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ORIGINAL ARTICLE

A Retrospective Comparative Analysis of Epidural Analgesia and Its Impact on Neutrophil-to-Lymphocyte and Platelet-to-Lymphocyte Ratios During Vaginal Delivery

Epidural Analjezi ve Vajinal Doğum Sırasında Nötrofil-Lenfosit ve Trombosit-Lenfosit Oranları Üzerindeki Etkisi: Karşılaştırmalı Bir Analiz

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ABSTRACT

Introduction: Epidural analgesia is a widely used method for managing labor pain. While effective in pain relief, its potential effects on maternal systemic inflammation during labor remain unclear. The neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) are established biomarkers for systemic inflammation and may provide insights into the inflammatory dynamics associated with epidural analgesia. This study aims to investigate the impact of epidural analgesia on NLR and PLR values in women undergoing normal vaginal delivery.
Methods: A retrospective case-control study was conducted involving 100 women with singleton pregnancies, evenly divided into two groups based on whether they received epidural analgesia. Hematological parameters, including NLR and PLR, were measured and analyzed. Labor duration and white blood cell (WBC) counts were also compared between groups.
Results: No significant differences in NLR ($p = 0.79$) or PLR ($p = 0.59$) values were observed between the epidural and non-epidural groups. However, WBC counts were significantly higher in the epidural group ($p = 0.007$), and labor duration was prolonged ($p < 0.001$) compared to the non-epidural group.
Conclusion: Epidural analgesia does not significantly influence NLR and PLR values, suggesting minimal systemic inflammatory effects. However, the observed increase in WBC counts and prolonged labor duration highlight the need for individualized monitoring and care. These findings provide further evidence supporting the safe use of epidural analgesia in normal vaginal delivery while identifying areas for future research.

Keywords: epidural analgesia, inflammation, neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio, vaginal delivery

ÖZ

Giriş: Epidural analjezi, doğum ağrısını yönetmek için yaygın olarak kullanılan bir yöntemdir. Ağrıyı gidermede etkili olsa da, doğum sırasında maternal sistemik inflamasyon üzerindeki potansiyel etkileri belirsizliğini korumaktadır. Nötrofil-lenfosit oranı (NLR) ve trombosit-lenfosit oranı (PLR), sistemik inflamasyon için belirlenmiş biyobelirteçlerdir ve epidural analjezi ile ilişkili inflamasyon dinamiklerine dair içgörüler sağlayabilir. Bu çalışma, normal vajinal doğum yapan kadınlarda epidural analjezinin NLR ve PLR değerleri üzerindeki etkisini araştırmayı amaçlamaktadır.
Yöntemler: Tekil gebelikleri olan 100 kadını içeren retrospektif bir vaka kontrol çalışması yürütüldü ve epidural analjezi alıp almamalarına göre eşit olarak iki gruba ayrıldı. NLR ve PLR dahil hematolojik parametreler ölçüldü ve analiz edildi. Doğum süresi ve beyaz kan hücresi (WBC) sayıları da gruplar arasında karşılaştırıldı.
Bulgular: Epidural ve epidural olmayan gruplar arasında NLR ($p = 0,79$) veya PLR ($p = 0,59$) değerlerinde anlamlı bir fark gözlenmedi. Ancak, epidural grupta WBC sayıları anlamlı şekilde daha yüksekti ($p = 0,007$) ve doğum süresi epidural olmayan gruba kıyasla daha uzundu ($p < 0,001$).
Sonuç: Epidural analjezi, NLR ve PLR değerlerini anlamlı şekilde etkilemez ve bu da minimal sistemik inflamatuar etkiler olduğunu düşündürmektedir. Ancak, WBC sayılarında gözlemlenen artış ve uzamış doğum süresi, bireyselleştirilmiş izleme ve bakıma olan ihtiyacı vurgulamaktadır. Bu bulgular, normal vajinal doğumda epidural analjezinin güvenli kullanımını destekleyen daha fazla kanıt sağlarken gelecekteki araştırma alanlarını belirlemektedir.

Anahtar Kelimeler: epidural analjezi, inflamasyon, nötrofil-lenfosit oranı, trombosit-lenfosit oranı, vajinal doğum

Introduction

Lumbar epidural analgesia is one of the most effective methods for pain management during vaginal delivery. Globally, 30-60% of women in labor prefer this method. Epidural analgesia increases maternal comfort by reducing labor pain, contributing to muscle relaxation and decreasing physiological stress during labor. However, this method is also associated with complications such as severe headaches, permanent nerve damage, significant drops in blood pressure, meningitis, epidural abscess, and hematoma (1).

In recent years, the role of inflammatory responses during labor has attracted attention. Neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) are indicators of inflammation and are potentially significant biomarkers for assessing maternal inflammatory status during labor (2). In the literature, NLR and PLR have been reported to be associated with obstetric conditions such as preterm labor, gestational

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diabetes, and preeclampsia (3, 4). However, there is insufficient research evaluating the effects of epidural analgesia on these markers.

The mechanisms through which epidural analgesia might influence inflammatory responses have been discussed in the literature. The immunomodulatory effects of local anesthetics on inflammation and the suppression of stress hormones could explain changes in inflammatory markers (5, 6). This study aimed to evaluate the effects of epidural analgesia on hematological inflammatory markers and contribute to scientific knowledge regarding the role of this method in labor.

Material and methods

Study Design and Patient Population

This retrospective case-control study was conducted at two centers in the Obstetrics and Gynecology Departments. The research was carried out in accordance with the principles of the Helsinki Declaration and received ethical committee approval (approval number: 2024/504, approval date: 08.10.2024). Data were collected from hospital databases between October 2021 and September 2024.

A total of 100 pregnant women with singleton pregnancies between 37 and 41 weeks of gestation who presented with regular uterine contractions were included in the study. Half of the cases were selected from women who received epidural analgesia, while the other half were selected from those who did not. The exclusion criteria were as follows:

• Multiple pregnancies,

• Significant structural anomalies in the fetus,

• Chromosomal aneuploidy,

•Risky pregnancy findings during follow-up (gestational diabetes mellitus, preeclampsia or eclampsia, intrauterine growth restriction, premature rupture of membranes, preterm birth, macrosomia, polyhydramnios, or oligohydramnios),

• Smoking or alcohol use,

• Chronic systemic disease in the mother,

• History of instrumental delivery (vacuum, forceps).

In the epidural analgesia group, a combination of lidocaine–epinephrine (2%) and fentanyl (100 mcg) was used. Epidural fentanyl 100 mcg after lidocaine–epinephrine test dose has been shown to provide adequate analgesia in early labor in previous studies (7). Analgesia was initiated when cervical dilation reached 4 cm during active labor. The epidural catheter was placed in the L3-L4 interspace, and all procedures were performed by an experienced anesthesia team. The same analgesia protocol was applied in both centers.

All hemogram parameter measurements were performed using a blood count analyzer within half an hour of blood collection. Laboratory parameters, including platelet count, neutrophil count, lymphocyte count, NLR, and PLR, were recorded for both groups.

Statistical analyses

The statistics software package SPSS 25 (IBM, Armonk, NY: IBM Corp.) was used for the statistical evaluations in the present study. In this study, statistical analyses were conducted to compare the Neutrophil-Lymphocyte Ratio (NLR) and Platelet-Lymphocyte Ratio (PLR) between two groups: those who underwent epidural anesthesia and those who did not. The first step involved calculating the measures of central tendency (mean) and dispersion (standard deviation) for each group to understand the distribution of NLR and PLR values. To determine if there were significant differences between the two groups, independent sample t-tests were performed for both NLR and PLR. The t-test is used to compare the means of two independent groups to see if they differ significantly. A p-value of less than 0.05 was considered statistically significant, indicating that the difference between the groups is not due to random chance.For each parameter (NLR and PLR), we computed the mean, standard deviation, and the number of participants for both groups. The results are presented in tables that summarize these statistics and the outcomes of the t-tests, including the t-statistics and p-values, along with an indication of whether the differences were statistically significant.

Results

NLR and PLR Analyses

According to Table 1, there were no statistically significant differences in NLR and PLR values between the epidural and non-epidural groups ($p = 0.79$ and $p = 0.59$, respectively). This indicates that epidural analgesia does not significantly impact inflammatory responses.

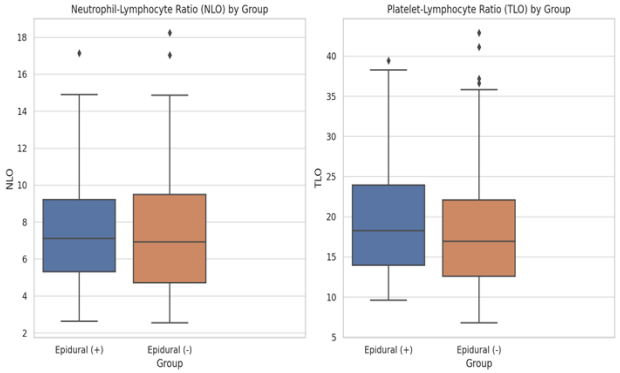
Table 1. NLR and PLR Statistics for Epidural and Non-Epidural Groups

Groups	Parame-ters	Mean	Standard Deviation	Patient Count	P value
Epidural (+)	NLR	7.70	3.10	50	p = 0.79
Epidural (-)	NLR	7.52	3.61	50	
Epidural (+)	PLR	19.76	7.39	50	p = 0.59
Epidural (-)	PLR	18.87	8.79	50	

NLR: neutrophil-lymphocyte ratio, PLR: platelet-lymphocyte ratio

The boxplots in Figure 1 show the distributions of NLR and PLR for both groups. The median values and distributions visually confirm the lack of significant differences between the groups.

Figure 1. The following boxplots display the distribution of Neutrophil-Lymphocyte Ratio (NLO) and Platelet-Lymphocyte Ratio (TLO) between the Epidural (+) and Epidural (-) groups.



Comparison of Other Parameters

As shown in Table 2, demographic and clinical parameters such as age, gravida, parity, abortus, BMI, hemoglobin (Hb), and platelet counts did not differ significantly between the two groups ($p > 0.05$).

Table 2. Comparison of Parameters Between Groups

Parameter	Group 1 Mean	Group 1 Std	Group 2 Mean	Group 2 Std	T-Statistic	P-Value	Significance
Age	30.52	4.75	31.2	4.76	-0.715	0.476	No
Gravity	2.04	1.38	2.28	0.88	-1.034	0.304	No
Parity	0.76	0.94	0.98	0.68	-1.339	0.184	No
Abortus	0.28	0.64	0.3	0.46	-0.179	0.858	No
BMI	25.62	2.97	25.96	2.88	-0.588	0.558	No
WBC	16.5	3.71	14.44	3.79	2.751	0.007	Yes
Hemoglobin	10.92	1.19	11.21	1.27	-1.193	0.236	No
Platelet	215.52	44.29	211.84	59.47	0.351	0.726	No
Weight	3366.3	366.81	3223.6	391.95	1.88	0.063	No
Labor duration	8.66	4.73	3.88	2.98	6.048	0.0	Yes

Group 1: Epidural (+) group, Group 2: Epidural (-) group, BMI: Body mass index, WBC: White blood cells

• WBC Count: WBC levels were significantly higher in the epidural group ($p = 0.007$). This supports the hypothesis that epidural analgesia may trigger an inflammatory response.

• Labor Duration: Labor duration was significantly longer in the epidural group ($p < 0.001$). This may be associated with the effects of epidural analgesia on muscle activity and pushing force.

The bar plots in Figure 2 present the mean values of other parameters for both groups. The differences in labor duration and WBC are particularly notable.

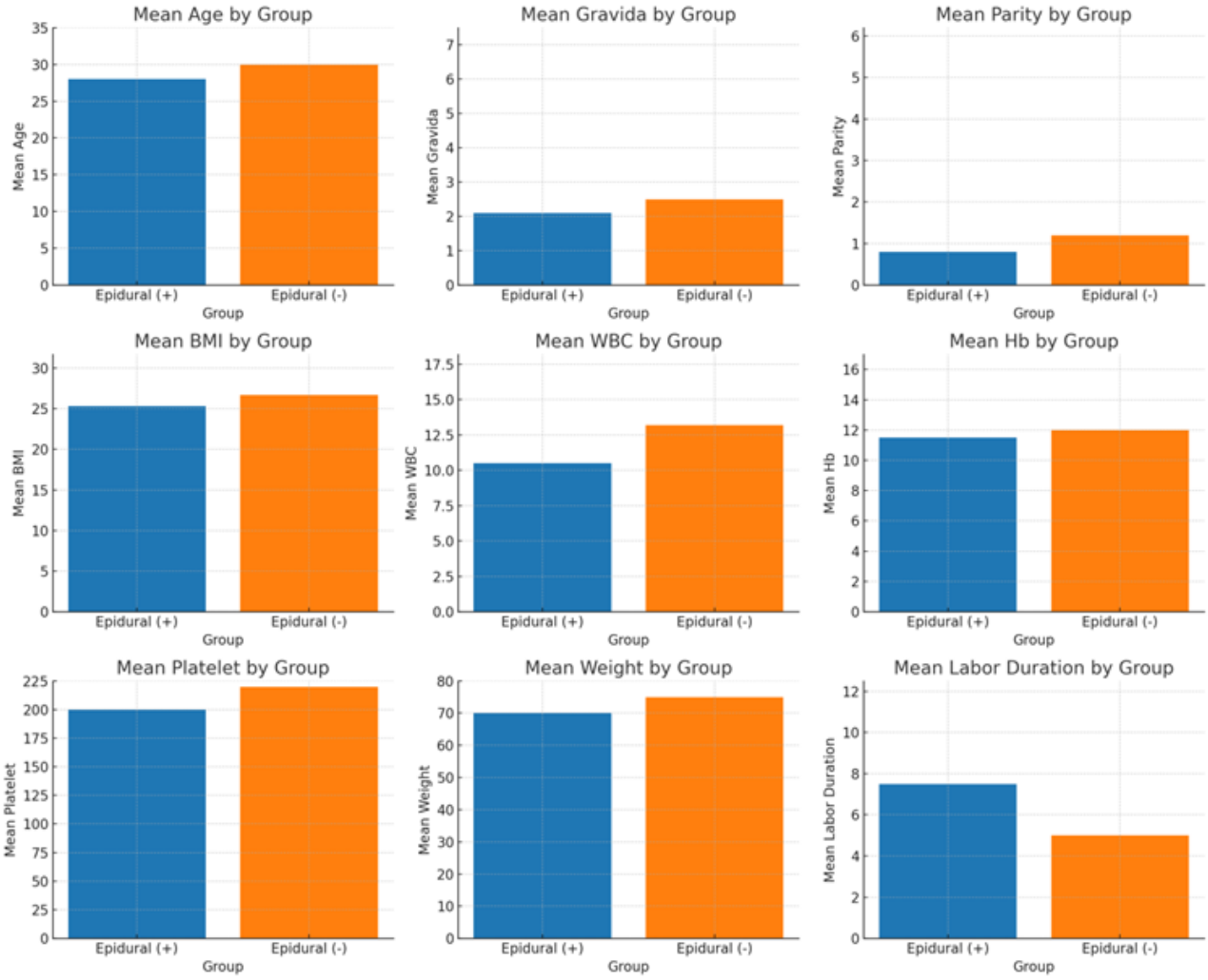
Discussions

This study contributes to the growing body of evidence regarding the effects of epidural analgesia on maternal inflammatory markers and labor outcomes. Epidural analgesia is widely used for pain management during vaginal delivery, yet its potential impact on systemic inflammation remains an area of active investigation.

The finding of no significant difference in NLR and PLR values between epidural and non-epidural groups aligns with previous studies suggesting that epidural analgesia does not significantly alter systemic inflammatory markers (8, 9). For instance, it's reported that NLR and PLR values were consistent across different modes of analgesia during labor, indicating that the physiological stress of labor itself might overshadow any minor effects of analgesia on these markers (10).

In the obstetrics field, several studies have examined the association between maternal WBC count and maternal or neonatal adverse outcomes (11-13). Shigemi et al. investigated the association between maternal WBC count on the day after operative vaginal delivery and sequential maternal adverse events during hospitalization (14). In this study, there was no significant association of WBC count on the day after operative vaginal delivery with maternal adverse outcomes. The observed increase in WBC levels

Figure 2. The following bar plots show the mean values of various parameters (Age, Gravida, Parity, BMI, WBC, Hb, Platelet, Weight, LaborDuration) between the Epidural (+) and Epidural (-) groups.



in the epidural group warrants further exploration. While elevated WBC levels could be indicative of an inflammatory response triggered by epidural administration, it is also possible that this reflects a stress-related physiological adaptation rather than pathological inflammation. Similar findings by Zhang et al. suggest that WBC elevations in epidural groups may not necessarily correlate with adverse maternal or neonatal outcomes, but rather reflect transient responses to procedural stress (15).

Prolonged labor duration in the epidural group is a well-documented phenomenon. A Cochrane review by Anim-Somuah et al. found that epidural analgesia is associated with a modest increase in the duration of both the first and second stages of labor, potentially due to reduced maternal pushing efforts and altered uterine contractility (16). The current study's findings are consistent with this literature and further emphasize the need for monitoring and supportive interventions to mitigate potential delays in labor progression.

In light of these findings, the potential immunological implications of epidural analgesia during labor merit further attention. Hawkins et al. (17) demonstrated that epidural analgesia may attenuate the systemic release of pro-inflammatory cytokines, potentially reducing the risk of excessive inflammatory responses. This could explain the lack of significant differences in NLR and PLR observed in this study, as epidural analgesia might modulate systemic inflammation without overtly impacting hematological markers. Moreover, the observed increase in WBC levels in our study might reflect a localized stress or inflammatory reaction, aligning with the hypothesis that the procedure triggers a transient physiological response

rather than a pathological one. This modulation of maternal inflammatory and stress responses could have important clinical implications, particularly in high-risk pregnancies where exaggerated inflammatory states may exacerbate complications such as preeclampsia or fetal distress. Future research should explore these mechanisms in greater depth to enhance our understanding of epidural analgesia's impact on labor outcomes and recovery.

The clinical implications of these findings are significant. Epidural analgesia remains a safe and effective method for pain relief during labor. However, the observed changes in WBC levels and labor duration underscore the importance of individualized patient care. Future research should focus on elucidating the mechanisms underlying these observations and exploring whether specific patient populations may require tailored management strategies.

Some potential confounding factors like maternal BMI and gestational age can change the results of our study. When the Table 2 examination, we see the same BMI results for both groups. In future studies, including patients in the same gestational week may increase the scientific power of the study.

This study has several limitations. First, the retrospective nature of the study, which may introduce biases in data collection and patient selection. Second, a limited sample size, potentially restricting the ability to detect subtle differences in inflammatory markers. Third, The absence of data on potential confounding factors, such as nutritional status, comorbidities, or subclinical conditions, that could influence the results and finally, the lack of evaluation of long-term maternal or neonatal outcomes related to the observed changes in inflammatory markers and labor duration. Future prospective, multicenter studies with larger sample sizes are needed to validate these findings and explore underlying mechanisms in greater detail.

In conclusion, epidural analgesia effectively reduces labor pain while having minimal effects on inflammatory markers. However, the associated prolongation of labor duration should be carefully monitored. These findings provide encouraging evidence for the safe use of epidural analgesia in obstetric practice.

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Conflict of interest

The authors report no conflict of interest.

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