-024-02202-x
9. Tang Y, Fang CL, Huang JR, Chen XM, Cai X, Wu J, et al. Comparison of rapid recovery outcomes between vNOTES hysterectomy and laparoscopic hysterectomy: a prospective study. *BMC Surg.* 2025;25(1):189. doi:10.1186/s12893-025-02906-9
10. Kaya C, Yıldız Ş, Alay İ, Karakaş S, Durmuş U, Güraslan H, et al. Comparison of Surgical Outcomes of Total Laparoscopic Hysterectomy and vNOTES Hysterectomy for Undescended-Enlarged Uteri. *J Invest Surg.* 2022;35(4):918-923. doi:10.1080/08941939.2021.1958111
11. Halışçelik MA, Oğlak SC, Bağlı İ, Akgöl S, Can B, Arkan K, et al. Comparison of conventional laparoscopic hysterectomy and vNOTES hysterectomy in previous pelvic surgery: a retrospective study. *Sci Rep.* 2025;15(1):30629. doi:10.1038/s41598-025-16525-0
12. Fang S, Xia Y, Jin J, Zhang J, Lu L. Comparison of Surgical Outcomes Between Vaginally Assisted NOTES Hysterectomy and Laparoscopic Hysterectomy in Primary Hospitals: A Prospective Cohort Study. *J Invest Surg.* 2025;38(1):2515054. doi:10.1080/08941939.2025.2515054
13. Özceltik G, Hortu I, İtil İM, Yeniel AO. Impact of transvaginal natural orifice transluminal endoscopic surgery on hysterectomy practice. *J Gynecol Obstet Hum Reprod.* 2022;51(1):102241. doi:10.1016/j.jogoh.2021.102241
14. Zhang W, Deng L, Yang F, Liu J, Chen S, You X, et al. Comparing the efficacy and safety of three surgical approaches for total hysterectomy (TSATH): protocol for a multicentre, single-blind, parallel-group, randomised controlled trial. *BMJ Open.* 2024;14(1):e074478. doi:10.1136/bmjopen-2023-074478
15. Pickett CM, Seeratan DD, Mol BWJ, Nieboer TE, Johnson N, Bonestroo T, et al. Surgical approach to hysterectomy for benign gynaecological disease. *Cochrane Database Syst Rev.* 2023;8(8):CD003677. doi:10.1002/14651858.CD003677.pub6
16. Kaya C, Yıldız Ş, Alay İ, Aslan Ö, Aydın İE, Yaşar L. The Comparison of Surgical Outcomes following Laparoscopic Hysterectomy and vNOTES Hysterectomy in Obese Patients. *J Invest Surg.* 2022;35(4):862-867. doi:10.1080/08941939.2021.1927262

Anormal Uterin Kanaması Olan Ergenlerde ABO Kan Gruplarının Kanama Şiddeti ve Seyri ile İlişkisi

The Relationship Between ABO Blood Groups and the Severity and Clinical Course of Abnormal Uterine Bleeding in Adolescents

¹Demet AYĞÜN ARI¹, ²Gürses ŞAHİN², ³Semra ÇETİNKAYA³

¹Ankara Etlik Şehir Hastanesi, Çocuk Sağlığı ve Hastalıkları, Ergen Sağlığı Kliniği, Ankara, Türkiye

²Ankara Etlik Şehir Hastanesi, Çocuk Sağlığı ve Hastalıkları, Çocuk Onkoloji Kliniği, Ankara, Türkiye

³Ankara Etlik Şehir Hastanesi, Çocuk Sağlığı ve Hastalıkları, Çocuk Endokrinoloji Kliniği, Ankara, Türkiye

ÖZ

Amaç: O kan grubuna sahip bireylerde von Willebrand faktör (vWF) düzeylerinin O kan grubu olmayan gruplara kıyasla daha düşük olduğu bilinmektedir. Bu nedenle O kan grubunda kanama riskinin daha yüksek olabileceği düşünülmektedir. Bu çalışmada, anormal uterin kanama (AUK) ile başvuran ergenlerde ABO kan grupları ile vWF düzeyleri, kanama şiddeti ve klinik seyri arasındaki ilişkinin değerlendirilmesi amaçlanmıştır.

Gereç ve Yöntemler: Haziran 2019–Haziran 2023 tarihleri arasında Ergen Sağlığı Polikliniğine başvuran ve AUK tanısı alan ergenler retrospektif olarak değerlendirildi. Anovulatuvar AUK tanılı, sistemde ABO kan grubu bilgisi bulunan ve vWF, vWF ristocetin kofaktörü (vWF:RCO) ile faktör VIII düzeyleri normal olan hastalar çalışmaya dahil edildi. Yapısal, iatrojenik, endokrin veya hematolojik nedenlere bağlı AUK olguları ile koagülopati veya von Willebrand hastalığı şüphesi olanlar çalışma dışında bırakıldı. Demografik veriler, menstrual özellikler, kanama şiddeti, tedavi gereksinimi ve laboratuvar sonuçları O ve O dışı kan grupları arasında karşılaştırıldı.

Bulgular: Toplam 98 ergen çalışmaya dahil edildi (%33 O kan grubu, %67 O dışı kan grubu). Demografik özellikler, antropometrik ölçümler, menarş yaşı ve menarştan itibaren geçen süre iki grup arasında benzerdi (tüm karşılaştırmalar için $p>0,05$). AUK geliştiğinde kanama şiddeti, hastaneye yatış oranı, eritrosit süspansiyonu gereksinimi ve hormonal veya traneksamik asit tedavisi gereksinimi açısından gruplar arasında anlamlı fark yoktu (tüm karşılaştırmalar için $p>0,05$). Tüm koagülasyon parametreleri normal aralıkta olmasına rağmen; O kan grubunda vWF, vWF:RCO ve faktör VIII düzeyleri anlamlı olarak daha düşük bulundu (sırasıyla $p=0,009$; $p=0,002$; $p=0,029$).

Sonuç: AUK tanılı ergenlerde O kan grubuna sahip olanlarda vWF düzeyleri daha düşük saptanmış olsa da bunun kanama şiddeti veya klinik sonuçlar üzerinde belirgin bir etkisi olmadığı görülmüştür.

Anahtar Kelimeler: Anormal uterin kanama, ergenlik, kan grubu

ABSTRACT

Aim: Individuals with blood group O are known to have lower levels of von Willebrand factor (vWF) compared with those with non-O blood groups. Therefore, bleeding risk is thought to be higher in individuals with blood group O. This study aimed to evaluate the relationship between ABO blood groups and vWF levels, bleeding severity, and clinical outcomes in adolescents presenting with abnormal uterine bleeding (AUB).

Materials and Methods: Adolescents who presented to the Adolescent Health Clinic with a diagnosis of AUB between June 2019 and June 2023 were retrospectively reviewed. Patients with anovulatory AUB who had documented ABO blood group information and normal levels of vWF, vWF ristocetin cofactor (vWF:RCO), and factor VIII were included. Those with AUB due to structural, iatrogenic, endocrine, or hematologic causes, as well as patients diagnosed with coagulopathy or von Willebrand disease, were excluded. Demographic data, menstrual characteristics, bleeding severity, treatment requirements, and laboratory results were compared between the O and non-O blood groups.

Results: A total of 98 adolescents were included in the study (33% blood group O, 67% non-O). Demographic characteristics, anthropometric measurements, age at menarche, and time since menarche were similar between the two groups ($p>0.05$ for all comparisons). When AUB occurred, bleeding severity, hospitalization rate, need for red blood cell transfusion, and the requirement for hormonal therapy or tranexamic acid did not differ significantly between the groups. Although all coagulation parameters were within normal ranges, levels of vWF, vWF:RCO, and factor VIII were significantly lower in the O blood group ($p=0.009$, $p=0.002$, and $p=0.029$, respectively).

Conclusion: Although vWF levels were lower in adolescents with AUB who had blood group O, this difference did not appear to influence bleeding severity or clinical outcomes.

Keywords: Abnormal uterine bleeding, adolescence, blood group.

Cite as: Aygün Arı D, Şahin G, Çetinkaya S. Anormal Uterin Kanaması Olan Ergenlerde ABO Kan Gruplarının Kanama Şiddeti ve Seyri ile İlişkisi. Jinekoloji-Obstetrik ve Neonatoloji Tıp Dergisi 2026;23(2):203–208.

Geliş/Received: 01.12.2025 • Kabul/Accepted: 11.02.2026

Sorumlu Yazar/Corresponding Author: Demet Aygün Arı, Ankara Etlik Şehir Hastanesi, Çocuk Sağlığı ve Hastalıkları, Ergen Sağlığı Kliniği, Ankara, Türkiye

E-mail: demetaygunari@gmail.com

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

GİRİŞ

Anormal uterin kanama (AUK) miktar, sıklık, süre ve/veya düzen açısından anormal olan, uterus kaynaklı kanamayı tanımlar (1) Ergenlerde yapısal nedenler çok nadirdir; en sık neden ise hipotalamus-hipofiz-over aksının immatürasyonuna bağlı anovulasyondur (2).

AUK olan ergenlerin %20'sinde altta yatan bir kanama bozukluğu olduğu, hastane yatışı gereken ergenlerde ise bu oranın %33'e yükseldiği bildirilmiştir (3). AUK ile başvuran ergenlerde en sık görülen kanama bozukluğu von Willebrand hastalığıdır ve prevalansı ergen ve erişkinlerin dahil edildiği bir derlemede %13 olarak bulunmuştur (4).

Von Willebrand hastalığı, von Willebrand faktör (vWF) eksikliği veya işlev bozukluğu olarak tanımlanır. vWF, endotel damar hasarı bölgelerine trombositleri yönlendirerek birincil hemostaza katılan, kollajene ve trombositlere bağlanarak trombosit tıkaçının oluşmasına yardımcı olan büyük, multimerik bir glikoproteindir. Ayrıca vWF, koagülasyon faktörü VIII'in taşıyıcısıdır; onun klirensini azaltarak fibrin oluşumuna katkıda bulunur. Bu nedenle, vWF'deki herhangi bir nicel veya nitel bozukluk, kanama riskinin artmasına neden olmaktadır (5). vWF molekülleri, A ve B kan grubu antijenlerine de ait olan oligosakkaridleri içerir. Bu antijenlerin varlığı vWF moleküllerinin vücuttan temizlenmesini azaltır. Bu nedenle A, B ve AB kan grubuna sahip bireyler, O kan grubuna sahip olanlardan yaklaşık %25 daha yüksek vWF seviyelerine sahiptir (6). Bu etkileşim nedeniyle, ABO kan grubunun kanama veya trombotik olayların gelişme olasılığını etkileyebileceği düşünülmüş, bu yönde çalışmalar yapılmıştır. O dışı kan gruplarının erişkinlerde bazı vasküler hastalıklar ile ilişkili olduğu (7), özellikle venöz tromboembolizm olan hastalarda O dışı kan grubu prevalansının, O kan grubuna göre daha yüksek olduğu gösterilmiştir (8).

O kan grubunun kanama için bir risk faktörü olduğu düşünülmektedir, ancak literatürde, ABO kan grupları ile kanama eğilimi arasındaki korelasyon konusunda çelişkili çalışmalar bulunmaktadır. ABO kan grubu ile hemorajik bozuklukların ilişkisinin değerlendirildiği bir meta-analizde; O kan grubu prevalansı, kanamalı hastalarda kontrollere göre istatistiksel olarak anlamlı şekilde daha yüksek bulunmuştur ve O kan grubunun kanama için potansiyel olarak önemli bir genetik risk faktörü olduğu şeklinde yorumlanmıştır (9). Üst gastrointestinal sistem kanaması olan hastalarda da O kan grubu sıklığı, kontrol grubuna göre anlamlı olarak artmış bulunmuştur (10). Bununla birlikte, başka bir çalışma, kan grupları ile majör serebral veya serebral olmayan kanamalar arasında herhangi bir ilişki olmadığını göstermiştir (11).

Literatürde erişkin kadınlarda gebelik ve sonrasında kanama ile ABO kan gruplarının ilişkisini değerlendiren çalışmalarda da farklı sonuçlar bildirilmiştir. Gebelikte kanama ile ABO kan gruplarının ilişkisinin değerlendirildiği bir çalışmada, doğum öncesi, doğumda ve doğum sonrası kanama ile ABO kan grupları arasında bir ilişki saptanmamıştır (12). Geniş çaplı bir çalışmada ise erken postpartum kanama ve hemoglobin düşüşü açısından O kan grubunun, O dışı kan gruplarına göre artmış risk taşıdığı bildirilmiştir. Ancak kan grupları arasında ağır hemoglobin düşüşü veya transfüzyon gereksinimi açısından fark saptanmamıştır (13). Buna karşın, mevcut çalışmalar erişkin popülasyona odaklanmakta olup, ergen yaş grubunda ABO kan grupları ile kanama eğilimi arasındaki ilişkiyi sistematik olarak değerlendiren yeterli veri bulunmamaktadır. Bildiğimiz kadarıyla literatürde ergenlerde ABO kan gruplarının AUK ve kanama şiddeti ile ilişkisini değerlendiren çalışma yoktur. Bu çalışmada, ergen sağlığı polikliniğimize AUK nedeniyle başvuran ergen hastalarda ABO kan gruplarına göre vWF düzeylerinin, kanama şiddetinin ve seyrinin karşılaştırılması amaçlanmıştır.

GEREÇ VE YÖNTEM

Çalışma Grubu

Araştırmaya Haziran 2019-Haziran 2023 tarihleri arasında hastanemiz Ergen Sağlığı polikliniğine başvuran, AUK tanısı alan hastalar dahil edildi. Uzamış ve/veya fazla miktarda adet kanaması tarifleyen, etiyolojide diğer nedenler ekarte edilerek anovulatuvar uterin kanaması olduğu saptanan hastalardan; kan grubu sistemde olan, vWF, vWF ristosetin kofaktörü (vWF:RCO), faktör VIII düzeyi bakılmış ve normal saptanmış olan hastalar çalışmaya dahil edildi. AUK etiyolojisinde yapısal, iyatrojenik veya başka bir neden olan hastalar; koagülopati, von Willebrand hastalığı, faktör VIII eksikliği saptanan hastalar çalışma dışında bırakıldı. Hastaların başvuru ve takip verileri hastane elektronik kayıtlarından elde edildi. Vücut kitle indeksi (VKİ), vücut ağırlığının (kg) boyun metre cinsinden karesine bölünmesiyle hesaplandı.

Hastaların başvuru anındaki yaş (yıl), vücut ağırlığı (kg), boy (cm), VKİ (kg/m²) verileri, menarş yaşları (yıl), menarştan sonra geçen süre (ay), normal adet düzenleri, son adet tarihleri; AUK geliştiğinde adet süreleri, siklus sıklıkları ve günlük kullanılan ped sayıları ve kanama şiddetleri, hastane yatış durumları, eritrosit süspansiyonu gereksinimleri, hormon tedavileri veya traneksamik asit kullanımları elektronik tıbbi kayıtlardan elde edildi. AUK geliştiğinde hastaneye başvurdıklarında bakılan hemogram, demir, serum demir bağlama kapasitesi, ferritin, prolaktin, tiroid stimulan hormon (TSH), serbest T4 (sT4), vWF, vWF:RCO, faktör VIII düzeyleri ve sistemde bulunan kan grupları not edildi.

Tanımlar

Adet kanamasının uzun sürmesi (≥ 8 gün) veya miktarının fazla olması (>6 ped/gün veya 80 ml/gün), siklus süresinin kısa olması (<21 gün) AUK olarak tanımlandı. Etiyolojide yapısal nedenlerin, kanama bozukluğunun, endokrinopatilerin, iyatrojenik nedenlerin ekarte edildiği kanamalar anovulatuvar kanama olarak kabul edildi.

Hafif AUK; adet süresinin uzaması veya siklusların normalden daha sık olması durumunda, kanamanın hafif-orta düzeyde artmış olması ve hemoglobin değerinin normal (>12 g/dL) ya da hafif düşük ($10-12$ g/dL) olması şeklinde tanımlandı. Orta AUK; adet süresinin uzaması veya siklus sıklığının artmasıyla birlikte orta-ağır düzeyde kanama bulunması ve hemoglobin düzeyinin ≥ 10 g/dL olması şeklinde sınıflandırıldı. Ağır AUK ise; ağır kanama ile birlikte hemoglobin düzeyinin <10 g/dL olması olarak tanımlandı.

Etik Kurul Onayı

Bu retrospektif, gözlemsel, karşılaştırmalı çalışma Dr. Sami Ulus Kadın Doğum, Çocuk Sağlığı ve Hastalıkları Eğitim ve Araştırma Hastanesi Klinik Araştırmalar Etik Kurulu'ndan 2020-KAEK-141/442 sayılı numarası ile onay alındı.

İstatistiksel Analiz

Verilerin değerlendirilmesinde, istatistiksel analizler için IBM SPSS StatisticsforWindows, Version 27.0 (Armonk, NY: IBM Corp.) programı kullanıldı. Kategorik değişkenler sayı ve % ile tanımlandı. Sürekli değişkenler için normal dağılım gösterenler ortalama $\pm$ standart sapma ile, normal dağılım göstermeyenler ise ortanca (çeyrekler arası aralık, Q1–Q3) şeklinde gösterildi. Parametrelerin normal dağılıma uygunluğu “Kolmogorov-Smirnov” ve “Shapiro-Wilk” testi ile değerlendirildi. Sürekli değişkenler parametrik test varsayımları

sağlanıyorsa Student t testi, sağlanmıyorsa Mann-Whitney U testi ile karşılaştırıldı. Kategorik değişkenler Ki-kare veya Fisher–Freeman–HaltonExact Test ile analiz edildi. p değeri $<0,05$, istatistiksel olarak anlamlı kabul edildi.

BULGULAR

Çalışmaya, yaş ortalaması $13,79\pm 1,95$ yıl olan, 32'si (%33) O kan grubuna, 66'sı (%67) O dışı kan grubuna sahip (45 hasta A, 18 hasta B ve 3 hasta AB), 98 AUK tanılı olgu dahil oldu. Olguların ortalama menarş yaşları $11,93\pm 1,14$ yıl, menarştan sonra geçen süre ortancası 17,5 (IQR: 7,75-34,25) ay idi. Olguların 32'sinin (%32,7) hastaneye yatırılarak izlenmesi gerektiği, 16'sının (%16,3) eritrosit süspansiyonu gereksinimi olduğu, 66'sının (%67,3) hormon tedavisi aldığı, 4'ünün (%4,1) traneksamik asit tedavisi aldığı saptandı. Olguların 33'ünün (%33,7) kanama şiddeti hafif, 24'ünün (%24,5) orta, 41'inin (%41,8) ağır düzeyde idi. Olguların aktive parsiyel tromboplastin zamanı (aPTT), Uluslararası Normalleştirilmiş Oran ('International Normative Ratio'; INR) ve trombosit sayısı normal sınırlarda idi. Tüm olguların human koryonik gonadotropin (hCG) testleri negatif idi.

O ve O dışı kan grubuna sahip olguların yaşları ve antropometrik verileri benzer idi (Tablo 1). O kan grubuna sahip olgularda; ortalama menarş yaşı $11,86\pm 1,03$ yıl, menarştan beri geçen süre ortanca 20 (5,25-38,25) ay iken; O dışı kan grubuna sahip olan olgularda ise; bu süreler $11,96\pm 1,20$ yıl ve 16,50 (8-34,25) ay idi ve iki grup arasında anlamlı fark yoktu (sırasıyla $p=0,677$, $p=0,791$). AUK şiddetleri (hafif, orta, ağır) iki grup arasında benzer bulundu

Tablo 1. Hastaların demografik ve antropometrik verilerinin karşılaştırılması.

	O Kan Grubu n: 32	O Dışı (A, B, AB) Kan Grupları n: 66	p
	Ortalama $\pm$ SD Medyan (IQR)	Ortalama $\pm$ SD Medyan (IQR)	
Yaş (yıl)	13,90 $\pm$ 2,18	13,74 $\pm$ 1,84	0,694
Vücut ağırlığı (kg)	52,60 (46,13-60,44)	50,00 (45,00-57,66)	0,117
Vücut ağırlığı persentil	61,79 (28,13-92,46)	55,77 (13,11-79,03)	0,158
Vücut ağırlığı SDS	0,30 (-0,59-1,44)	0,15 (-1,12-0,81)	0,148
Boy (cm)	157,02 $\pm$ 7,79	156,39 $\pm$ 6,78	0,687
Boy persentil	48,05 $\pm$ 30,84	46,12 $\pm$ 27,93	0,758
Boy SDS	-0,10 $\pm$ 1,10	-0,17 $\pm$ 1,14	0,772
VKİ (kg/m ²)	21,27 (19,69-25,08)	20,31 (18,23-24,02)	0,115
VKİ persentil	67,72 (34,48-94,32)	57,34 (15,97-90,29)	0,157
VKİ SDS	0,73 $\pm$ 1,46	0,18 $\pm$ 1,50	0,094

VKİ: Vücut kitle indeksi

Tablo 2. Menstrual verilerin gruplar arasında karşılaştırılması.

	O Kan Grubu n: 32	O Dışı (A, B, AB) Kan Grupları n: 66	p
	Ortalama ± SD	Ortalama ± SD	
Menarş yaşı (yıl)	11,86±1,03	11,96±1,20	0,677
	Medyan (IQR)	Medyan (IQR)	p
Menarştan beri geçen süre (ay)	20,00 (5,25-38,25)	16,50 (8,00-34,25)	0,791
	n (%)	n (%)	p
Kanama şiddeti			
-Hafif	10 (%31,3)	23 (%34,8)	0,271
-Orta	11 (%34,4)	13 (%19,7)	
-Ağır	11 (%34,4)	30 (%45,5)	
Hastane yatışı			
-Var	10 (%31,3)	22 (%33,3)	0,837
-Yok	22 (%68,8)	44 (%66,7)	
ES almış mı?			
-Evet	7 (%21,9)	9 (%13,6)	0,301
-Hayır	25 (%78,1)	57 (%86,4)	
Tedavi			
-Almamış	8 (%25)	20 (%30,3)	0,852*
-Hormonal tedavi	23 (%71,9)	43 (%65,2)	
-Traneksamik asit	1 (%3,1)	3 (%4,5)	

* Fisher-Freeman-Halton Exact Test

ES: Eritrosit süspansiyonu

(p=0,271). O kan grubuna sahip olguların 23'ü hormonal tedavi (20 olgu kombine oral kontraseptif, 3 olgu progesteron), biri transamin; O dışı kan grubuna sahip olguların 43'ü hormonal tedavi (39 olgu kombine oral kontraseptif, 4 olgu progesteron), üçü transamin tedavisi almıştı. İki grubun klinik ve izlem özellikleri Tablo 2'de sunulmuştur (Tablo 2).

vWF, vWF:RCo ve faktör VIII düzeyleri O kan grubuna sahip grupta, diğer gruba göre istatistiksel olarak anlamlı şekilde daha düşük (sırasıyla p=0,009, p=0,002, p=0,029) iken, diğer laboratuvar verilerinin iki grup arasında benzer olduğu saptandı (Tablo 3). O kan grubu olan grupta, O dışı kan grubu olan gruba göre vWF düzeyinin %17, vWF:RCo düzeyinin %23,8 ve faktör VIII düzeyinin %14 daha düşük olduğu bulundu.

Tablo 3. Gruplara göre laboratuvar değerleri ve gruplar arası karşılaştırılması.

	O Kan Grubu n: 32	O Dışı (A, B, AB) Kan Grupları n: 66	p
	Ortalama ± SD Medyan (IQR)	Ortalama ± SD Medyan (IQR)	
Hemoglobin (g/dL)	11,35 (7,63-12,08)	10,4 (7,3-13,0)	0,782
Trombosit sayısı (x10 ³ /μL)	321,38±119,35	334,98±85,60	0,520
Demir (mcg/dl)	24,0 (11,5-41,0)	23,0 (13,0-49,0)	0,472
SDBK (mcg/dl)	439,0±73,1	425,1±72,7	0,739
Ferritin (ng/ml)	6,00 (2,05-11,85)	5,50 (2,55-16,95)	0,679
PRL (ng/ml)	12,88 (9,84-17,70)	10,72 (7,85-16,07)	0,211
TSH (mIU/ml)	2,12±0,88	2,41±1,26	0,267
sT4 (ng/dl)	1,16±0,17	1,10±0,19	0,182
vWF (%)	85,5 (62,8-119,5)	103,0 (79,8-138,3)	0,009
vWF:RCo (%)	61,7 (52,3-80,0)	81 (61-101)	0,002
Faktör VIII (%)	92,0 (62,0-141,5)	107,0 (86,5-144,3)	0,029

PRL: Prolaktin, SDBK: Serum demir bağlama kapasitesi, sT4: Serbest T4, TSH: Tiroid stimulan hormon, vWF: VonWillebrand faktör, vWF:RCo: vWF Ristosetin kofaktör.

TARTIŞMA

Çalışmamızda O kan grubuna sahip olguların, vWF düzeylerinin yaklaşık %25 daha düşük olması nedeniyle; AUK olan ergenlerde ABO kan gruplarının; AUK şiddetine ve seyrine etkisini değerlendirdik. Kan gruplarına göre, vWF, vWF:RCo ve faktör VIII düzeyleri ile değerlendirme yaptığımız çalışmamızda; vWF, vWF:RCo ve faktör VIII düzeyleri tüm olgularımızda normal aralıkta olmakla birlikte, O kan grubu olan olgularımızda, O dışı kan grubu olan olgularımıza göre anlamlı şekilde düşük bulduk. Ancak bu düşüklüğün klinik olarak kanama şiddeti, hastane yatış oranı ve eritrosit süspansiyonu ihtiyacı açısından kan gruplarına göre farklılık oluşturmadığını saptadık.

Çalışmamızda 45 (%45,9) hastada A, 32 (%32,7) hastada O, 18 (%18,4) hastada B ve 3 (%3,1) hastada AB kan grubu saptanmıştır. Türk toplumunda ise ABO kan grubu dağılımı A %42,1, O %34,0, B %16,4 ve AB %7,5 olarak bildirilmektedir (14). Hasta grubumuzdaki O ve O dışı kan grubu dağılımının, Türk toplumunda bildirilen dağılımla benzer olduğu görülmüştür.

O kan grubu olan grupta, O dışı kan grubu olan gruba göre vWF düzeyinin %17, vWF:RCo düzeyinin %23,8 ve faktör VIII düzeyinin %14 daha düşük olduğu saptandı. Literatürde de vWF, vWF:RCo ve faktör VIII düzeylerinin O kan grubu olanlarda O dışı kan grubu olanlara göre düşük olduğu gösterilmiştir (15). Bu bilgiye dayanarak, pıhtılaşmada önemli olan vWF düzeyinin daha yüksek olduğu O dışı kan gruplarında tromboz riskinin; vWF düzeyinin daha düşük olduğu O kan grubunda ise kanama riskinin artacağı düşünülmektedir. O kan grubu olan bireylerde, kanama riskinin artıp artmadığı farklı çalışmalarla değerlendirilmiştir. Sistematik bir gözden geçirme ve meta-analiz çalışmasında O kan grubu kanama için risk faktörü olarak tanımlanmıştır (9). Postpartum kanamanın değerlendirildiği bir çalışmada, O kan grubunda kanamanın daha sık olduğu, ancak bunun klinik olarak anlamlı bir fark yaratmadığı gösterilmiş (16), daha geniş çaplı başka bir çalışmada ise ABO kan grubu ile postpartum kanama arasında ilişki gösterilmemiştir (17). Doğum şekline göre ABO kan grupları ile doğum sonrası kanama oranlarının ilişkisine bakılan bir çalışmada ise, vajinal doğumda gruplar arasında fark yokken, sezaryen doğumda O kan grubu olanlarda kanamanın daha sık olduğu, ancak klinik seyrin değişmediği belirtilmiştir (18). Yine kardiyak cerrahide, AB kan grubunun anlamlı ölçüde daha az transfüzyonla ilişkili olduğu ve uzun dönem sağkalımın bu grupta daha iyi olduğu gösterilmiştir (19). Yani obstetrik kanamaların ve kanamanın klinik seyrinin, ABO kan gruplarına göre belirgin değişiklik göstermediği; ancak obstetrik veya başka bir cerrahi işlem söz konusu olduğunda, ABO kan grubunun önem kazandığı anlaşılmaktadır.

AUK olan ergenlerde ABO kan gruplarına göre kanamanın şiddetinin değişmediğini, klinik izlemde hastane yatış oranlarının, eritrosit süspansiyonu ve tedavi gereksiniminin gruplar arasında benzer olduğunu gösterdik. Nedeni bilinmeyen hafif-orta şiddette kanaması olan, 16 yaş ve üzeri hastaların değerlendirildiği bir çalışmada O kan grubu, kanaması olan hastalarda kontrol grubuna göre daha sık görülmüş ve artmış kanama şiddeti ile ilişkili bulunmuştur. Oral mukozal kanama görülme sıklığının da, O kan grubunda, O dışı kan gruplarına göre anlamlı olarak daha yüksek olduğu saptanmıştır. Ancak bu ilişkinin, vWF, vWF:RCo ve faktör VIII düzeylerinden bağımsız olduğu belirtilmiştir. Bu durum O kan grubunda vWF düzeyinden bağımsız, başka mekanizmalarla da kanama riskinin ve şiddetinin artabileceği şeklinde yorumlanmış ve tartışılmıştır (20). Ancak ABO kan gruplarına göre kanama şiddetini, özellikle uterin kanamalarda şiddeti değerlendiren yeterli çalışma olmadığından; O kan grubunun kanama şiddetine etkili olduğu söylenemez. Çalışma sonuçlarımız da bunu desteklemektedir. Ancak literatürdeki cerrahi ilişkili çalışmalar göz önüne alındığında, cerrahi gerektiren durumlarda kan grubunun göz önünde bulundurulması önerilebilir.

Bu çalışmanın bazı kısıtlılıkları vardır. Yalnızca vWF, vWF:RCo ve faktör VIII düzeyleri ölçülmüş hastaların çalışmaya dahil edilmesi, AUK tanılı tüm olgular arasında, kan grubu dağılımının değerlendirilememesine neden olmuştur. Ayrıca örneklem büyüklüğü, kan grubunun kanama şiddeti üzerindeki etkisini göstermede yetersiz kalmış olabilir. Bununla birlikte, bildiğimiz kadarıyla çalışmamız, AUK olan ergenlerde vWF düzeylerini ve kan gruplarının kanama şiddeti ile klinik seyr üzerindeki olası etkilerini birlikte inceleyen ilk araştırmadır ve gelecekte yapılacak daha kapsamlı çalışmalara zemin oluşturmaktadır.

Sonuç olarak çalışmamızda AUK olan ergenlerde, O kan grubu olan hastalarda vWF düzeyi daha düşük olsa da bunun kanama şiddeti ve klinik seyr üzerinde bir etkisi olmadığı saptanmıştır.

KAYNAKLAR

1. Munro MG, Critchley HO, Broder MS, Fraser IS. FIGO classification system (PALM-COIN) for causes of abnormal uterine bleeding in nonpregnant women of reproductive age. *Int J Gynaecol Obstet.* 2011;113(1):3-13.
2. Practice bulletin no. 128: diagnosis of abnormal uterine bleeding in reproductive-aged women. *Obstet Gynecol.* 2012;120(1):197-206.
3. Screening and management of bleeding disorders in adolescents with heavy menstrual bleeding: ACOG COMMITTEE OPINION, Number 785. *Obstet Gynecol.* 2019;134(3):e71-e83.
4. Shankar M, Lee CA, Sabin CA, Economides DL, Kadir RA. von Willebrand disease in women with menorrhagia: a systematic review. *Bjog.* 2004;111(7):734-40.
5. Kabra R, Fisher M. Abnormal uterine bleeding in adolescents. *Curr Probl Pediatr Adolesc Health Care.* 2022;52(5):101185.
6. Blustin JM, McBane RD, Mazur M, Ammash N, Sochor O, Grill DE, et al. The association between thromboembolic complications and blood group in patients with atrial fibrillation. *Mayo Clin Proc.* 2015;90(2):216-23.

7. Wu O, Bayoumi N, Vickers MA, Clark P. ABO(H) blood groups and vascular disease: a systematic review and meta-analysis. *J Thromb Haemost.* 2008;6(1):62-9.
8. Dentali F, Sironi AP, Ageno W, Turato S, Bonfanti C, Frattini F, et al. Non-O blood type is the commonest genetic risk factor for VTE: results from a meta-analysis of the literature. *Semin Thromb Hemost.* 2012;38(5):535-48.
9. Dentali F, Sironi AP, Ageno W, Bonfanti C, Crestani S, Frattini F, et al. Relationship between ABO blood group and hemorrhage: a systematic literature review and meta-analysis. *Semin Thromb Hemost.* 2013;39(1):72-82.
10. Bayan K, Tüzün Y, Yılmaz S, Dursun M, Canoruc F. Clarifying the relationship between ABO/Rhesus blood group antigens and upper gastrointestinal bleeding. *Dig Dis Sci.* 2009;54(5):1029-34.
11. Franchini M, Crestani S, Rossi C, Frattini F, Mengoli C, Giacomini I, et al. O blood group and the risk of major bleeding: a single-center survey. *J Thromb Thrombolysis.* 2013;35(1):65-6.
12. Clark P, Walker ID, Govan L, Wu O, Greer IA. The GOAL study: a prospective examination of the impact of factor V Leiden and ABO(H) blood groups on haemorrhagic and thrombotic pregnancy outcomes. *Br J Haematol.* 2008;140(2):236-40.
13. Drukker L, Srebnik N, Elstein D, Levitt L, Samueloff A, Farkash R, et al. The association between ABO blood group and obstetric hemorrhage. *J Thromb Thrombolysis.* 2016;42(3):340-5.
14. Sağdur L, Karaca A, Günçikan MN, Yılmaz M, Kinik K. Blood group profile of Türkiye with regional and demographic differences: a 23-year retrospective study. *Turk J Med Sci.* 2025;55(4):961-70.
15. Moeller A, Weippert-Kretschmer M, Prinz H, Kretschmer V. Influence of ABO blood groups on primary hemostasis. *Transfusion.* 2001;41(1):56-60.
16. Kahr MK, Franke D, Brun R, Wisser J, Zimmermann R, Haslinger C. Blood group O: A novel risk factor for increased postpartum blood loss? *Haemophilia.* 2018;24(4):e207-e12.
17. Ali-Saleh M, Lavie O, Abramov Y. Evaluation of blood type as a potential risk factor for early postpartum hemorrhage. *PLoS One.* 2019;14(4):e0214840.
18. Burd JE, Quist-Nelson JA, Edwards SE, Suhag A, Berghella VP, Nijjar JB. Blood type and postpartum hemorrhage by mode of delivery: A retrospective cohort study. *Eur J Obstet Gynecol Reprod Biol.* 2021;256:348-53.
19. Welsby IJ, Phillips-Bute B, Mathew JP, Newman MF, Becker R, Rao S, et al. ABO blood group influences transfusion and survival after cardiac surgery. *J Thromb Thrombolysis.* 2014;38(3):402-8.
20. Mehic D, Hofer S, Jungbauer C, Kaider A, Haslacher H, Eigenbauer E, et al. Association of ABO blood group with bleeding severity in patients with bleeding of unknown cause. *Blood Adv.* 2020;4(20):5157-64.

The Effect of Sexual Health Education and Pelvic Floor Exercises on Body Image and Anxiety Levels in Women Diagnosed with Vaginismus

Vajinismus Tanısı Konmuş Kadınlarda Cinsel Sağlık Eğitimi ve Pelvik Taban Egzersizlerinin Vücut Algısı ve Kaygı Düzeyleri Üzerindeki Etkisi

 Gonca TURKER ERGUN¹,  Ayşe KUYULU AKMAN¹

¹Ankara Bilkent City Hospital, Department of Obstetrics and Gynecology, Ankara, Türkiye

ABSTRACT

Aim: This study was conducted to determine the effects of sexual health education and pelvic floor exercises on body image perception and anxiety levels in women diagnosed with vaginismus.

Materials and Methods: The sample of this prospective study consisted of married women aged 18 years and older who were diagnosed with vaginismus, had no psychiatric disorders, and presented to the Sexual Function Disorders Outpatient Clinic of the Department of Obstetrics and Gynecology at Ankara Bilkent City Hospital between 2024 and 2025. A total of 120 women were included in the study, comprising 60 participants in the intervention group who received sexual health education and pelvic floor exercises and 60 participants in the control group. The Beck Anxiety Inventory (BAI) and the Body Image Scale (BIS) were administered to both groups.

Results: The mean age of the women was 28.7 ± 5.5 years, and the mean age of their partners was 31.3 ± 5.2 years. Seventy percent of the women were university graduates, and 59.2% were employed. When vaginal penetration success among women diagnosed with vaginismus was evaluated, the overall success rate was 56.7%. A statistically significant difference was observed between pre- and post-intervention Body Image Scale total scores following sexual health education and pelvic floor exercises ($p < 0.05$). After the intervention, the total Beck Anxiety Inventory score of the intervention group (17.7 ± 14.0) was significantly lower than that of the control group (43.8 ± 15.3).

Conclusion: Sexual health education and pelvic floor exercises play a critical role in improving sexual quality of life. Regular and effective exercise programs supported by vaginismus treatment teams and women's health professionals have a positive impact on anxiety levels and body image perception.

Keywords: Vaginismus, sexual health education, pelvic floor exercises

ÖZ

Amaç: Araştırma vajinismus tanılı kadınlarda cinsel sağlık eğitimi ve pelvik taban egzersizlerinin beden algısı ve anksiyete düzeyine etkisini belirlemek amacıyla yapılmıştır.

Gereç ve Yöntemler: Bu prospektif araştırmanın örneklemini; Ankara Bilkent Şehir Hastanesi Kadın Doğum ve Hastalıkları Cinsel Fonksiyon Bozuklukları Polikliniğine 2024-2025 tarihleri arasında vajinismus tanılı, 18 yaş ve üzeri evli ve psikiyatrik bir tanısı olmayan kadınlar oluşturmuştur. Araştırmaya cinsel sağlık eğitimi ve pelvik taban egzersizleri uygulanan 60 vaka - 60 kontrol grubu kadın dahil edilmiştir. Her iki gruba da Beck Anksiyete Ölçeği (BAI) ve Beden İmajı Ölçeği (BİÖ) uygulanmıştır.

Bulgular: Araştırmadaki kadınların yaş ortalaması $28,7 \pm 5,5$, partner yaş ortalaması $31,3 \pm 5,2$ ve kadınların %70'nin üniversite mezunu olduğu gözlenmiş olup %59,2'sinin çalıştığı belirlenmiştir. Vajinismus tanılı kadınların penetrasyon gerçekleştirme durumu incelendiğinde; başarı oranı %56,7'dir. CSE(cinsel sağlık eğitimi) ve PTE (pelvik taban egzersiz) öncesi ve sonrası BİÖ toplam puanı arasında istatistiksel olarak anlamlı bir fark görülmüştür ($p < 0,05$). CSE ve PTE sonrası vaka grubunun BAI toplam puanı ($17,7 \pm 14,0$) kontrol grubunun ($43,8 \pm 15,3$) toplam puanından düşük olduğu sonucuna varılmıştır.

Sonuç: CSE ve PTE'nin cinsel yaşam kalitesi açısından yeri çok önemlidir. Düzenli ve etkili yapılan egzersizlerin vajinismus ve kadın sağlığı çalışan ekiplerce desteklenmesi pozitif anlamda etkilediği sonucuna ulaşılmıştır.

Anahtar Kelimeler: Vajinismus, cinsel sağlık eğitimi, pelvik taban egzersizleri

Cite as: Turker Ergun G, Kuyulu Akman A. The Effect of Sexual Health Education and Pelvic Floor Exercises on Body Image and Anxiety Levels in Women Diagnosed with Vaginismus. Jinekoloji-Obstetrik ve Neonatoloji Tıp Dergisi 2026;23(2):209–214.

Geliş/Received: 12.01.2026 • **Kabul/Accepted:** 12.02.2026

Sorumlu Yazar/Corresponding Author: Gonca Turker Ergun, Ankara Bilkent City Hospital, Department of Obstetrics and Gynecology, Ankara, Türkiye

E-mail: drgoncaturker@gmail.com

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

INTRODUCTION

Although vaginismus is one of the most common sexual dysfunctions, its exact prevalence in gynecology clinics cannot be clearly determined, as patients often refrain from seeking medical help due to feelings of embarrassment during the application process and difficulties in expressing themselves (1). In a cross-sectional study conducted in Turkey on sexual dysfunctions, the prevalence of vaginismus has been reported as 41%, 41.7%, and between 66% and 75.9% (1, 2).

As a treatment method for vaginismus, interventions aimed at increasing awareness of the vaginal muscles and promoting relaxation through the use of vaginal dilators, sexual therapy, and cognitive behavioral therapy are frequently employed. In addition, eye movement desensitization and reprocessing (EMDR), hypnotherapy, and pharmacological approaches may also be used (3). Furthermore, the Information–Motivation–Behavioral Skills (IMB) Model is among the models widely utilized to promote and improve sexual health through a holistic approach (4). The IMB model may provide a structured framework for vaginismus treatment by addressing women's knowledge about genital anatomy and pain mechanisms, enhancing motivation to overcome fear and avoidance, and developing practical behavioral skills such as pelvic floor relaxation and graded vaginal exposure. In this context, applying the IMB components to vaginismus management may facilitate treatment adherence and support the acquisition of adaptive sexual behaviors. Studies in the literature employing the IMB Model have predominantly focused on sexual health, sexually transmitted diseases, substance use disorders, and chronic illnesses (5).

Individuals' perceptions of their physical appearance—that is, their internalized body image—are considered one of the most important factors influencing self-esteem. Body image affects individuals' lives across a wide spectrum, ranging from social anxieties to sexual behaviors (6). In a study examining the relationship between body image and sexuality, individuals with a healthy sexual life were investigated. The results of the study demonstrated that individuals who derive pleasure from sexuality tend to have a positive body image (7). Furthermore, La Rocque and Cioe (8), as well as Van den Brink et al. (9), concluded that individuals of both sexes with a negative body image are more likely to avoid sexual activity compared to those with a positive body image.

The process of sexual education and counseling includes providing individuals with information on sexual health, anatomical knowledge, physiological responses, and positive experiences related to sexual intercourse. In addition, it focuses on correcting

misconceptions about sexual activity, addressing fears, improving body image, and enhancing skills related to relaxation and the ability to experience pleasure during sexual intercourse. Sexual education and counseling constitute an essential component of a multidisciplinary approach to the treatment of vaginismus and, when used in conjunction with other therapeutic methods, contribute to achieving more effective outcomes (10).

In behavioral treatment models of vaginismus, the vaginal response represents a conditioned fear response to a specific (sexual) stimulus. From this perspective, the ability to control the pelvic muscle system plays a crucial role in the perception and maintenance of sexuality, as well as in feelings of shame related to body image. Hypertonic pelvic floor muscles in women are associated with myofascial pain, vulvodynia, dyspareunia, and vaginismus. In genito-pelvic pain disorders such as dyspareunia and vaginismus, pelvic floor rehabilitation is considered an important treatment modality within a multidisciplinary approach, as it facilitates relaxation of hypertonic pelvic floor muscles, normalizes muscle activity at rest, enhances muscle awareness, and improves vaginal flexibility (11, 12).

In this study, it is planned to examine the processes of improvement in sexual well-being and the treatment of vaginismus in patients who receive sexual education based on the IMB model, accompanied by pelvic floor exercises.

MATERIALS AND METHODS

The study population consisted of women aged 18 years and older who presented with complaints of vaginismus to the Sexual Function Disorders Outpatient Clinic of the Department of Obstetrics and Gynecology at Ankara Bilkent City Hospital between 2024 and 2025, who were married and had no diagnosed psychiatric disorders. Ethical approval for the study was obtained from the Ankara Bilkent City Hospital Institutional Ethics Committee (Decision No: TABED 1-24-757, Code No: 757).

None of the women had previously performed any exercises or treatment for vaginismus.

A total of 120 women were included in the study, comprising 60 participants in the intervention group who received sexual health education and pelvic floor exercises, and 60 participants in the control group who did not receive any intervention. Group allocation of the current study was based on voluntary participation. Women who agreed to receive the structured sexual health education and pelvic floor exercise program were assigned to the intervention

group. Face-to-face interviews were conducted with both groups at least twice, and follow-up evaluations and testing procedures were performed under clinical conditions one week later. The common characteristics of both groups were being married, having no psychiatric history, and the absence of vaginal penetration.

The exclusion criteria were as follows: age under 18 years, unmarried status, presence of a known psychiatric disorder, lost to follow-up, and inability to participate due to insufficient data.

Patients included in the intervention group received sexual health education, pelvic floor exercises, and an intervention based on the Information–Motivation–Behavioral Skills (IMB) model. Sexual health education covered fundamental concepts of sexuality, sexual myths, sexual health during adolescence and reproductive age, sexual behaviors, sexual identity, anatomy and physiology of the female and male reproductive systems, sexual identity development, universal values related to sexuality, sexually transmitted infections, and family planning.

Pelvic floor exercises included Kegel exercises, diaphragm breathing, stress management techniques, calming suggestions, focusing on silence and internal impulses, and supplementation with magnesium glycinate (13).

The IMB model, developed by Fisher in 1992, is a three-component sexual health model consisting of Information, Motivation, and Behavioral Skills. This model was used to provide structured education and exercise support to patients with vaginismus (13).

Demographic characteristics of the participants (such as age, educational level, and employment status) and variables related to the vaginismus treatment process (including session duration, penetration status, and receipt of psychological or urological support) were recorded.

The Beck Anxiety Inventory (BAI) and the Body Image Scale (BIS) were administered at baseline and at the final assessment (14).

The Body Image Scale (BIS) was developed by Secord and Jourard (1953) to assess individuals' satisfaction with various body parts and bodily functions (15). The validity and reliability study of the scale in Turkish was conducted by Hovardaoğlu (1992) (16). The scale consists of 40 items related to body organs, parts, or functions and is scored on a 5-point Likert scale ranging from "do not like at all (1)" to "like very much (5)." Higher scores indicate greater body satisfaction.

The Beck Anxiety Inventory (BAI) is a self-report scale used to assess the frequency of anxiety symptoms experienced by individuals. It

consists of 21 items rated on a Likert scale from 0 to 3. Higher scores indicate greater severity of anxiety. Scores between 0–7 indicate minimal anxiety/normal, 8–15 indicate mild anxiety, 16–25 indicate moderate anxiety, and 26–63 indicate severe anxiety. The validity and reliability of the Turkish version of the BAI were established by Ulusoy et al (17).

Penetration success was defined as the participant's ability to achieve vaginal penetration with the partner's penis without intolerable pain and without involuntary pelvic floor muscle contraction that prevented intercourse. Success was considered present when the participant reported at least one episode of completed vaginal penetration during the post-intervention assessment period.

Statistical Analysis

Statistical analyses were conducted by evaluating the normality of the distribution of variables using the Shapiro–Wilk and Kolmogorov–Smirnov tests, as well as skewness and kurtosis values and histogram plots. Continuous numerical variables were expressed as mean $\pm$ standard deviation and median (minimum–maximum). Categorical variables were expressed as numbers and percentages. For comparisons between independent groups involving non-normally distributed continuous variables, the Mann–Whitney U test was used. For comparisons of non-normally distributed continuous variables within dependent groups (repeated measurements), the Wilcoxon signed-rank test was applied. A p-value of <0.05 was considered statistically significant in all analyses, which were performed using SPSS version 25.0.

RESULTS

The mean age of the women was 28.7 ± 5.5 years, and the mean age of their partners was 31.3 ± 5.2 years. Most participants were university graduates (70%), and 59.2% were employed. The majority of women (89.2%) reported premarital romantic relationships, and the median duration of marriage was 7 (1–56) months. Psychological counseling was received by 23.3 % of couples, and 74.2% of male partners underwent urological evaluation (Table 1).

In the intervention group, the mean duration of sexual health education was 17.2 ± 8.9 days, and the mean duration of pelvic floor muscle training was 34.6 ± 14.9 minutes per session. A history of sexual abuse or violence was reported by 6.7% of women, and successful vaginal penetration was achieved by 56.7% of participants with vaginismus (Table 1).

Following sexual health education and pelvic floor muscle training, the mean total Beck Anxiety Inventory (BAI) score significantly

Table 1. Selected Sociodemographic Characteristics of the Participants

Variable	n	%
Group		
Patient	60	50.0
Control	60	50.0
Age, years		
Mean $\pm$ SD = 28.7 $\pm$ 5.5; Median (min-max) = 27 (18-42)		
Educational status		
Secondary school graduate	8	6.7
High school graduate	28	23.3
University graduate	84	70.0
Employment status		
Employed	49	40.8
Unemployed	71	59.2
Type of marriage		
Dating	107	89.2
Arranged marriage	13	10.8
Duration of marriage, months		
Mean $\pm$ SD = 8.9 $\pm$ 8.6; Median (min-max) = 7 (1-56)		
Spouse's age, years		
Mean $\pm$ SD = 31.3 $\pm$ 5.2; Median (min-max) = 30 (21-48)		
Psychological support		
Yes	28	23.3

Table 2. Beck Anxiety Inventory (BAI) and Subscale Scores of Participants Before and After Exercise (n = 60)

BAI	Before Exercise	After Exercise	p-value*
Subjective anxiety	25.9 $\pm$ 5.0	11.0 $\pm$ 8.4	<0.001
	25 (12-39)	11 (0-33)	
Somatic symptoms	14.7 $\pm$ 4.0	6.7 $\pm$ 5.6	<0.001
	16 (1-24)	7 (0-23)	
Total score	39.6 $\pm$ 8.1	17.7 $\pm$ 14.0	<0.001
	41 (13-63)	18 (0-56)	

*Wilcoxon Signed-Rank Test
Data are presented as mean $\pm$ SD and median (min-max).

Table 3. Body Image Scale (BIS) Scores of Participants Before and After Exercise (n = 60)

Time point	BIS score	p-value*
Before exercise	104.2 $\pm$ 24.4; 104 (54-160)	
After exercise	161.9 $\pm$ 21.6; 166 (49-194)	<0.001

*Wilcoxon signed-rank test.

decreased from 39.6 $\pm$ 8.1 to 17.7 $\pm$ 14.0 ($p < 0.05$). Both cognitive/subjective anxiety and somatic symptom subscale scores demonstrated significant post-intervention reductions (Table 2).

The mean Body Image Scale score increased significantly from 104.2 $\pm$ 24.4 at baseline to 161.9 $\pm$ 21.6 after the intervention ($p < 0.05$) (Table 3).

When comparing the intervention and control groups before the intervention, the mean total BAI score was 39.6 $\pm$ 8.1 in the case group and 43.8 $\pm$ 15.3 in the control group (Table 4).

After sexual health education and pelvic floor exercises, a statistically significant difference was found between the intervention and control groups in terms of total Beck Anxiety Inventory scores ($p < 0.001$). The total BAI score of the case group (17.7 $\pm$ 14.0) was significantly lower than that of the control group (43.8 $\pm$ 15.3) (Table 5)

No significant between-group difference was observed in baseline Body Image Scale scores ($p = 0.256$). However, post-intervention Body Image Scale scores were significantly higher in the intervention group compared with the control group ($p < 0.001$) (Table 6).

Table 4. Comparison of Beck Anxiety Inventory (BAI) Scores Between Patients (Before Exercise) and Controls (n = 120)

BAI score	Patients (n = 60)	Controls (n = 60)	p-value*
Subjective anxiety	24.9 $\pm$ 5.0; 25 (12-39)	27.1 $\pm$ 9.8; 28 (0-39)	0.009
Somatic symptoms	14.7 $\pm$ 4.0; 16 (1-24)	16.7 $\pm$ 5.6; 17 (1-24)	0.007
Total BAI score	39.6 $\pm$ 8.1; 41 (13-63)	43.8 $\pm$ 15.3; 45 (1-63)	0.002

*Mann-Whitney U test.

Table 5. Comparison of Beck Anxiety Inventory (BAI) Scores Between Patients (After Exercise) and Controls (n = 120)

BAI score	Patients (n = 60)	Controls (n = 60)	p-value*
Subjective anxiety	11.0 $\pm$ 8.4; 11 (0-33)	27.1 $\pm$ 9.8; 28 (0-39)	<0.001
Somatic symptoms	6.7 $\pm$ 5.6; 7 (0-23)	16.7 $\pm$ 5.6; 17 (1-24)	<0.001
Total BAI score	17.7 $\pm$ 14.0; 18 (0-56)	43.8 $\pm$ 15.3; 45 (1-63)	<0.001

*Mann-Whitney U test.

Table 6. Comparison of Body Image Scale (BIS) Scores Between Patients and Controls (n = 120)

Time point	Patients (n = 60)	Controls (n = 60)	p-value*
Before exercise	104.2 ± 24.4; 104 (54–160)	108.0 ± 47.4; 81 (40–200)	0.256
After exercise	161.9 ± 21.6; 166 (49–194)	108.0 ± 47.4; 81 (40–200)	<0.001

*Mann-Whitney U test.

DISCUSSION

This study evaluated changes in anxiety levels and body image perception among women diagnosed with vaginismus attending a sexual dysfunction outpatient clinic following sexual health education and pelvic floor muscle training. At baseline, no statistically significant differences in Beck Anxiety Inventory scores, and body image scale were observed between the intervention and control groups. After the intervention, lower post-intervention anxiety level scores observed in the intervention group. In addition, post-intervention Body Image Scale scores were significantly higher in the intervention group.

Pelvic floor muscle training aims to alleviate symptoms by regulating increased pelvic floor muscle activation in patients with vaginismus. This approach is important for contributing to the improvement of heightened anxiety symptoms and for supporting treatment adherence throughout the process.

Lankveld et al. reported that a sexual therapy protocol incorporating sexual education, relaxation exercises, gradual exposure, and group-based cognitive behavioral therapy was effective in the cognitive-behavioral treatment of vaginismus (18). In a study involving sixty women with vaginismus, commonly used interventions such as finger and vaginal dilator exercises aimed at promoting relaxation and voluntary control of the vaginal muscles were evaluated (19). In this study, the intervention group received pelvic floor muscle training combined with vaginal dilator therapy, while the control group was treated with a behavioral approach consisting of systematic desensitization and vaginal dilator therapy. The authors concluded that the combined use of pelvic floor muscle training and vaginal dilators represented a simple, practical, and highly effective treatment modality for vaginismus, yielding superior outcomes compared with the behavioral sexual therapy approach applied in the control group (19).

Consistent with previous studies, our study's findings indicate that sexual health education combined with pelvic floor muscle training is associated with greater reductions in anxiety levels among women with vaginismus. Additionally, body image scores were higher following the intervention. This improvement may be related

to reduced anxiety levels, which could contribute to enhanced self-confidence in affected women.

Seo et al reported that, in women with vaginismus, pelvic floor muscle relaxation was achieved through the use of functional electrical stimulation and biofeedback, followed by sexual cognitive behavioral therapy once patients became tolerant of vaginal manipulation (10). After an eight-week intervention period, all participants were able to engage in vaginal intercourse. Functional electrical stimulation and biofeedback, when combined with sexual cognitive behavioral therapy, were shown to be effective adjuncts in facilitating pelvic floor muscle control in women with vaginismus and may therefore enhance treatment success.

In a study examining the relationship between pelvic floor dysfunction and sexual dysfunction, a significant correlation was reported between pelvic floor muscle dysfunction, sexual dysfunction, and FSFI scores (20). The Female Sexual Function Index (FSFI) is widely used as a standardized assessment tool in studies addressing sexual dysfunction (21). In women with multiple sclerosis, a pelvic floor physiotherapy program designed to treat lower urinary tract symptoms was found to result in improved FSFI scores following the intervention (21).

Additionally, a study evaluating the effects of sexual counseling and pelvic floor relaxation on sexual function in women undergoing treatment for vaginismus reported significant improvements in sexual functioning and Vaginal Penetration Cognition Scale scores following the intervention (22).

Vaginismus remains underreported and underresearched due to sociocultural stigma, particularly in conservative settings. Addressing anxiety and body image alongside treatment is a notable strength of this study. The use of the Beck Anxiety Inventory (BAI) and the Body Image Scale (BIS)—both validated in Turkish populations—enhances the reliability and interpretability of the findings.

A limitation is the lack of randomization, this may have introduced selection bias. Participants were recruited from a single tertiary hospital and were all married. Therefore, findings may not be

generalizable to the population. Additionally, this study's findings reflect only short-term outcomes, as long-term follow-up data were not available.

In conclusion, this study demonstrates that sexual health education based on the IMB model combined with pelvic floor muscle exercises significantly reduces anxiety levels and improves body image perception in women with vaginismus. These findings highlight the importance of both psychological and physical components of vaginismus. Future randomized, multicenter studies with more diverse populations are needed.

Ethics Committee Approval: Ethical approval for the study was obtained from the Ankara Bilkent City Hospital Institutional Ethics Committee (Decision No: TABED 1-24-757, Code No: 757).

Conflict of Interest: No conflicts of interest.

REFERENCES

- Baranowski C. A Hidden Struggle: An Exploration of the Experiences of People with Vaginismus: University of Leicester; 2024.
- Yavuzkir Ş, Aslan M, Yurt N, Baykara S. Association between non-penetrative sexual activities and depression in women with vaginismus: a cross-sectional study. *Journal of International Medical Research*. 2024;52(4):03000605241244762.
- Maseroli E, Scavellio I, Rastrelli G, Limoncin E, Cipriani S, Corona G, et al. Outcome of medical and psychosexual interventions for vaginismus: a systematic review and meta-analysis. *The journal of sexual medicine*. 2018;15(12):1752-64.
- Newby LK, Jesse RL, Babb JD, Christenson RH, De Fer TM, Diamond GA, et al. ACCF 2012 expert consensus document on practical clinical considerations in the interpretation of troponin elevations: a report of the American College of Cardiology Foundation task force on Clinical Expert Consensus Documents. *Journal of the American College of Cardiology*. 2012;60(23):2427-63.
- Jiang H, Chen X, Li J, Tan Z, Cheng W, Yang Y. Predictors of condom use behavior among men who have sex with men in China using a modified information-motivation-behavioral skills (IMB) model. *BMC public health*. 2019;19(1):261.
- Tylka TL, Wood-Barcalow NL. What is and what is not positive body image? Conceptual foundations and construct definition. *Body image*. 2015;14:118-29.
- Woertman L, Van den Brink F. Body image and female sexual functioning and behavior: A review. *Journal of sex research*. 2012;49(2-3):184-211.
- La Rocque CL, Cioe J. An evaluation of the relationship between body image and sexual avoidance. *Journal of sex research*. 2011;48(4):397-408.
- Amagir A, Groot W, Maassen van den Brink H, Wilschut A. A review of financial-literacy education programs for children and adolescents. *Citizenship, Social and Economics Education*. 2018;17(1):56-80.
- Seo JT, Choe JH, Lee WS, Kim KH. Efficacy of functional electrical stimulation-biofeedback with sexual cognitive-behavioral therapy as treatment of vaginismus. *Urology*. 2005;66(1):77-81.
- Pollock I, Alshaigh B, Bradley A, Krogstie BR, Kumar V, Ott L, et al. 5 degrees of separation: Computer science education in the age of the anthropocene. *Proceedings of the Working Group Reports on Innovation and Technology in Computer Science Education 2019*. p. 1-25.
- Deliktas Demirci A, Buyuk A, Kabukcuoglu K. Effects of positive sex education and pelvic floor strengthening program on sexual and pelvic health among youngest old: a randomized controlled trial. *BMC geriatrics*. 2025;25(1):488.
- Anderson RP, Aschkenazi SO. *Complementary and Alternative Therapies for the Overactive Pelvic Floor*. The Overactive Pelvic Floor: Springer; 2016. p. 305-19.
- Hopwood P, Fletcher I, Lee A, Al Ghazal S. A body image scale for use with cancer patients. *European journal of cancer*. 2001;37(2):189-97.
- Secord PF, Jourard SM. The appraisal of body-cathexis: body-cathexis and the self. *Journal of consulting psychology*. 1953;17(5):343.
- Hakan K, Seval F. CIPP evaluation model scale: development, reliability and validity. *Procedia-Social and Behavioral Sciences*. 2011;15:592-9.
- Ulusoy M, Sahin NH, Erkmen H. Turkish version of the Beck Anxiety Inventory: psychometric properties. *Journal of cognitive psychotherapy*. 1998;12(2):163.
- Omidvar Z, Bayazi MH, Faridhosseini F. Comparing the effectiveness of mindfulness-based cognitive therapy training and cognitive-behavioral therapy on sexual satisfaction of women with vaginismus disorder. *Journal of Fundamentals of Mental Health*. 2021;23(4):267-71.
- Jokar F, Fani M, Isfahani NT, Sabahi R. Effectiveness of Biofeedback with Dilator Therapy for Sexual Function in Women with Primary Vaginismus: Randomized Controlled Trial Study. *International urogynecology journal*. 2025;36(3):557-65.
- Bortolami A, Vanti C, Banchelli F, Guccione AA, Pillastrini P. Relationship between female pelvic floor dysfunction and sexual dysfunction: an observational study. *The journal of sexual medicine*. 2015;12(5):1233-41.
- FARIAS JGT, de Araújo GT, Brito HBB. Os efeitos das abordagens fisioterapêuticas no tratamento do vaginismo. *PROJEÇÃO, SAÚDE E VIDA*. 2023;4(1):1-9.
- Seo S, Herr A, Lim J-W, Richardson GA, Richardson H, Kroll KL. Geminin regulates neuronal differentiation by antagonizing Brg1 activity. *Genes & development*. 2005;19(14):1723-34.

Change in Liver Function Tests After Liver Mobilization for Gynecologic Cancers; Does Metastasectomy Affect the Course?

Jinekolojik Kanserlerde Karaciğer Mobilizasyonu Sonrası Karaciğer Fonksiyon Testlerindeki Değişim; Metastazektomi Seyri Etkiler mi?

Halise Meltem BATUR¹, Burak ERSKİ¹, Mehmet UNSAL¹, Günsu Kimyon COMERT¹, Mert İshak KAYA², Melih Emre TORUN²,
Gonca TÜRKER ERGÜN², Aziz Ahmet SUREL³, Taner TURAN¹

¹Department of Gynecologic Oncology, Ankara Bilkent City Hospital, University of Health Sciences, Ankara, Türkiye

²Department of Obstetrics and Gynecology, Ankara Bilkent City Hospital, Ankara, Türkiye

³Department of General Surgery, Ankara Bilkent City Hospital, University of Health Sciences, Ankara, Türkiye

ABSTRACT

Aim: Evaluate the fluctuation of aminotransferase levels after liver mobilization for gynecologic cancers and determine the effect of liver metastasectomy on this change.

Materials and Methods: We retrospectively evaluate the patients who underwent liver mobilization for gynecologic cancers from 09/2019 to 10/2022. Alanine aminotransferase (ALT), aspartate aminotransferase (AST) and bilirubin serum levels were monitored.

Results: 69 patients were enrolled in the study. Liver function tests (LFTs) immediately tended to increase following surgery. ALT levels peaked at the postoperative 6 th hour (median: 119.5 U/L; range: 13-762) and AST peaked in the 2 nd hour after the surgery (median: 204 U/L; range: 11-717). Both ALT and AST tended to normalize on the 6 th postoperative day (24/28 U/L). Liver tumor resection was performed on 26 patients. Liver metastasectomy caused high both AST and ALT levels ($p=0.013$ and $p=0.022$, respectively) on the 2 nd postoperative day. This effect continued especially in ALT from the 2 nd day to the 10 th postoperative day. Subsequently, both groups became similar. Liver metastasectomy caused higher AST and ALT on the 2 nd postoperative day compared with the non-metastasectomy group.

Conclusion: Both liver mobilization and liver metastasectomy procedures are associated with a transient increase in LFTs. Although liver mobilization in itself causes high LFTs in the immediate postoperative period, this effect is more significant in liver metastasectomy. High LFTs returned to normal values within 2 weeks in both two groups. Fluid replacement and avoidance of hepatotoxic drugs can prevent the aggravation of the clinical course.

Keywords: Liver mobilization, liver metastasectomy, liver function tests, ovarian cancer

ÖZ

Amaç: Jinekolojik kanserler nedeniyle yapılan karaciğer mobilizasyonu sonrası aminotransferaz düzeylerindeki dalgalanmaları değerlendirmek ve karaciğer metastazektomisinin bu değişim üzerindeki etkisini belirlemek.

Gereç ve Yöntemler: 09/2019 ile 10/2022 tarihleri arasında jinekolojik kanserler nedeniyle karaciğer mobilizasyonu uygulanan hastalar retrospektif olarak değerlendirildi. Alanin aminotransferaz (ALT), aspartat aminotransferaz (AST) ve bilirubin serum düzeyleri ölçüldü.

Bulgular: Çalışmaya 69 hasta dahil edildi. Karaciğer fonksiyon testleri (KCFT) ameliyat sonrasında hemen yükselme eğilimindeydi. ALT düzeyleri ameliyat sonrası 6. saatte (medyan: 119.5 U/L; aralık: 13-762) ve AST düzeyleri 2. saatte en yüksek seviyeye ulaştı (medyan: 204 U/L; aralık: 11-717). ALT ve AST düzeyleri postoperatif 6. günde normale dönme eğilimindeydi (24/28 U/L). 26 hastaya karaciğerden metastazektomi yapıldı. Karaciğer metastazektomisi, postoperatif 2. günde hem AST hem de ALT düzeylerinde yüksekliğe neden oldu (sırasıyla $p=0.013$ ve $p=0.022$). Bu etki özellikle ALT düzeyinde postoperatif 2. günden 10. güne kadar devam etti. Takip eden süreçte her iki grup benzer hale geldi. Karaciğer metastazektomisi, metastazektomi uygulanmayan grupla karşılaştırıldığında postoperatif 2. günde daha yüksek AST ve ALT düzeylerine yol açtı.

Sonuç: Karaciğer mobilizasyonu ve karaciğer metastazektomisi işlemleri geçici KCFT artışı ile ilişkilidir. Karaciğer mobilizasyonu tek başına erken postoperatif dönemde KCFT yüksekliğine yol açsa da, bu etki metastazektomi yapılan hastalarda daha belirgindir. Her iki grupta da KCFT değerleri 2 hafta içinde normale dönmektedir. Sıvı replasmanı ve hepatotoksik ilaçlardan kaçınılması, klinik seyrin kötüleşmesini önleyebilir.

Anahtar Kelimeler: Karaciğer mobilizasyonu, karaciğer metastazektomi, karaciğer fonksiyon testleri, over kanseri

Cite as: Batur HM, Erskı B, Unsal M, Comert GK, Kaya Mİ, Torun ME et al. Change in Liver Function Tests After Liver Mobilization for Gynecologic Cancers; Does Metastasectomy Affect the Course? Jinekoloji-Obstetrik ve Neonatoloji Tıp Dergisi 2026;23(2):215–220.

Geliş/Received: 12.09.2025 • Kabul/Accepted: 06.12.2025

Sorumlu Yazar/Corresponding Author: Mehmet Unsal, Department of Gynecologic Oncology, Ankara City Hospital, Ankara, Türkiye

E-mail: munsal174@hotmail.com

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

INTRODUCTION

Liver mobilization, which is used in right upper quadrant surgeries, liver metastasectomy, diaphragm stripping, and full-thickness resection provides adequate exposure for surgical resection. Diaphragm metastases, especially to the right diaphragm because of the anticlockwise direction of peritoneal fluid flow, are common in epithelial ovarian cancer (EOC) [1]. Eisenkop et al. suggested that up to 40% of patients with EOC present with bulky metastatic disease to the diaphragm and resectability of the tumor can be one of the major obstacles to achieving optimal cytoreductive surgery (CRS) with <1 cm visible tumor after surgery [2]. Previous reports showed that resection of these implants improved the survival of patients with advanced ovarian cancer [3].

In this procedure, freeing the ligaments and peritoneal attachment of the liver may cause a transient increase in liver function tests (LFTs). Liver cell damage markers (liver fatty acid-binding protein, arginase-1, glutathione-s-transferase-a and cell-free circulating albumin mRNA) increase significantly during mobilization of the liver [4, 5]. However, relevant clinical results are not defined clearly in studies. Although elevated enzyme levels may be asymptomatic, progression to liver failure is also observed. In relevant studies, high levels of LFTs tend to normalize in 1 week. Patient-dependent factors may further worsen the clinical course [6, 7].

Our study's primary endpoint was to define the fluctuation of aminotransferase levels in liver mobilization. The secondary endpoint was to determine the effect of liver metastasectomy on this change.

MATERIALS AND METHODS

Sixty-nine patients who underwent liver mobilization during CRS for gynecologic cancer at our institution from September 2019 to October 2022 were enrolled in the study. Total abdominal hysterectomy, bilateral salpingo-oophorectomy, total omentectomy and systematic lymphadenectomy were performed as standard surgical procedures. In addition, extensive surgical procedures requiring liver mobilization including unilateral/bilateral diaphragm stripping, diaphragm full-thickness resection, cardiophrenic lymph node dissection, tumor resection at the porta hepatis, liver parenchyma, or capsular metastasectomy were performed to achieve non-residue tumors at the end of CRS. To mobilize the liver, the ligamentum teres was divided. The anterior right coronary ligament was dissected by protecting the inferior vena cava and distal right hepatic vein. Then, the right hepatic lobe was mobilized medially. All surgical procedures were performed by gynecologic

oncologists. The study was approved by the Non-Interventional Clinical Research Institutional Review Board. Informed consent was received from all patients before surgery to use their medical data in medical research.

All patients were followed up in the postoperative intensive care unit and administered antibiotic therapy, paracetamol, and non-steroid anti-inflammatory drugs for pain palliation as routine clinical practice. Complete blood count, alanine aminotransferase (ALT), aspartate aminotransferase (AST), total bilirubin, direct bilirubin, and indirect bilirubin serum levels were monitored at the postoperative 2nd and 6th hours and daily thereafter from the first postoperative day to discharge. Normal reference ranges were used as <35 U/L AST, and <50 ALT U/L. Preoperative blood tests were performed at least 1 week before the surgery.

The demographic characteristics of the patients were retrospectively retrieved from the electronic medical record system and the patients' files. Surgical notes were used to determine whether liver tumor resection was performed.

Statistical Analysis

Statistical analyses were performed using the Statistical Package for the Social Sciences version 25.0 software package (IBM SPSS Inc, Chicago, IL, USA). Descriptive statistics are expressed as median (min-max) for continuous variables and number/percentage for categorical variables. The ANOVA Table Test was used for continuous parameters. A p-value of less than 0.05 was considered statistically significant.

RESULTS

The mean age of the study group was 58.3±10.67 (range; 27-79) years. Of all 69 patients, 54 (78.2%) had ovarian cancer, 14 (20.2%) had endometrium cancer, and one (1.4 %) had extragenital malignancy. Forty-seven patients underwent primary CRS, 18 patients underwent interval CRS, and four patients underwent secondary CRS. Forty-seven patients had co-morbidities. Clinicopathologic features are detailed in Table 1.

Preoperative ALT values were above the upper reference limit (median: 21.5 U/L; range: 8-89) in 10.6% of total patients, and AST values were normal (median: 19 U/L; range: 2-47) in the entire study group. LFTs immediately tended to increase following surgery. Both ALT and AST serum levels tended to normalize on the 6th postoperative day (24/28 U/L). On the 6th postoperative day, only 26.1% of patients had ALT and 18.8% of patients had AST values above the upper reference limit. Serum levels AST increased in 95.5% of the patients in the 2nd hour after the surgery and this

Table 1. Clinical features

Clinical Features		Mean $\pm$ SD	Median (Range)
Age		58.3 $\pm$ 10.67	59 (27-79)
Size of liver tumor metastasectomy (cm)		2.6 $\pm$ 2.27	2 (1-12)
		n	%
Liver tumor metastasectomy	Not performed	43	62.3
	Performed	26	37.7
Co-morbidities	Absent	22	31.9
	Present	47	68.1
Primary site	Ovary	54	78.3
	Endometrium	14	20.3
	Extra-genital	1	1.4
Surgical procedure	Primary cytoreduction	47	68.1
	Interval cytoreduction after NACT	18	26.1
	Secondary cytoreduction	4	5.8

SD: Standard Deviation

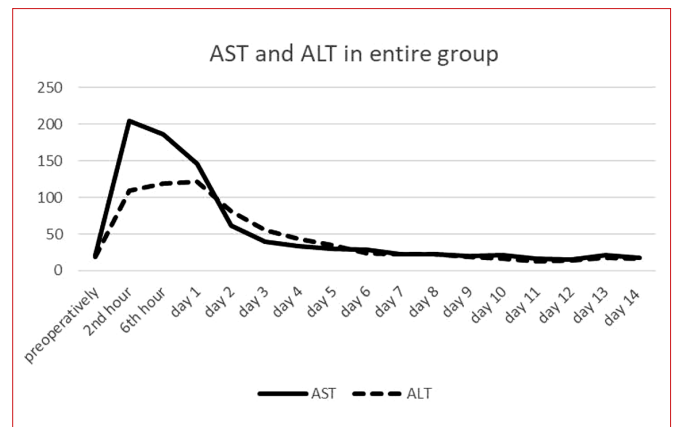
NACT: Neoadjuvant chemotherapy

Table 2. The values for postoperative LFTs in entire cohort

Time Mean $\pm$ SD		AST (U/L)			ALT (U/L)		
		Median (Range)	Above the reference value (%) ¹	Mean $\pm$ SD	Median (Range)	Above the reference value (%) ²	Mean $\pm$ SD
Preoperatively		24.6 $\pm$ 12.33	21.5 (8-89)	10.6	20.6 $\pm$ 9.25	19 (2-47)	0
Postoperatively	2 nd hour	232 $\pm$ 165.27	204 (11-717)	95.5	156.1 $\pm$ 140.39	109 (6-702))	85.1
	6 th hour	240 $\pm$ 212.42	186.5 (24-1261)	96.4	177.6 $\pm$ 163.51	119.5 (13-762)	89.3
	Day 1	227.1 $\pm$ 338.33	146 (19-2562)	94	162.1 $\pm$ 167.59	122 (10-1031)	80.6
	Day 2	243.6 $\pm$ 695.85	61 (12-4007)	100	202.4 $\pm$ 527.76	81 (8-3234)	60
	Day 3	246.9 $\pm$ 1242.62	40 (8-3210)	60.7	137.8 $\pm$ 392.23	56 (8-3234)	54.1
	Day 4	219.1 $\pm$ 1248.36	33 (4-9615)	47.8	124.8 $\pm$ 394.36	43 (4-2859)	30.4
	Day 5	44.1 $\pm$ 50.30	30 (5-283)	42.1	62.1 $\pm$ 100.34	35 (7-590)	35.1
	Day 6	35 $\pm$ 23.51	28 (10-114)	26.1	49.6 $\pm$ 67.48	24 (2-349)	18.8
	Day 7	26.9 $\pm$ 18.47	22 (7-90)	8.7	45.2 $\pm$ 57.81	22 (7-252)	10.1
	Day 8	25.7 $\pm$ 14.59	22.5 (9-65)	8.7	35.5 $\pm$ 39.74	22 (4-174)	8.7
	Day 9	25.1 $\pm$ 13.69	20.5 (10-58)	7.2	35 $\pm$ 37.42	19 (5-125)	7.2
	Day 10	23.2 $\pm$ 12.69	21 (9-48)	2.9	30.1 $\pm$ 33.22	16 (6-104)	4.3
	Day 11	20.3 $\pm$ 10.94	16 (8-53))	1.4	20.9 $\pm$ 19.03	13 (5-64)	2.9
	Day 12	18.5 $\pm$ 9.21	15 (9-40)	1.4	14 $\pm$ 5.53	14 (7-23)	0
	Day 13	21.3 $\pm$ 11.00	21 (5-48)	1.4	21.6 $\pm$ 20.87	17 (4-81)	1.4
	Day 14	19.7 $\pm$ 10.78	17 (5-44)	1.4	15.7 $\pm$ 9.72	16 (4-35)	0

¹: The reference limit of AST <35 U/L²: The reference limit of ALT <50 U/L

rate increased to 100% on the 2nd postoperative day. AST levels peaked in the 2nd hour after the surgery (median: 204 U/L; range: 11-717) and decreased gradually by the following period. AST levels normalized 98.6% of all patients on the 11th postoperative day. Similar to AST, ALT values rose in 85.1% of the study group in the 2nd hour after the surgery. ALT levels peaked at the postoperative 6th hour (median: 119.5 U/L; range: 13-762) and gradually decreased in the following days. The highest value of ALT (median: 122 U/L; range: 10-1031) on the postoperative 1st day tended to decrease from the 2nd postoperative day and regressed to the normal level in all patients on the 12th day. The transient increase was observed in only 1.4% of the total study group on the 14th postoperative day;

**Figure 1.** The fluctuation of ALT and AST after liver mobilization

ALT values normalized in all patients (Table 2) (Figure 1). Multiorgan failure was observed in only one patient. We performed Morrison's pouch stripping, bilateral diaphragm stripping, and liver parenchyma metastasectomy in addition to standard staging surgery. The tumor removed from the liver in this patient was 1x0.3x0.3 cm. Maximal cytoreduction was achieved (no visible tumor after surgery) in this case. Although the first two postoperative days the laboratory tests are normal; the LFTs began to rise (creatinine: 1.11 mg/dL, ALT: 3234 U/L, AST: 3210 U/L, total bilirubin: 2.7 mg/dL, direct bilirubin: 1.8 mg/dL, INR: 5.5) on the 3rd postoperative day. Hepatotoxic drugs were avoided and adequate fluid replacement was administered. The

patient was followed in the intensive care unit. Multiorgan failure developed on the postoperative 3rd day and the patient died on the postoperative 4th day. Bilirubin values were normal in the total study group except for this patient.

Liver tumor resection was performed on 26 patients. The median tumor size was 2 (range 1-12) cm. It was statistically significant that liver metastasectomy caused high both AST and ALT levels ($p=0.013$ and $p=0.022$, respectively) on the 2nd postoperative day. This effect continued especially in ALT from the 2nd day to the 10th postoperative day. Subsequently, both groups became similar (Table 3) (Figure 2 and Figure 3).

Tablo 3. The values for postoperative LFTs in liver metastasectomy group

Time		Enzyme	Tumor Resection Group		Non Tumor Resection Group		P value
			Mean±SD	Median (Range)	Mean±SD	Median (Range)	
Preoperatively		AST	25.6±14.84	21.5 (8-89)	23.1±6.93	21.5 (13-39))	0.430
		ALT	21.3±6.58	20 (2-47)	19.5±8.78	18 (6-40)	0.434
Postoperatively	2 nd hour	AST	224±165.84	186 (19-717)	244.7±166.83	212 (11-661)	0.620
		ALT	139.6±107.40	107 (13-423)	182.1±180.10	115 (6-702)	0.230
	6 th hour	AST	229.6±236.37	173 (24-1261)	254±179.54	212.5 (42-752))	0.674
		ALT	173.3±164.29	109 (13-762)	183.3±165.82	131.5 (16-694)	0.824
	Day 1	AST	177±169.16	135 (19-882)	306.2±495.77	153 (27-2562)	0.129
		ALT	136.4±107.88	113 (10-477)	202.6±229.65	131 (13-1031)	0.116
	Day 2	AST	75.9±66.86	56 (12-396)	512±1077.97	87 (13-4007)	0.013
		ALT	85±64.95	74 (9-275))	390.3±822.26	95 (8-3234)	0.022
	Day 3	AST	42.5±26.60	38.5 (8-160)	636.2±2094.81	48 (10-9615)	0.076
		ALT	58.9±41.97	45 (8-173)	288.2±649.54	73 (12-2859)	0.029
	Day 4	AST	40.9±44.01	27 (4-257)	498.1±1993.0	42 (10-9615)	0.042
		ALT	41.8±30.08	36 (4-149)	254.7±616.18	56 (6-2859)	0.172
	Day 5	AST	41.5±45.52	29.5 (5-257)	48.5±58.54	32 (8-283)	0.619
		ALT	41.1±29.47	33 (7-133)	98±156.57	40 (9-590)	0.037
	Day 6	AST	35.3±26.06	28 (10-114)	34.4±18.68	28 (18-78)	0.897
		ALT	35.6±28.86	24 (2-116)	75.1±103.64	24 (9-349)	0.051
	Day 7	AST	25.4±20.34	25 (7-90)	28.7±16.48	19.5 (14-58)	0.622
		ALT	27.1±25.19	18 (7-110)	67.1±77.38	32 (7-252)	0.054
	Day 8	AST	23.5±12.161	23 (9-53)	28.62±17.35	22 (11-65)	0.353
		ALT	22.9±18.65	15.5 (4-71)	53±53.71	28 (10-174)	0.035
	Day 9	AST	21.5±11.43	18 (10-42)	30.2±15.64	25 (11-58)	0.144
		ALT	19.9±21.94	15 (5-88)	55±45.24	28 (6-125)	0.029
	Day 10	AST	19.1±10.38	17 (10-39)	27.8±14.44	24.5 (9-48)	0.234
		ALT	13.9±6.74	15 (6-23)	49±42.38	43 (7-104)	0.052
	Day 11	AST	18±7.31	16 (8-29)	23.7±15.04	17 (14-53)	0.344

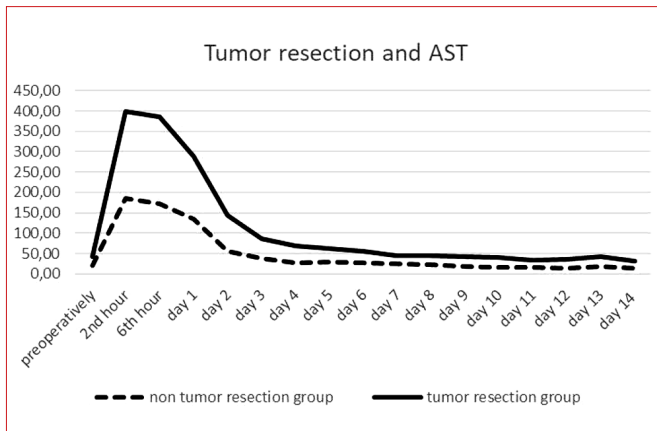


Figure 2. The fluctuation of AST in liver tumor metastasectomy and non-metastasectomy group

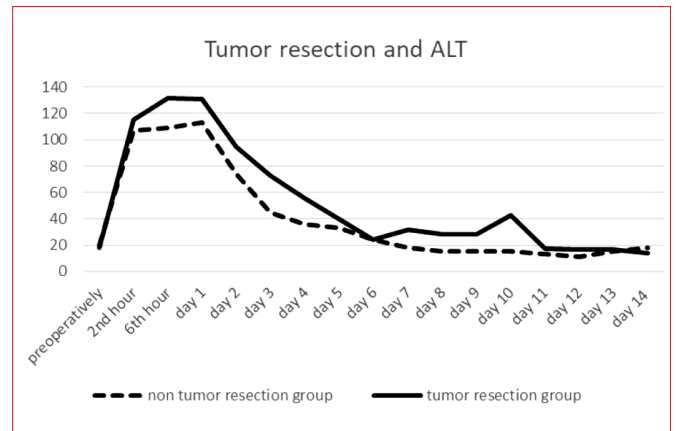


Figure 3. The fluctuation of ALT in liver tumor metastasectomy and non-metastasectomy group

DISCUSSION

Risk factors and etiologies have been suggested for postoperative liver injury after right upper quadrant surgery with liver mobilization and liver metastasectomy. Clamping of the portal triad (inflow occlusion), also called the Pringle Maneuver, which is used to decrease blood loss, can cause hepatocellular apoptosis, necrosis, and eventually liver dysfunction with the ischemia/reperfusion mechanism [8]. According to Matzinger's Danger Model, injured cells and their intracellular necrotic products, which could potentially be a danger signal, activate antigen-presenting cells and this cascade leads to a systemic inflammatory response [9]. Liver injury can be observed as a clinical manifestation of the systemic inflammatory response [10].

Studies showed that mobilization of the liver in itself causes hepatocellular injury [9, 11]. Besides mobilization, surgical techniques, duration and type of anesthetic agents, chemotherapy history, and biliary surgery may lead to postoperative liver function impairment [11-13]. Different surgical techniques may be preferred to avoid extensive mobilization of the liver. Laparoscopic liver resection or choosing liver resection using the anterior approach compared with conventional surgery with extensive mobilization may protect against hepatocellular damage or hepatic inflammation [14, 15].

In our study, we noted an increase in LFTs following liver mobilization. The AST serum levels were high in all patients on the 2nd day. ALT levels peaked at the postoperative 6th hour and gradually decreased in the following days. These high levels of both transferases spontaneously normalized at 11-12 postoperative days, in keeping with the only study that evaluated the postoperative trends in hepatic function following extensive right upper quadrant surgery [6]. In that study, Nasser et al.

evaluated 132 patients with advanced epithelial ovarian cancer. All patients underwent right upper quadrant surgery. ALT appeared to be the most fluctuant LFT, which peaked on the postoperative 1st day and returned to normal 5 days postoperatively. The bilirubin levels did not reflect similar fluctuation. Naik et al. showed ALT and AST levels 10-12 times above the reference limit in all three arms of liver transplantation patients (acute cellular rejection in adults; pediatrics and non-acute cellular rejection in adults). Increased transaminases reached normal levels within a week in uncomplicated cases [16].

In our data, liver metastasectomy caused more high both AST and ALT levels on the 2nd postoperative day compared with the non-metastasectomy group. Whereas ALT increased more significantly, both ALT and AST became similar and normalized in the following days. High levels persisted in only one patient. The patient was discharged on the 14th day of hospitalization because they had no clinical symptoms relevant to liver functions. LFTs normalized in the outpatient follow-up. Multiorgan failure developed in only one patient who had diabetes and mitral valve replacement in her medical history. Liver tumor metastasectomy was performed in addition to standard surgery. Sufficient fluid replacement was administered, we avoided hepatotoxic drugs, and the patient was followed in the intensive care unit. Clinical worsening and death were attributed to high-risk comorbid diseases rather than extensive surgery. In a study by Nasser et al., only one patient died within 5 days of surgery. The development of liver failure in this case was attributed to the neuroendocrine component and cytokines released from the neuroendocrine tumor, rather than excessive mobilization. This patient did not respond to the fluid resuscitation and avoidance of hepatotoxic medication, which was suggested to prevent liver failure. As known, there is no consensus on the adequate minimal volume of the liver to avoid

liver failure after resection. The volume range from 10% to 40% is adequate [17]. However, hepatic failure can also be observed in adequate liver volume [18]. In our study, insufficient residual liver volume was not observed.

This study has limitations. The number of metastatic lesions in the liver and the total volume of the tumors were not assessed in our retrospectively designed study. However, in our study, we compared fluctuations of LFTs in the groups that underwent liver mobilization without metastasectomy and liver metastasectomy. Laboratory parameters were followed daily during the immediate postoperative period until discharge. To our knowledge, no study has compared the serum levels of LFTs in these two groups in gynecologic oncology.

In conclusion, both liver mobilization and liver metastasectomy procedures are associated with a transient increase in LFTs. Although liver mobilization in itself causes high LFT values in the immediate postoperative period, this effect is more significant in liver metastasectomy. High serum levels of LFTs returned to normal values within 2 weeks in both two groups. Studies have not demonstrated the clinical significance of this increase and its role in predicting liver failure. Adequate fluid replacement and avoidance of hepatotoxic drugs can prevent the aggravation of the clinical course.

Ethics approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The study protocol has been approved by the research institute's committee on human research.

Funding Sources: The study was not funded by any institution.

Conflicts of interest: The authors declare that they have no conflict of interest.

Informed consent: Informed consent was obtained from all individual participants included in the study

Consent for publication: All authors read and approved the final manuscript.

Availability of data and material: Data and material is available.

Code availability: Not applicable.

Author contributions: H.M.B: Conceptualization, data curation, methodology, validation, writing the original draft, and review and editing. B.E : Review and editing. M.U., G.K.C., A.A.S: Data curation, validation. A.A.S. and T.T: visualization, supervision, methodology, validation, review and editing.

REFERENCES

1. Carmignani, C.P., et al., Intraperitoneal cancer dissemination: mechanisms of the patterns of spread. *Cancer Metastasis Rev*, 2003. 22(4): p. 465-72.
2. Eisenkop, S.M. and N.M. Spirtos, What are the current surgical objectives, strategies, and technical capabilities of gynecologic oncologists treating advanced epithelial ovarian cancer? *Gynecol Oncol*, 2001. 82(3): p. 489-97.
3. Eisenhauer, E.L., et al., The addition of extensive upper abdominal surgery to achieve optimal cytoreduction improves survival in patients with stages IIIC-IV epithelial ovarian cancer. *Gynecol Oncol*, 2006. 103(3): p. 1083-90.
4. van de Poll, M.C., et al., Elevated plasma arginase-1 does not affect plasma arginine in patients undergoing liver resection. *Clin Sci (Lond)*, 2008. 114(3): p. 231-41.
5. van de Poll, M.C., et al., Liver manipulation causes hepatocyte injury and precedes systemic inflammation in patients undergoing liver resection. *World J Surg*, 2007. 31(10): p. 2033-8.
6. Nasser, S., et al., Impact of right upper quadrant cytoreductive techniques with extensive liver mobilization on postoperative hepatic function and risk of liver failure in patients with advanced ovarian cancer. *Gynecol Oncol*, 2018. 151(3): p. 466-470.
7. Cliby, W., et al., Diaphragm resection for ovarian cancer: technique and short-term complications. *Gynecol Oncol*, 2004. 94(3): p. 655-60.
8. Choukér, A., et al., Alpha-gluthathione S-transferase as an early marker of hepatic ischemia/reperfusion injury after liver resection. *World J Surg*, 2005. 29(4): p. 528-34.
9. Matzinger, P., The danger model: a renewed sense of self. *Science*, 2002. 296(5566): p. 301-5.
10. Rolando, N., et al., The Systemic Inflammatory Response Syndrome in Acute Liver Failure. *Hepatology*, 2000. 32(4): p. 734-739.
11. Oh, S.K., et al., Comparison of the Postoperative Liver Function Between Total Intravenous Anesthesia and Inhalation Anesthesia in Patients with Preoperatively Elevated Liver Transaminase Levels: A Retrospective Cohort Study. *Ther Clin Risk Manag*, 2020. 16: p. 223-232.
12. Hasukic, S., D. Kosuta, and K. Muminhodzic, Comparison of postoperative hepatic function between laparoscopic and open cholecystectomy. *Med Princ Pract*, 2005. 14(3): p. 147-50.
13. van den Broek, M.A., et al., Liver manipulation during liver surgery in humans is associated with hepatocellular damage and hepatic inflammation. *Liver Int*, 2013. 33(4): p. 633-41.
14. Nsadi, B., et al., Consequences of pneumoperitoneum on liver ischemia during laparoscopic portal triad clamping in a swine model. *J Surg Res*, 2011. 166(1): p. e35-43.
15. Lai, E.C., et al., Anterior approach for difficult major right hepatectomy. *World J Surg*, 1996. 20(3): p. 314-7; discussion 318.
16. Naik, P., et al., A single centre prospective study of liver function tests in post liver transplant patients. *Indian J Clin Biochem*, 2013. 28(1): p. 38-45.
17. Clavien, P.A., et al., Protection of the liver during hepatic surgery. *J Gastrointest Surg*, 2004. 8(3): p. 313-27.
18. Yanaga, K., et al., Significance of liver size in hepatic surgery. *HPB Surg*, 1997. 10(4): p. 195-9; discussion 199-200.

Laparoscopic Surgical Staging in Gynecologic Cancers: Nodal Adequacy and Perioperative Outcomes in 105 Patients

Jinekolojik Kanserlerde Laparoskopik Cerrahi Evreleme: 105 Hastada Nodal Yeterlilik ve Perioperatif Sonuçlar

Özgün CEYLAN¹, Tuba ZENGİN AKSEL¹, Mustafa ŞAHİN²

¹Department of Gynecologic Oncology, Etlik City Hospital, Ankara, Türkiye

²Department of Gynecologic Oncology, Konya City Hospital, Konya, Türkiye

ABSTRACT

Aim: To evaluate the feasibility and nodal adequacy of laparoscopic surgical staging for gynecologic malignancies at a tertiary gynecologic oncology center, with particular attention to perioperative tolerability in an obese population.

Materials and Methods: This single-center retrospective study included 105 consecutive patients who underwent laparoscopic surgical staging for histologically confirmed gynecologic malignancy over a 24-month period. Demographic, clinicopathologic, surgical, and perioperative hematologic data were extracted from institutional records. Surgical adequacy was defined a priori as a pelvic lymph node count ≥ 10 and a paraaortic lymph node count ≥ 5 .

Results: The median age was 62 years (IQR 55–66) and the mean body mass index was 32.6 ± 5.2 kg/m²; 68.6% of patients were obese. Endometrial cancer accounted for 93.3% of cases, and 88.6% had early-stage (FIGO I–II) disease. The median pelvic nodal yield was 18 (IQR 13–23), with adequacy achieved in 95.2% of patients; paraaortic lymphadenectomy was performed in 68.6%, all meeting the adequacy threshold. Nodal metastasis was detected in 10.5%, and nodal yield was preserved across body mass index strata ($\rho=0.166$, $p = 0.091$). The median 24-hour hemoglobin drop was 1.1 g/dL (IQR 0.8–1.6), with a drop of ≥ 2 g/dL in 14.3%. During a median follow-up of 8 months, recurrence occurred in two patients (2.0%).

Conclusion: Laparoscopic surgical staging for gynecologic malignancies achieved high rates of nodal adequacy with limited perioperative hematologic impact, supporting its routine use in tertiary gynecologic oncology practice, including in obese populations.

Keywords: Laparoscopy; genital neoplasms, female; endometrial neoplasms; lymph node excision; obesity

ÖZ

Amaç: Jinekolojik malignitelerde uygulanan laparoskopik cerrahi evrelemenin uygulanabilirliğini ve nodal yeterliliğini, obezite yükü yüksek bir kohortta perioperatif tolerabilite de göz önünde bulundurularak tersiyer bir jinekolojik onkoloji merkezinde değerlendirmektir.

Gereç ve Yöntemler: Bu tek merkezli retrospektif çalışma, 24 aylık bir dönemde histolojik olarak doğrulanmış jinekolojik malignite nedeniyle laparoskopik cerrahi evreleme uygulanan 105 ardışık hastayı kapsamaktadır. Demografik, klinikopatolojik, cerrahi ve perioperatif hematolojik veriler kurumsal kayıtlardan elde edildi. Cerrahi yeterlilik, pelvik lenf nodu sayısının ≥ 10 ve paraaortik lenf nodu sayısının ≥ 5 olması olarak önceden tanımlandı.

Bulgular: Medyan yaş 62 yıl (IQR 55–66) ve ortalama vücut kitle indeksi $32,6 \pm 5,2$ kg/m² idi; hastaların %68,6'sı obezdi. Endometrium kanseri olguların %93,3'ünü oluşturdu ve %88,6'sı erken evre (FIGO I–II) hastalığa sahipti. Medyan pelvik nodal çıkarım sayısı 18 (IQR 13–23) olup yeterlilik hastaların %95,2'sinde sağlandı; paraaortik lenfadenektomi %68,6 hastaya uygulandı ve tümü yeterlilik eşliğini karşıladı. Nodal metastaz %10,5 oranında saptandı ve nodal çıkarım sayısı vücut kitle indeksi katmanları arasında korundu ($\rho=0,166$, $p = 0,091$). Medyan 24 saatlik hemoglobin düşüşü 1,1 g/dL (IQR 0,8–1,6) olup ≥ 2 g/dL düşüşü %14,3 hastada gözlemlendi. Medyan 8 aylık takipte iki hastada (%2,0) nüks gelişti.

Sonuç: Jinekolojik malignitelerde laparoskopik cerrahi evreleme, obez popülasyonlar dahil olmak üzere, sınırlı perioperatif hematolojik etki ile yüksek oranda nodal yeterlilik sağlamış olup, tersiyer jinekolojik onkoloji pratiğinde rutin kullanımını desteklemektedir.

Anahtar Kelimeler: Laparoskopi; kadın genital neoplazileri; endometrium neoplazileri; lenf nodu eksizyonu; obezite

Cite as: Ceylan Ö, Zengin Aksel T, Şahin M. Laparoscopic Surgical Staging in Gynecologic Cancers: Nodal Adequacy and Perioperative Outcomes in 105 Patients. Jinekoloji-Obstetrik ve Neonatoloji Tıp Dergisi 2026;23(2):221–227.

Geliş/Received: 21.04.2026 • Kabul/Accepted: 24.05.2026

Sorumlu Yazar/Corresponding Author: Özgün Ceylan, Department of Gynecologic Oncology Etlik City Hospital, Ankara, Türkiye

E-mail: ozguncyln@hotmail.com

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

INTRODUCTION

Endometrial cancer is the most common gynecologic malignancy in developed countries, predominantly affecting postmenopausal women, while epithelial ovarian cancer remains the leading cause of gynecologic cancer death (1) whereas around one in nine men and one in 12 women die from it. Lung cancer was the most frequently diagnosed cancer in 2022, responsible for almost 2.5 million new cases, or one in eight cancers worldwide (12.4% of all cancers globally). According to the International Federation of Gynecology and Obstetrics (FIGO) 2023 classification, surgical staging of endometrial cancer comprises peritoneal cytology, total extrafascial hysterectomy with bilateral salpingo-oophorectomy, and pelvic and paraaortic lymphadenectomy in selected patients; omentectomy is additionally recommended for non-endometrioid histologies (2,3). In apparent early-stage epithelial ovarian cancer, comprehensive staging further encompasses omentectomy, peritoneal biopsies, and appendectomy in mucinous histology (4). The aims of this surgical effort are to confirm the anatomical extent of disease, establish prognosis, and rationally triage patients for adjuvant therapy.

Surgical staging, historically performed through laparotomy, has progressively shifted toward minimally invasive approaches since the 1990s. The Gynecologic Oncology Group LAP2 trial established laparoscopy as a safe alternative to laparotomy for uterine cancer staging, with fewer complications, less blood loss, and shorter hospital stays without compromising oncologic outcomes (5); these advantages have been consistently reproduced in subsequent endometrial and early-stage ovarian cancer series (6–8). Current European Society of Gynaecological Oncology (ESGO) guidelines endorse minimally invasive staging in early-stage endometrial cancer, including high–intermediate and high-risk disease, and ESGO–ESMO consensus statements acknowledge laparoscopy as an acceptable option for early-stage ovarian cancer in experienced hands (9,10). However, the Laparoscopic Approach to Cervical Cancer (LACC) trial has reinforced the need for tumor-specific scrutiny of oncologic outcomes after minimally invasive surgery (11).

Several practical questions relevant to tertiary-center practice nevertheless remain. Comparative studies are often restricted to endometrial or ovarian cancer in isolation, whereas a single minimally invasive program typically serves patients with heterogeneous malignancies. The feasibility and nodal adequacy of laparoscopic staging in obese women, and the perioperative hematologic impact of the procedure, have not been systematically reported in contemporary real-world cohorts (12–14).

We therefore conducted a single-center retrospective study of 105 consecutive patients who underwent laparoscopic surgical staging for gynecologic malignancy at our tertiary gynecologic oncology unit, evaluating the feasibility and nodal adequacy of the procedure, as well as perioperative hematologic outcomes and short-term clinicopathologic findings.

MATERIALS AND METHODS

Study design and patient selection

This single-center retrospective observational study, reported in accordance with the STROBE statement, was conducted at the Department of Gynecologic Oncology of Etlik City Hospital, a tertiary referral hospital in Ankara, Türkiye. Consecutive women aged ≥ 18 years who underwent laparoscopic surgical staging for a histologically confirmed gynecologic malignancy between January 2024 and January 2026 were identified from the institutional database. Patients were excluded if they had undergone sentinel lymph node biopsy or bulky nodal sampling, laparoscopic staging for locally advanced cervical carcinoma before chemoradiotherapy, intraoperative conversion to laparotomy, or follow-up outside our institution. Only operations performed by senior gynecologic oncologists with at least two years of subspecialty experience and an annual laparoscopic caseload exceeding 100 procedures — consistent with thresholds defined for high-volume minimally invasive gynecologic oncology practice (12) — were included. The composition of the surgical team remained stable throughout the 24-month study period. The study was approved by the institutional Ethics Committee (AEŞH-BADEK2-2026-242, 24/03/2026); the requirement for informed consent was waived given the retrospective design. Patient selection is shown in Figure 1.

Surgical technique

All procedures were performed in the dorsal lithotomy position using conventional multi-port laparoscopic access with pneumoperitoneum at 12–14 mmHg, following institutional protocols aligned with ESGO and ESMO guidelines. Pelvic lymphadenectomy was performed within standard anatomical boundaries (common iliac, external iliac, internal iliac regions, and the obturator fossa up to the obturator nerve). Paraaortic lymphadenectomy was performed in selected patients, extending to the inferior mesenteric artery in most cases and to the left renal vein in those with high-risk histology or suspected upper paraaortic involvement. Omentectomy was routinely performed in serous, clear cell, carcinosarcoma, undifferentiated carcinoma, uterine sarcoma, and all epithelial ovarian malignancies; in endometrioid endometrial carcinoma, omentectomy was additionally performed in selected cases at the surgeon's discretion. Hysterectomy was performed by standard technique, with the uterine specimen extracted intact through the vaginal cuff (no morcellation). Bilateral salpingo-oophorectomy was performed routinely, except in rare premenopausal low-risk endometrioid cases and in two 20-year-old patients with an ovarian granulosa cell tumor and a mucinous carcinoma, respectively, in whom fertility-sparing surgery was performed. Operative technique — including port configuration, pneumoperitoneum settings, energy devices, and the anatomical boundaries of pelvic and paraaortic lymphadenectomy — was standardized according to institutional protocol and remained unchanged throughout the study period.

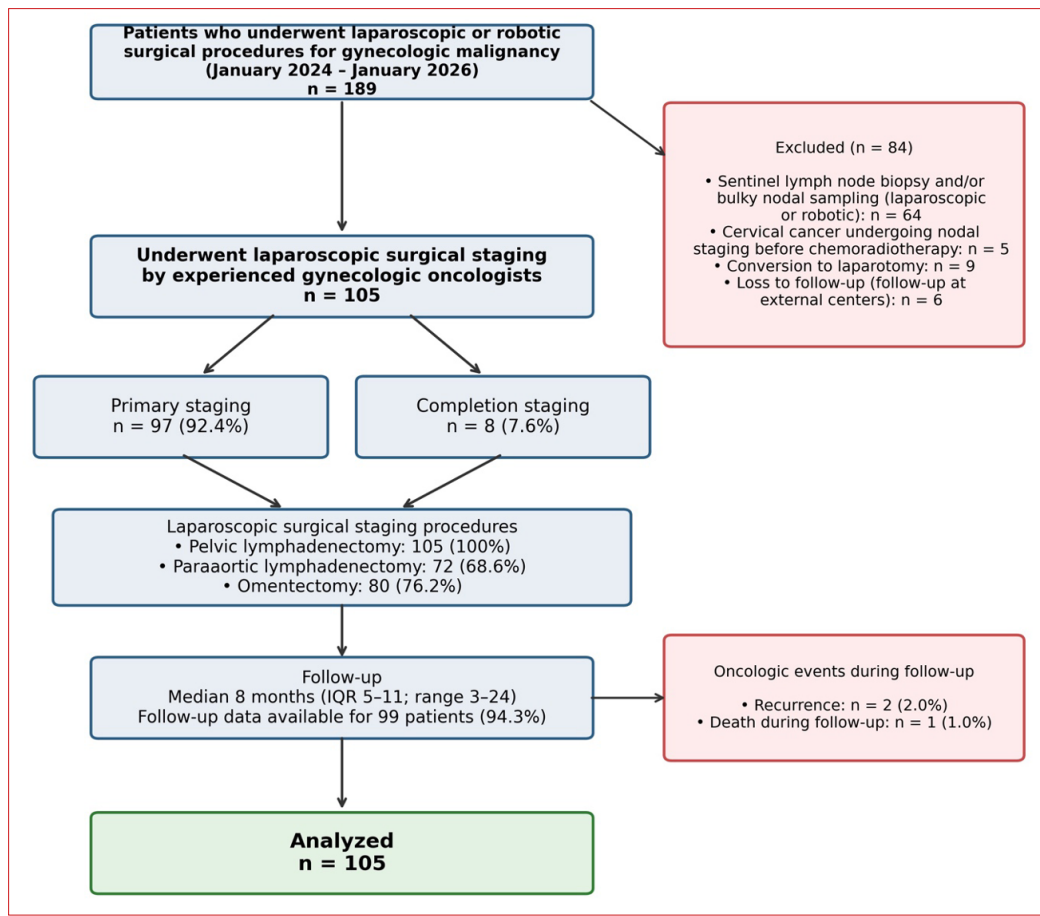


Figure 1. Flow diagram of patient selection. Of 189 patients who underwent laparoscopic or robotic surgical procedures for gynecologic malignancy at our institution between January 2024 and January 2026, 84 were excluded based on pre-specified criteria, and 105 consecutive patients who underwent laparoscopic surgical staging by senior gynecologic oncologists were included in the final analysis.

Data collection, outcomes, and follow-up

Clinical, surgical, and pathologic data — including demographics, tumor characteristics (histology, FIGO 2023 stage, grade), perioperative hematologic parameters, and follow-up — were extracted from the institutional electronic medical record. Obesity was defined as body mass index (BMI) ≥ 30 kg/m². The primary endpoint was surgical adequacy, defined a priori as a pelvic lymph node count ≥ 10 and a paraaortic lymph node count ≥ 5 (7,9). Secondary endpoints included nodal and omental metastatic involvement, perioperative hematologic outcomes, and adjuvant therapy distribution. Adjuvant decisions were made by the institutional multidisciplinary tumor board in accordance with ESGO/ESTRO/ESP and NCCN guidelines.

Statistical analysis

Normality was assessed with the Shapiro–Wilk test. Continuous variables are presented as mean $\pm$ standard deviation or median with interquartile range (IQR), and categorical variables as frequencies and percentages. Between-group comparisons used the Mann–Whitney U or Pearson χ^2 /Fisher exact test as appropriate;

paired hematologic comparisons used the Wilcoxon signed-rank test. Associations between continuous variables were assessed with Spearman rank correlation and differences across groups with the Kruskal–Wallis test. A two-sided $p < 0.05$ was considered statistically significant. Analyses were performed using Python 3.11 with the SciPy and pandas libraries.

RESULTS

Study population and baseline characteristics

Over the 24-month study period, 105 consecutive patients underwent laparoscopic surgical staging for gynecologic malignancy. The median age was 62 years (IQR 55–66), and 89 patients (84.8%) were postmenopausal. Mean BMI was 32.6 ± 5.2 kg/m²; 72 patients (68.6%) were obese and 34 (32.4%) had class II or greater obesity. The primary tumor was of endometrial origin in 98 patients (93.3%) and ovarian origin in 7 (6.7%); endometrioid endometrial carcinoma was the most frequent subtype (71 patients, 67.6%), followed by uterine serous carcinoma (18, 17.1%) and clear cell carcinoma (3, 2.9%). According to the surgical-pathologic

Table 1. Baseline demographic, clinicopathologic, surgical, perioperative, and outcome characteristics of 105 patients who underwent laparoscopic surgical staging for gynecologic malignancy.

Variable	All patients (n = 105)
Demographic characteristics	
Age (years), median (IQR) [range]	62 (55–66) [20–81]
BMI (kg/m ²), mean ± SD [range]	32.6 ± 5.2 [21–48]
Postmenopausal status, n (%)	89 (84.8)
Histologic diagnosis, n (%)	
Endometrioid endometrial carcinoma	71 (67.6)
Uterine serous carcinoma	18 (17.1)
Other uterine tumors*	9 (8.6)
High-grade serous ovarian carcinoma	2 (1.9)
Other ovarian tumors [†]	5 (4.8)
FIGO stage and grade	
FIGO stage (I–II), n (%)	93 (88.6)
FIGO stage (III–IV), n (%)	12 (11.4)
Tumor grade 1–2, n (%)	70 (66.7)
Tumor grade 3, n (%)	35 (33.3)
Tumor diameter (mm), median (IQR) [range]	50 (25–62) [5–150]
Surgical procedure	
Pelvic lymphadenectomy, n (%)	105 (100)
-Pelvic nodes removed, median (IQR) [range]	18 (13–23) [9–40]
Paraaortic lymphadenectomy, n (%)	72 (68.6)
-Paraaortic nodes removed [‡] , median (IQR) [range]	13 (9–18) [5–43]
Omentectomy, n (%)	80 (76.2)
Pathologic nodal and omental findings	
Any positive lymph node, n (%)	11 (10.5)
Positive pelvic nodes, n (%)	8 (7.6)
Positive paraaortic nodes [§] , n (%)	8 (11.1)
Omental metastasis [§] , n (%)	1 (1.2)
Perioperative hematologic parameters	
Preoperative hemoglobin (g/dL), median (IQR) [range]	12.4 (11.2–13.2) [9.4–14.8]
24-h postoperative hemoglobin (g/dL), median (IQR) [range]	11.1 (10.1–11.9) [8.1–14.4]
Hemoglobin drop (g/dL), median (IQR) [range] [¶]	1.1 (0.8–1.6) [–1.3–3.6]
Preoperative WBC (/ μ L), mean ± SD	7,780 ± 1,565
24-h postoperative WBC (/ μ L), median (IQR)	11,040 (9,320–13,470)
WBC change (/ μ L), median (IQR) [¶]	+3,100 (+2,050 to +4,840)
Preoperative CA-125 (U/mL), median (IQR) [range]	12.0 (8.2–18.7) [3.0–120.0]
Adjuvant therapy, n (%)	
None (observation)	36 (34.3)
Radiotherapy only	13 (12.4)
Chemotherapy only	13 (12.4)
Chemoradiotherapy	43 (41.0)

Data are presented as median (interquartile range, IQR) with full range [minimum–maximum], mean ± standard deviation, or number of patients (percent), as appropriate.

*Includes three clear cell carcinomas, two undifferentiated carcinomas, two carcinosarcomas, and two endometrial stromal sarcomas (one high-grade, one low-grade).

[†]Includes two ovarian endometrioid carcinomas, one granulosa cell tumor, one seromucinous borderline tumor, and one ovarian mucinous carcinoma.

[‡]Calculated for the 72 patients who underwent paraaortic lymphadenectomy.

[§]Calculated for the 80 patients who underwent omentectomy.

[¶]Paired pre- vs 24-h postoperative comparisons were statistically significant by Wilcoxon signed-rank test ($p < 0.001$ for both hemoglobin and WBC change).

Abbreviations: BMI, body mass index; CA-125, cancer antigen 125; FIGO, International Federation of Gynecology and Obstetrics; HG, high grade; IQR, interquartile range; LG, low grade; SD, standard deviation; WBC, white blood cell count.

FIGO classification, 93 patients (88.6%) had early-stage (FIGO I–II) and 12 (11.4%) advanced (FIGO III) disease, with a median tumor diameter of 50 mm (IQR 25–62). Detailed baseline characteristics are presented in Table 1 and Figure 2.

Surgical procedures and lymph node yield

All 105 patients underwent pelvic lymphadenectomy; paraaortic lymphadenectomy was performed in 72 (68.6%) and omentectomy in 80 (76.2%). Primary laparoscopic staging was performed in 97 patients (92.4%), and 8 (7.6%) underwent laparoscopic completion staging for incidentally diagnosed malignancy.

The median pelvic nodal yield was 18 (IQR 13–23); the adequacy threshold of ≥ 10 nodes was achieved in 100 patients (95.2%), and ≥ 15 nodes in 68 (64.8%). Among the 72 patients undergoing paraaortic lymphadenectomy, the median paraaortic nodal count was 13 (IQR 9–18), and all 72 (100%) met the ≥ 5 -node adequacy threshold. Nodal yield was preserved across BMI strata, with median pelvic nodal counts of 15, 20, and 17 in non-obese, obese (BMI 30–34.9), and class II or greater obese patients, respectively (Kruskal–Wallis $p = 0.037$); the Spearman correlation between continuous BMI and pelvic nodal yield was non-significant ($\rho = 0.166$, $p = 0.091$). Age was not associated with nodal yield ($\rho = -0.108$, $p = 0.272$).

Pathologic nodal and omental involvement

Nodal metastasis was identified in 11 of 105 patients (10.5%): 8 (7.6%) had positive pelvic nodes, 8 of 72 (11.1%) had paraaortic involvement, and 5 (4.8%) had concomitant pelvic and paraaortic metastasis. Omental metastasis was detected in only 1 of the 80 patients who underwent omentectomy (1.2%). Nodal positivity increased non-significantly with tumor grade (4.3% in grade 1, 16.7% in grade 2, 14.3% in grade 3; $\chi^2 p = 0.186$). Preoperative serum CA-125 elevation above 35 U/mL was observed in 3 of 11 node-positive patients (27.3%) versus 5 of 94 node-negative patients (5.3%), a statistically significant difference (Fisher exact $p = 0.036$; Table 2).

Perioperative hematologic parameters

Median preoperative and 24-hour postoperative hemoglobin levels were 12.4 g/dL (IQR 11.2–13.2) and 11.1 g/dL (IQR 10.1–11.9), respectively, yielding a median drop of 1.1 g/dL (IQR 0.8–1.6; Wilcoxon $p < 0.001$). A clinically meaningful drop (≥ 2 g/dL) occurred in 15 patients (14.3%). The median white blood cell count increased from 7,780/ μ L preoperatively to 11,040/ μ L (IQR 9,320–13,470) at 24 hours (Wilcoxon $p < 0.001$). Preoperative serum CA-125 was elevated above 35 U/mL in 8 patients (7.6%).

Adjuvant therapy and follow-up

Based on surgical-pathologic risk assessment, 36 patients (34.3%) were observed, 13 (12.4%) received radiotherapy, 13 (12.4%)

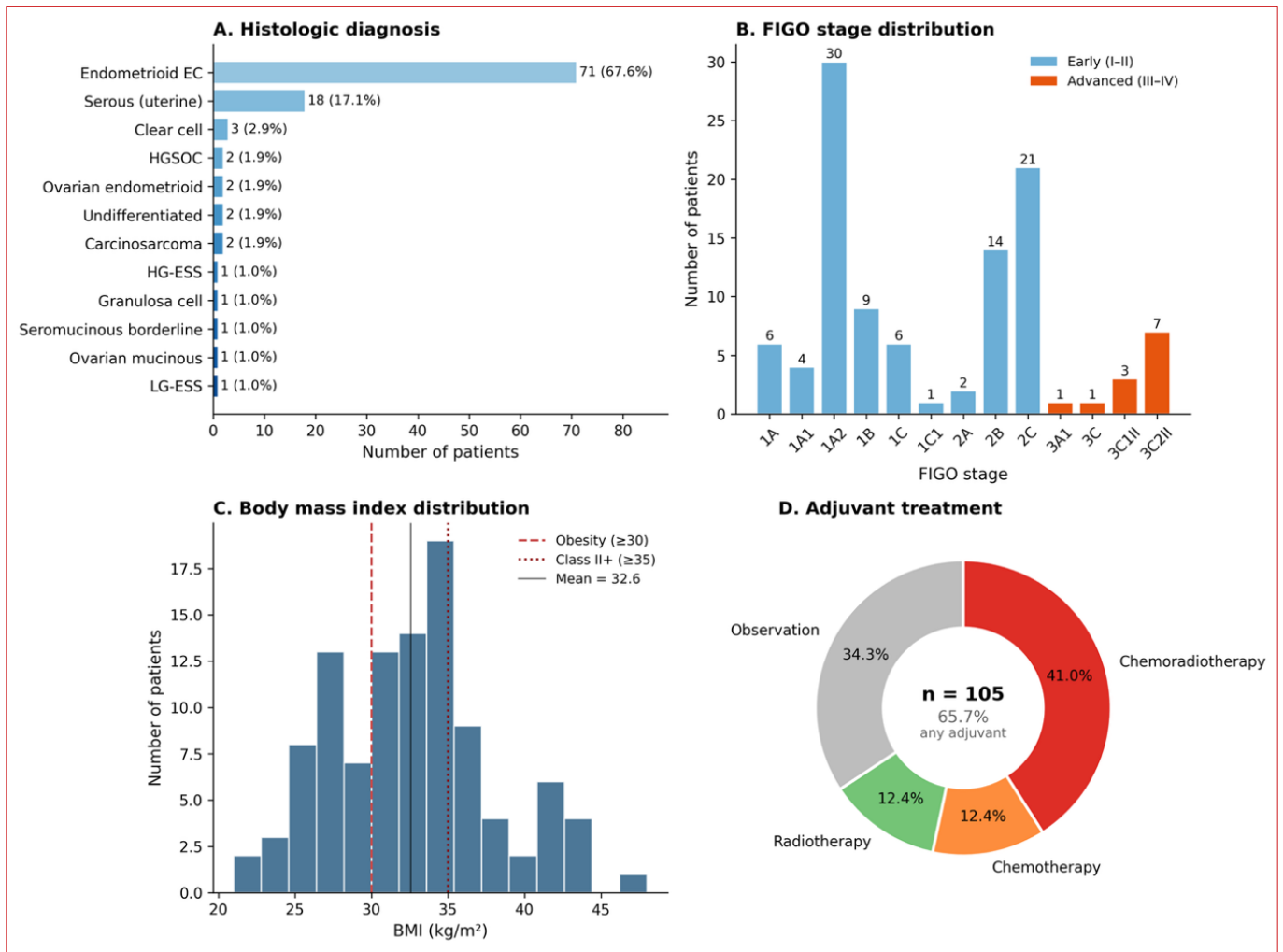


Figure 2. Baseline characteristics of the study population (n = 105). Distribution of (A) histologic subtypes, (B) FIGO 2023 stage, (C) body mass index categories, and (D) adjuvant therapy received. The cohort was predominantly composed of endometrial carcinoma (93.3%) and early-stage (FIGO I-II) disease (88.6%), with 68.6% of patients classified as obese (BMI ≥ 30 kg/m²).

Abbreviations: BMI, body mass index; CCC, clear cell carcinoma; CRT, chemoradiotherapy; CT, chemotherapy; FIGO, International Federation of Gynecology and Obstetrics; HGSOC, high-grade serous ovarian carcinoma; RT, radiotherapy.

chemotherapy, and 43 (41.0%) combined chemoradiotherapy; overall, 69 patients (65.7%) received adjuvant therapy. Use of any adjuvant treatment differed significantly between stage groups: all 12 advanced-stage patients (100%) versus 57 of 93 early-stage patients (61.3%) (Fisher exact $p = 0.007$; Table 2).

The median follow-up was 8 months (IQR 5–11), with data available for 99 of 105 patients (94.3%). Two patients (2.0%) developed recurrence. One patient (1.0%) — a woman with stage IIC serous endometrial carcinoma who declined recommended adjuvant therapy — died 3 months postoperatively of disease-related causes.

Subgroup comparisons

Patients with advanced disease had a higher median BMI (34.5 vs 32.0 kg/m²; $p = 0.047$) and more frequently underwent paraaortic lymphadenectomy (100% vs 64.5%; $p = 0.016$) than those with

early-stage disease. The 24-hour hemoglobin drop did not differ between stage groups (1.1 vs 1.0 g/dL; $p = 0.199$) (Table 2). Node-positive patients showed a non-significant trend toward higher preoperative CA-125 (median 15.4 vs 11.7 U/mL; $p = 0.101$) and clustered almost exclusively within advanced-stage disease (11 of 12 advanced-stage patients vs 0 of 93 early-stage; $p < 0.001$). Other baseline variables did not differ significantly by nodal status.

DISCUSSION

In this single-center retrospective study of 105 consecutive patients who underwent laparoscopic surgical staging for gynecologic malignancy at a tertiary gynecologic oncology unit, we demonstrated that the procedure was associated with a high rate of surgical adequacy and limited perioperative hematologic impact

Table 2. Comparison of baseline, surgical, perioperative, and adjuvant characteristics by FIGO stage group.

Variable	Early stage (I-II) (n = 93)	Advanced stage (III-IV) (n = 12)	P value
Age (years), median (IQR)	62 (53–67)	61 (57–64)	0.755
BMI (kg/m ²), median (IQR)	32 (28–35)	34.5 (33–39)	0.047
Postmenopausal, n (%)	78 (83.9)	11 (91.7)	0.687
Tumor diameter (mm), median (IQR)	50 (25–62)	47 (39–64)	0.361
Tumor grade 3, n (%)	30 (32.3)	5 (41.7)	0.745
Preoperative CA-125 (U/mL), median (IQR)	12 (8–18)	13.3 (10–32)	0.292
Para-aortic lymphadenectomy, n (%)	60 (64.5)	12 (100)	0.016
Pelvic nodes removed, median (IQR)	16 (13–23)	19 (18–21)	0.230
Para-aortic nodes removed†, median (IQR)	13 (8–18)	15 (11–17)	0.528
Any positive lymph node, n (%)	0 (0.0)	11 (91.7)	<0.001
24-h hemoglobin drop (g/dL), median (IQR)	1.1 (0.9–1.6)	1.0 (0.6–1.2)	0.199
Any adjuvant therapy, n (%)	57 (61.3)	12 (100)	0.007

Continuous variables are presented as median (interquartile range). Categorical variables are presented as number of patients (percent).

P values were calculated by Mann-Whitney U test for continuous variables and χ^2 or Fisher exact test for categorical variables, as appropriate. Two-sided $p < 0.05$ was considered statistically significant (shown in bold).

†Restricted to patients who underwent para-aortic lymphadenectomy (n = 60 in early-stage group and n = 12 in advanced-stage group).

Abbreviations: BMI, body mass index; CA-125, cancer antigen 125; FIGO, International Federation of Gynecology and Obstetrics; IQR, interquartile range.

in a predominantly obese, postmenopausal cohort. Pelvic nodal adequacy, defined a priori as a nodal count of ≥ 10 , was achieved in 95.2% of patients, and para-aortic nodal adequacy, defined as ≥ 5 nodes, was achieved in all patients who underwent para-aortic dissection. The median pelvic nodal yield of 18 (interquartile range 13–23) and the nodal metastasis detection rate of 10.5% were consistent with the thresholds reported in contemporary comparative series. Importantly, nodal yield was preserved across body mass index strata, and the median 24-hour hemoglobin drop was limited to 1.1 g/dL, with a clinically meaningful drop (≥ 2 g/dL) observed in only 14.3% of patients. Collectively, these findings support the feasibility and surgical quality of laparoscopic staging in routine tertiary-center practice.

The nodal adequacy rates observed in our cohort compare favorably with those reported in contemporary series of laparoscopic staging for endometrial cancer. In the landmark Gynecologic Oncology Group LAP2 trial, Walker et al. reported a median pelvic nodal yield of 17 nodes in the laparoscopic arm, with pelvic and para-aortic lymph nodes successfully harvested in 92% of patients, and confirmed non-inferior oncologic outcomes when compared with laparotomy (5). More recent single-institution and national cohort studies have reproduced these findings, with van Bommel et al. demonstrating in a Dutch population-based cohort of 941 women with high-intermediate and high-risk endometrial cancer that laparoscopic and robot-assisted laparoscopic staging achieved comparable nodal counts and disease-free survival to laparotomy (7). The Cochrane systematic review by Galaal et al., incorporating nine randomized trials and nearly 4000 women, similarly concluded that laparoscopy is an effective and oncologically equivalent alternative to laparotomy for early-stage endometrial cancer (15). Our median pelvic yield of 18 and complete para-aortic adequacy therefore situate our results within the upper range of published benchmarks.

A distinctive feature of our cohort is the high prevalence of obesity (68.6% obese, 32.4% class II or greater), which has historically been cited as a relative barrier to minimally invasive staging owing to concerns regarding surgical access and nodal yield (13). Despite this, median pelvic nodal yield was preserved across body mass index strata, and the Spearman correlation between body mass index and nodal count was non-significant ($\rho = 0.166$, $p = 0.091$) — consistent with subanalyses of the LAP2 trial and subsequent series demonstrating the feasibility of laparoscopic staging in obese women (5,12). The perioperative hematologic impact was likewise limited, with a median 24-hour hemoglobin drop of only 1.1 g/dL, in line with the reduced blood loss consistently reported for laparoscopy in randomized trials and meta-analyses (15).

Two secondary findings deserve specific mention. First, preoperative CA-125 elevation above 35 U/mL was significantly associated with nodal metastasis (27.3% in node-positive vs 5.3% in node-negative patients, Fisher exact $p = 0.036$), suggesting that routinely available preoperative markers may complement histologic criteria in nodal risk stratification — although the small number of node-positive events requires cautious interpretation. Second, omentectomy was performed in 80 patients, of whom only one (1.2%) harbored microscopic omental metastasis. This rate is comparable to the very low incidence reported by Ozdal et al., who identified only a single omental metastasis among 186 patients with endometrioid endometrial carcinoma undergoing routine omentectomy, and concluded that the procedure is unnecessary in this histologic subgroup unless gross metastases are suspected intraoperatively (16). Although the small number of omental events in our cohort precludes strong inference, our observation is consistent with current European Society of Gynaecological Oncology recommendations favoring selective

rather than routine omentectomy in endometrioid endometrial carcinoma (2), and underscores the need for confirmation in larger prospective series.

Our study has several strengths, including consecutive enrollment from a high-volume tertiary gynecologic oncology unit, a homogeneous surgical cohort restricted to operations performed by senior gynecologic oncologists, intact transvaginal specimen extraction without morcellation, and the systematic reporting of perioperative hematologic parameters — an aspect incompletely documented in prior series. Of note, fertility-sparing laparoscopic staging was safely performed in two young patients with early-stage non-epithelial and mucinous ovarian tumors, consistent with current ESGO recommendations. Several limitations should also be acknowledged. First, the retrospective single-center design and the absence of a laparotomy comparator group preclude direct inferences regarding comparative effectiveness. Second, the median follow-up of 8 months is short and precludes formal survival analyses; extended follow-up is planned in a future analysis. Third, operative time, estimated blood loss, and conversion details were not retrievable from institutional records, and the rationale for omentectomy in individual endometrioid cases could not be reconstructed retrospectively.

CONCLUSION

In this single-center retrospective cohort, laparoscopic surgical staging for gynecologic malignancy achieved high rates of pelvic (95.2%) and paraaortic (100%) nodal adequacy with limited perioperative hematologic impact, including in a predominantly obese, postmenopausal population. Nodal yield was preserved across body mass index strata, and the low rate of omental metastasis in endometrioid endometrial carcinoma (1.2%), although based on a small number of events, is in line with current recommendations favoring selective rather than routine omentectomy in this histologic subgroup. Preoperative CA-125 elevation emerged as a potentially useful adjunct marker of nodal risk, warranting prospective validation. Collectively, these findings support laparoscopic staging as a feasible, oncologically adequate, and hematologically well-tolerated approach for routine tertiary-center practice.

Ethical approval statement: The study received ethical approval from the Ethics Committee of Etlik City Hospital (AESH-BADEK2-2026-242; date: 24/03/2026). 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 Statement: 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: ÖC: Design the method to achieve results, Analysis or Interpretation, Data collecting and processing, Literature scan, Article writing; TZA: Article writing, Critical examination; MŞ: Article writing, Critical examination

REFERENCES

- Bray F, Laversanne M, Sung H, Ferlay J, Siegel RL, Soerjomataram I, et al. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA A Cancer J Clinicians*. 2024 May;74(3):229–63. doi:10.3322/caac.21834
- Concin N, Matias-Guiu X, Vergote I, Cibula D, Mirza MR, Marnitz S, et al. ESGO/ESTRO/ESP guidelines for the management of patients with endometrial carcinoma. *Int J Gynecol Cancer*. 2021 Jan;31(1):12–39. doi:10.1136/ijgc-2020-002230 PubMed PMID: 33397713.
- Berek JS, Matias-Guiu X, Creutzberg C, Fotopoulou C, Gaffney D, Kehoe S, et al. FIGO staging of endometrial cancer: 2023. *International Journal of Gynecology & Obstetrics*. 2023;162(2):383–94.
- Minig L, Saadi J, Patrono MG, Giavedoni ME, Cárdenas-Rebollo JM, Perrotta M. Laparoscopic surgical staging in women with early stage epithelial ovarian cancer performed by recently certified gynecologic oncologists. *European Journal of Obstetrics & Gynecology and Reproductive Biology*. 2016;201:94–100.
- Walker JL, Piedmonte MR, Spirtos NM, Eisenkop SM, Schlaerth JB, Mannel RS, et al. Laparoscopy compared with laparotomy for comprehensive surgical staging of uterine cancer: Gynecologic Oncology Group Study LAP2. *Journal of Clinical Oncology*. 2009;27(32):5331–6.
- Perrone E, Capasso I, Pasciuto T, Giòè A, Alletti SG, Restaino S, et al. Laparoscopic vs. robotic-assisted laparoscopy in endometrial cancer staging: large retrospective single-institution study. *Journal of Gynecologic Oncology*. 2021;32(3):e45.
- Koek RC, Wenzel H, Jonges GN, Lok CA, Zweemer R, Gerestein CG. Oncological outcomes after laparotomic, laparoscopic, and robot-assisted laparoscopic staging for early high–intermediate or high-risk endometrial cancer. *International Journal of Gynecological Cancer*. 2025;35(7):101847.
- Merlier M, Kerbage Y, Pierache A, Ramdane N, Canlorbe G, Bolze PA, et al. Impact on prognosis of the surgical route, laparoscopy or laparotomy, for the surgical staging of early stage ovarian cancer—a study from the FRANCOGYN Group. *Journal of Clinical Medicine*. 2020;9(11):3528.
- Garcia NG, Moreno CS, Teixeira N, Lloret PE, Guibourg RL, Negre RR. Comparison of laparoscopy and laparotomy in the management of early-stage ovarian cancer. *Gynecology and Minimally Invasive Therapy*. 2023;12(2):83–9.
- Colombo N, Sessa C, du Bois A, Ledermann J, McCluggage WG, McNeish I, et al. ESMO–ESGO consensus conference recommendations on ovarian cancer: pathology and molecular biology, early and advanced stages, borderline tumours and recurrent disease. *International Journal of Gynecological Cancer*. 2019;29(4):728–60.
- Ramirez PT, Frumovitz M, Pareja R, Lopez A, Vieira M, Ribeiro R, et al. Minimally invasive versus abdominal radical hysterectomy for cervical cancer. *New England Journal of Medicine*. 2018;379(20):1895–904.
- Petousis S, Margioulas-Siarkou G, Margioulas-Siarkou C, Almpertis A, Guyon F, Dinas K. Laparoscopy in the Surgical Management of Gynecological Cancer: A Comprehensive Update. *Journal of Clinical Medicine*. 2025;14(21):7614.
- Smrz SA, Calo C, Fisher JL, Salani R. An ecological evaluation of the increasing incidence of endometrial cancer and the obesity epidemic. *American Journal of Obstetrics and Gynecology*. 2021;224(5):506–e1.
- Tse K, Ngan HY. The role of laparoscopy in staging of different gynaecological cancers. *Best Practice & Research Clinical Obstetrics & Gynaecology*. 2015;29(6):884–95.
- Galaal K, Donkers H, Bryant A, Lopes AD. Laparoscopy versus laparotomy for the management of early stage endometrial cancer. *Cochrane Gynaecological, Neuro-oncology and Orphan Cancer Group, editor. Cochrane Database of Systematic Reviews*. 2018 Oct 31;2018(10). doi:10.1002/14651858.CD006655.pub3
- Ozdağ B, Unlu B, Yakin H, Tapisiz O, Energin H, Besli M, et al. Role of omentectomy and appendectomy in surgical staging of endometrioid endometrial cancer. *European Journal of Gynaecological Oncology*. 2013;34(4).

Konjenital Kalp Hastalığı Nedeniyle İki Kez Fontan Ameliyatı Olan Hastada Gebelik ve Doğum: Olgu Sunumu

Pregnancy and Childbirth in a Patient Who Underwent Two Fontan Surgeries Due To Congenital Heart Disease: Case Report

 Vefa ŞAKAR¹,  Kübra Dilşad SÖNMEZ ÖZGÜR¹,  Özhan ÖZDEMİR¹

¹Sağlık Bilimleri Üniversitesi, Gülhane Tıp Fakültesi, Kadın Hastalıkları ve Doğum Anabilim Dalı, Ankara, Türkiye

ÖZ

Giriş: Fontan ameliyatı, biventriküler dolaşımı olmayan kompleks konjenital kalp hastalığı olan hastalarda palyasyon sağlama amacıyla gerçekleştirilir. Çocukluk çağında bu ameliyatı geçiren kadınların sayısı giderek artmakta ve bazıları hamile kalmaktadır. Fontan sirkülasyonu olan kadınların gebelik sırasında artmış maternal riske sahip olduğu bildirilmiştir. Gebelikte meydana gelen hemodinamik değişiklikler Fontan hastaları için özellikle zorlayıcı olmakta ve sonuçlar değişiklik göstermektedir. Bu olgu, bildiğimiz kadarıyla Türkiye'den bildirilen ilk vakadır.

Vaka Takdimi: Fontan ameliyatı geçirmiş, tekil spontan gebeliği olan 27 yaşında bir kadın hasta sunuyoruz. Hasta gebeliğin 30. Haftasında sezaryenle düşük doğum ağırlıklı canlı bir bebek doğurmuştur.

Sonuç: Bu olgu sunumu, uygun bir Fontan hastasında gebeliğin başarılı sonuçlarla tolere edilebileceğine dair bir kanıt sunmaktadır.

Anahtar kelimeler: Fontan ameliyatı, gebelik, sezaryen doğum, doğuştan kalp hastalığı

ABSTRACT

Introduction: The Fontan procedure is performed to provide palliation in patients with complex congenital heart disease without biventricular circulation. The number of women who undergo this procedure in childhood is increasing, and some of them become pregnant. It has been reported that women with Fontan circulation have an increased maternal risk during pregnancy. Hemodynamic changes that occur during pregnancy are particularly challenging for Fontan patients, and outcomes vary. This is, to our knowledge, the first case reported from Turkey.

Case Presentation: We present a 27-year-old female patient who underwent Fontan surgery and had a single spontaneous pregnancy. The patient delivered a live baby with low birth weight by cesarean section at 30 weeks of pregnancy.

Conclusion: This case presentation provides evidence that pregnancy can be tolerated with successful outcomes in an appropriate Fontan patient.

Keywords: Fontan surgery, pregnancy, cesarean delivery, congenital heart disease

GİRİŞ

Tek ventrikül palyasyonu olarak Fontan ameliyatı ilk kez 1971 yılında Fontan ve Baudet tarafından tanımlanmıştır [1]. Ergenlik çağına ulaşan kadınlar, yüksek maternal ve fetal riskler nedeniyle gebelikten kaçınmaları tavsiye edilmesine rağmen Fontan palyasyonundan sonra başarılı doğumlar yapabilmektedir. Gebelikte, artmış kan hacmi, azalmış hematokrit, azalmış sistemik vasküler direnç, artmış kalp hızı ve artmış kalp debisi gibi normal fizyolojik değişiklikler, Fontan palyasyonunda zaten tehlikede olan kalp debisi ve pulmoner kan akışını daha da kötüleştirebilir. Bu

durum aritmilere, siyanozun kötüleşmesine, kalp yetmezliğine ve egzersiz kapasitesinde bozulmaya yol açar[2]. İntrauterin büyüme geriliği, düşük doğum ağırlığı ve erken doğum şeklinde fetal komplikasyonlar da bildirilmiştir [3].

Fontan dolaşımı ile komplike gebeliği olan kadın hastalar, yüksek riske sahip olduğundan bu hastaların sıkı perinatal bakıma ihtiyacı vardır veya bazen gebelikten kaçınmaları önerilebilir. Gebelik sırasında Fontan dolaşımına eşlik eden sabit düşük kalp debisinin neden olduğu venöz veya intrakardiyak tromboz, aritmi ve kardiyak fonksiyonun azalmasına bilhassa önem verilmelidir. Tıptaki

Cite as: Şakar V, Sönmez Özgür KD, Özdemir Ö. Pregnancy and Childbirth in a Patient Who Underwent Two Fontan Surgeries Due To Congenital Heart Disease: Case Report. Jinekoloji-Obstetrik ve Neonatoloji Tıp Dergisi 2026;23(2):228–230.

Geliş/Received: 14.07.2025 • **Kabul/Accepted:** 24.11.2025

Sorumlu Yazar/Corresponding Author: Vefa Şakar, Sağlık Bilimleri Üniversitesi, Gülhane Eğitim ve Araştırma Hastanesi, Kadın Hastalıkları ve Doğum Anabilim Dalı, Ankara, Türkiye

E-mail: doctorvafa@hotmail.com

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

ilerlemeler sonucunda Fontan tedavisinin çeşitli modifikasyonları [4], hastalığın seyrini iyileştirdiğinden, üreme çağındaki Fontan dolaşımının insidansının önümüzdeki birkaç on yıl içinde artması beklenmektedir, ancak daha önce Fontan tedavisi olan kadınlarda gebelik ile ilgili raporlar hala çok nadirdir. Bu yazıda Fontan palyasyonu geçirmiş bir kadında başarılı gebelik ve doğumla sonuçlanan olgu sunulmuştur.

VAKA TAKDİMİ

27 yaşında primipar bir kadın 30. Gebelik haftasında dış merkezde yenidoğan yoğun bakımda yer olmaması üzerine hastanemize ppprom (preterm prematür membrane rüptürü) ön tanısıyla refere edildi. Geldiğinde serviks retropeze, açıklık 2 cm, silinme %30 ve aktif amniyon gelişi mevcuttu. Özgeçmişinde kompleks konjenital kalp hastalığı (hipoplastik sağ ventrikul ,asd,vsd, ps,trikuspit atrezisi tanıları) mevcuttu ve bunun için 6 ve 10 yaşında iki kez Total Cava-Pulmoner anastomoz (APC) ile Fontan ameliyatı geçirmişti.

New York Kalp Cemiyeti'nin (NYHA) konjestif kalp yetmezliği sınıflamasına göre sınıf III fonksiyonel durumu vardı. Nefes darlığı şikayeti yoktu. Periferik ödem yoktu. EKG normal sinüs ritmi gösteriyordu. Hastanın dış merkez takiplerinde 2 li testi normal,3 lü test yok,ayrıntılı ultrasonu normal,ogtt yapılmamıştı. Konjenital kalp hastalığı olduğu için amniyosentez önerilmiş, perinatoloji konseyi yapılmış, konsey sonucunda annenin ve bebeğin karşılaşabileceği riskler anlatılarak terminasyon önerilmiş ve hasta kabul etmemişti. İmza vererek gebeliğin devamını istemişti. Gebeliğin başından düzenli olarak oksapap 0,4, asetil salisilat asit (ASA) 100 mg, levotiron 1*62,5 ve tambacor 2*100 mg (flekainid) kullanmaktaydı. Hastaya fetal akciğer gelişimini artırmak için antenatal steroid (betametazon) uygulandı ve nöroprotektif amaçlı 4 gr magnezyum sulfat yükleme ve takiben idame tedavisi başlandı.Urofix takibine alındı. Pembisin ve azitromisin tedavisi başlandı. Acil kalp damar cerrahisi, kardioloji, anestezi, pediatrik kardioloji görüşleri alındı. Yatakbaşı yapılan EKO'sunda ejeksiyon fraksiyonu: 60, sat: 95, laboratuvar değerleri: hgb:13,9 g/dL, wbc:8,8*10⁹/L, aptt: 30,1, pTZ: 9

Flekainid tedavisine kardioloji görüşü de alınarak devam edildi. İlerleyen süreçte hastanın açıklığının 4-5 cm ve efasmanının %80 olması üzerine hasta sezaryene alındı.Sezaryen genel anestezi altında gerçekleştirildi. 6/8 Apgar ile 1154 gr ağırlığında erkek bebek doğurtuldu. Hastanın bebeği prematürite nedeniyle yenidoğan yoğun bakımda takibe alındı.

TARTIŞMA

Fontan operasyonu geçirmiş hastalarda gebeliğin yönetimi, yüksek riskli özellikleri nedeniyle mutlaka multidisipliner bir yaklaşım

gerektirir. Perinatoloji, kardioloji, anesteziyoloji ve neonatoloji uzmanlarının yer aldığı bir ekip, hem anne hem de fetüsün takibini koordine ederek olası komplikasyonlara hızlı müdahale edilmesini sağlar. Bu koordinasyon, gebelik planlamasından doğum sonrası döneme kadar uzanan süreçte maternal mortalite ve morbidite riskini azaltmada belirleyici rol oynamaktadır.

Olgumuz , Fontan operasyonu geçirmiş ve hayatta kalan hastalarda gebeliğin mümkün olduğunu ve başarılı olabileceğini doğrulamıştır [5,6,7,8]. Ancak gebeliği düşünen bir kadın kendisi ve bebeği için olası risklerin ve komplikasyonların farkında olmalıdır. Bonner ve ark. tarafından yayınlanan raporlarda Fanton operasyonu geçirmiş hastalarında %27-69'luk insidanda erken trimesterde düşük gözlemlenmiştir [9]. Bu sayılar Avrupa nüfusunda gözlemlenen %10-15'lik spontan düşük oranlarından çok daha yüksektir [10]. Bu durumun nedeni tam açık değildir, ancak abdominal venöz konjesyon, artmış venöz basınç ve kardiyak debiyi artıramama nedeniyle ortaya çıkabilir [5,6,11,12]. Fontan hastalarında prematürite oranları %60–82 arasında değişkenlik gösterebilir [9,16,17,18] ve normal gebe popülasyonuna göre altı–sekiz kat daha sık görülür [3].

Yayınlanmış verilerden de görüldüğü gibi, ikinci trimestere kadar devam eden gebelikler tamamlanmalıdır [8,9,13,14]. Hastaların fonksiyonel sınıfına ve Fontan dolaşımı için tipik olan komplikasyonlara göre kadınlar arasında yüksek (%93,3) bir düşük oranı gözlemlenmiştir.Ama iyi işlev gören Fontan hastalarının gebe kalma olasılığının daha yüksek olduğunu varsaymak mantıklıdır. Bu, Arif ve arkadaşları tarafından Fontan prosedüründen sonra kadınlarda 55 gebeliğin analizine istinaden de doğrulanmıştır [13].

Olgumuzda anne ve bebek ölümü olmadı. Yayınlanan verilere göre, hastaların %8.1–31.5'inde aritmi görülmektedir [13,15,16] Literatürde, bu gebe kadınlarda görülen en yaygın olumsuz olay supraventriküler aritmilerdir [5]. Fakat bizim hastamızda bu durumla karşılaşmadık.Buna ragmen kardioloji tarafından kullandığı flekainid ilacının 1 ay devamı ve 1 ay sonunda eko kontrolü önerildi.

Gebeliğin başarılı devamı, Fontan operasyonu geçirmiş kadınların gebelik öncesi klinik durumu ile sıkı bağlantılıdır [13] Bizim hastanın da konsepsiyondan 1 ay önce yapılan eko kontrolünde:İyi çalışan TCPC anastomozu(Total Cava Pulmoner Anastomoz), hafif sistemik AV yetersizliği mevcuttu ve EF: %70' ti.

Fontan operasyonu geçirmiş hastalarda postpartum dönemde tromboz riskinin artmış olması nedeniyle antikoagülasyon tedavisi önemlidir. Literatürde belirgin bir süre veya doz standardizasyonu olmamakla birlikte, bireysel risk değerlendirmesi esas alınmalıdır. Cauldwell ve arkadaşları, doğumdan sonra yalnızca 50 hamile kadından birinde venöz tromboemboli vakası göstermiştir [17].

New York Kalp Cemiyeti Sınıf 3 ve 4 KVS (kardiyovasküler sistem) hastalığı olanlara öncelikli olarak normal doğum önerse de bizim hasta kardiyoloji önerisi nedeniyle sezaryen ile doğum yaptı.

Bizim olgumuzda da kardiyoloji önerisi doğrultusunda postpartum dönemde antikoagülasyon tedavisini kesmemiş olup hâlen günlük 5 mg warfarin kullanmaktadır.

Önceki verilerde belirtildiği gibi, plasenta dekolmanı, erken membran rüptürü ve antepartum kanama gibi obstetrik komplikasyonlar, Fontan operasyonu olan gebelerde daha sık görülmektedir [3,5,15,16]. Bunun ana nedeni, fetoplasental ünitenin hipoperfüzyonu ve damarsal kardiyovasküler disfonksiyondur [6]. Bizim hastada da erken membrane rüptürü gelişmişti.

SONUÇ

Biz, Fontan operasyonu geçirmiş, gebeliğin erken döneminde terminasyon önerilmesine rağmen gebeliğine devam eden ve 30. Haftada preterm doğumla sonuçlanan bir vaka örneğini sunduk. Doğum sonrası kanama ve tromboz gözlemlemedik. Bebek ilk günden O2 desteği ile yenidoğan yoğun bakım ünitesinde takibe alındı ve 2000 gr olduktan sonra taburcu edildi. Hastamıza 1 ay sonra kardiyoloji poliklinik kontrolü önerildi.

Bu olgu sunumu, uygun bir Fontan hastasında gebeliğin başarılı sonuçlarla tolere edilebileceğine dair bir kanıt sunmaktadır.

Çatışma Beyanı: Bu çalışmada yer alan yazarlar, çıkar çatışması oluşturabilecek herhangi bir ticari veya finansal ilişkiye sahip olmadığını beyan eder.

Yazarlık Katkısı: Vefa Şakar: Yazının gözden geçirilmesi; Kübra Dilşad Sönmez Özgür: İlk taslağın yazımı; Özhan Özdemir: Yazının gözden geçirilmesi ve onayı

REFERANSLAR

- Fontan F, Baudet E. Surgical repair of tricuspid atresia. *Thorax*. 1971;26:240–8.
- Khairy P, Poirier N, Mercier LA. Univentricular heart. *Circulation*. 2007;115:800–12.
- Drenthen W, Pieper PG, RoosHesselink JW, Lottum WA, Voors AA, Mulder JM, Dijk APJ, Vliegen HW, et al. Pregnancy and delivery in women after Fontan palliation. *Heart*. 2006;92:1290–4.
- Therrien J, Dore A, Gersonny W et al. CCS Consensus Conference 2001 update: Recommendation for the management of adults with congenital heart disease. Part I. *Can J Cardiol*. 2001;17:940–959.
- Garcia Roperio, A.; Baskar, S.; Roos Hesselink, J.W.; Girnius, A.; Zentner, D.; Swan, L.; Ladouceur, M.; Brown, N.; Veldtman, G.R. Pregnancy in women with a Fontan circulation: A systematic review of the literature. *Circ. Cardiovasc. Qual. Outcomes*. 2018;11, e004575. (CrossRef)
- Ordóñez, M.V.; Trinder, J.; Curtis, S.L. Success in a Fontan pregnancy: How important is ventricular function? *Cardiol Young*. 2019;29:225–227. (CrossRef) (PubMed)
- RegitzZagrosek, V.; RoosHesselink, J.W.; Bauersachs, J.; BlomstromLundqvist, C.; Cifkova, R.; De Bonis, M.; Jung, B.; Johnson, M.R.; Kintscher, U.; Kranke, P.; et al. ESC Guidelines for the management of cardiovascular diseases during pregnancy. *Eur. Heart J*. 2018;39:3165–3241. (CrossRef)
- Wolfe, N.K.; Sabol, B.A.; Kelly, J.C.; Dombrowski, M.; Benhardt, A.C.; Fleckenstein, J.; Stout, M.J.; Lindley, K.J. Management of Fontan circulation in pregnancy: A multidisciplinary approach to care. *Am. J. Obstet. Gynecol. MFM*. 2021;3:100257. (CrossRef) (PubMed)
- Bonner, S.J.; Asghar, O.; Roberts, A.; Vause, S.; Clarke, B.; Keavney, B. Cardiovascular, obstetric and neonatal outcomes in women with previous Fontan repair. *Eur. J. Obstet. Gynecol. Reprod. Biol*. 2017;219:53–56. (CrossRef) (PubMed)
- Ford, H.B.; Schust, D.J. Recurrent pregnancy loss: Etiology, diagnosis, and therapy. *Rev. Obstet. Gynecol*. 2009;2:76–83. (PubMed)
- Ordóñez, M.V.; Biglino, G.; Caputo, M.; Kelly, B.; Mohan, A.; Trinder, J.; Curtis, S.L. Case of placental insufficiency and premature delivery in a Fontan pregnancy: Physiological insights and considerations on risk stratification. *Open Heart*. 2021;8:e001211. (CrossRef)
- Gewillig, M. The Fontan circulation. *Heart*. 2005;91:839–846. (CrossRef)
- Arif, S.; Chaudhary, A.; Clift, P.F.; Morris, R.K.; Selman, T.J.; Bowater, S.E.; Hudsmith, L.E.; Thompson, P.J.; Thorne, S.A. Pregnancy outcomes in patients with a Fontan circulation and proposal for a risk-scoring system: Single centre experience. *J. Congenit. Heart Dis*. 2017;1:10. (CrossRef)
- Walker, F. Pregnancy and the various forms of the Fontan circulation. *Heart*. 2007;93:152–154. (CrossRef)
- Gouton, M.; Nizard, J.; Patel, M.; Sassolas, F.; Jimenez, M.; Radojevic, J.; Mathiron, A.; Amedro, P.; Barre, E.; Labombarda, F.; et al. Maternal and fetal outcomes of pregnancy with Fontan circulation: A multicentric observational study. *Int. J. Cardiol*. 2015;187:84–89. (CrossRef)
- Pundi, K.N.; Pundi, K.; Johnson, J.N.; Dearani, J.A.; Bonnicksen, C.R.; Phillips, S.D.; Canobbio, M.C.; Driscoll, D.J.; Cetta, F. Contraception practices and pregnancy outcome in patients after Fontan operation. *Congenit Heart Dis*. 2016;11:63–70. (CrossRef)
- Cauldwell, M.; Steer, P.J.; Bonner, S.; Asghar, O.; Swan, L.; Hodson, K.; Head, C.E.G.; Jakes, A.D.; Walker, N.; Simpson, M.; et al. Retrospective UK multicentre study of the pregnancy outcomes of women with a Fontan repair. *Heart*. 2018;104:401–406. (CrossRef) (PubMed)
- Afshar, Y.; Tan, W.; Jones, W.M.; Canobbio, M.; Lin, J.; Reardon, L.; Lluri, G.; Aboulhossn, J.; Koos, B.J. Maternal Fontan procedure is a predictor of a small-for-gestational-age neonate: A 10-year retrospective study. *Am. J. Obstet. Gynecol. MFM*. 2019;1:100036. (CrossRef)