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Is early prediction of postpartum wound ınfection possible? A retrospective cohort study

Doğum sonrası yara enfeksiyonunun erken tahmini mümkün müdür? Retrospektif bir kohort çalışması

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ÖZET

AMAÇ: Çalışmada sezaryen sonrası yara enfeksiyonlarında delta-nötrofil indeksi (DNI) ve nötrofil/lenfosit oranı (NLR) değerlerinin prognostik önemi olup olmadığı araştırılmıştır.

GEREÇ VE YÖNTEM: 2015-2019 yılları arasında üçüncü basamak bir sağlık kuruluşunda yara enfeksiyonu gelişen ve sezaryen sonrası tekrar hastaneye yatırılan yüz on hasta çalışma grubunu oluşturdu. Kontrol grubunda da aynı sayıda hasta mevcuttu. Ameliyattan 12 saat önce (0. gün) ve 24 saat sonra (1. gün) ölçülen DNI, lökosit sayısı ve nötrofil yüzdesini içeren laboratuvar testleri değerlendirildi. Bu sonuçların yara enfeksiyonu için prediktif değeri olup olmadığı araştırıldı.

BULGULAR: Çalışmaya alınan hastaların yaş ortalaması 30,6 (17-55) yıl, vücut kitle indeksi 28,4±3,95 kg/m2 idi. NLR 0. gün için optimal eşik değeri 4.0 idi, %80 duyarlılık, %38.7 özgüllük, 1.31 pozitif olabilirlik oranı, 0.52 negatif olabilirlik oranı tespit edildi. Yara enfeksiyonu gelişimi için etkili olan faktörler NLR gün 0, 1 ve delta NLR olarak bulunmuştur. Ayrıca vücut kitle indeksinin 27'den büyük olması, sezaryen sayısının birden fazla, ameliyat süresinin 50 dakikadan fazla ve 30 dakikadan az olması da yara enfeksiyonu gelişimini etkileyen faktörler olarak saptanmıştır.

SONUÇ: Çalışmanın sonucunda, sezaryen sırasındaki NLR değerlerinin sezaryen sonrası enfeksiyon gelişimini öngördüğünü gösterdik.

Anahtar Kelimeler: Sezaryen, delta-nötrofil indeksi (DNI), nötrofil/lenfosit oranı (NLR)

ABSTRACT

AIM: This study investigated whether delta neutrophil index (DNI) and neutrophil-to-lymphocyte ratio (NLR) values have prognostic significance for wound infection after cesarean section.

MATERIAL AND METHOD: In this retrospective study, one hundred and ten patients who developed wound infection and were rehospitalized after cesarean section in a tertiary health center between 2015 and 2019 formed the study group. The same number of patients were in the control group. Laboratory tests including DNI, leukocyte count, and percentage of neutrophils which were measured 12 hours before surgery (day 0) and 24 hours after surgery (day 1) were assessed. It was investigated whether these findings had predictive value for wound infection.

RESULTS: The mean age of patients included in the study was 30.6 (17-55) years and body mass index was 28.4±3.95 kg/m2. The optimal cut-off value for NLR day 0 was 4.0, with a sensitivity of 80%, a specificity of 38.7%, a positive likelihood ratio of 1.31, a negative likelihood ratio of 0.52, and an area under the receiver operating characteristic curve (ROC) of 0.606. NLR day 0, 1, and delta NLR were factors that were effective in the development of wound infection. Additionally, it was discovered that the body mass index above 27, the frequency of cesarean sections over 1, and the length of the operation (more than 50 minutes or less than 30 minutes) all had an impact on the development of wound infection.

CONCLUSION: We showed that NLR values during cesarean section predicted the development of infections after cesarean section.

Keywords: Cesarean section, delta-neutrophil index(DNI), neutrophil/lymphocyte ratio (NLR)

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INTRODUCTION

Cesarean section (CS) is an important obstetric procedure to save the life of both mother and fetus. In 2012, an estimated 22.9 million deliveries were performed by cesarean section.[1] However, cesarean section is a surgical procedure associated with some complications, which include surgical site infections. The rate of wound infection after cesarean section varies from 3% to 15% worldwide.[2] This variation in incidence is influenced by many factors, including population risk factors, perioperative practices, and incisional procedures. Despite the increase in cesarean section rates, the risk of wound infection has declined rapidly over the past three decades. The most important factor in this success has been the development of hygiene conditions, antibiotic prophylaxis, and sterile procedures.[3] However, infection after cesarean section is still associated with increased maternal morbidity and mortality. It prolongs the mother's hospital stay and increases the cost of care. Surgical site infection is defined as an infection that occurs at the surgical site within 30 days of the procedure.[4] Staphylococcus aureus is the most common microorganism and is isolated in 15-20% of cases.[5] Identification of these risk factors and prognostic markers is critical for targeted interventions to reduce infection rates.

The delta-neutrophil index (DNI) is a calculation that indicates the percentage of immature granulocytes in whole blood.[6] It is calculated by measuring the light reflected from various leukocyte subtypes as a result of the cytochemical myeloperoxidase reaction and can be easily measured with an equipment that produces a complete blood count.[7] Increased immature granulocytes in peripheral blood are of prognostic and diagnostic significance in infections and sepsis.8 During stress or infection, newer forms of neutrophils enter the bloodstream in increasing numbers.[6,8] They have been found in the literature to be a useful marker for diagnosis and mortality in spontaneous bacterial peritonitis.[9] Cho et al. showed in an analysis of obstetric patients that DNI levels are higher in severe preeclampsia (PE) than in healthy or mild PE and can be used to determine the severity of the disease.[10] The neutrophil/lymphocyte ratio (NLR) is calculated by dividing the number of neutrophils by the number of lymphocytes.[11] Neutrophils and lymphocytes are known to play an important role in inflammation.[12] The NLR has been shown to play a predictive role in the prognosis of chronic and acute inflammatory processes, even when the total white blood cell count is normal.[13] With this in mind, we aimed to investigate whether DNI and NLR levels have prognostic value in postpartum wound infections after cesarean section.

MATERIAL AND METHOD

This study strictly complied with the provisions of the Declaration of Helsinki on Research Involving Human Subjects and was approved by the Ethics Committee (date: 04/21/2022, approval number: 05/27). All participants signed a written informed consent form and gave verbal consent.

For this retrospective study, postpartum patients who received care at a tertiary hospital maternity clinic and delivered by cesarean section between January 2015 and December 2019 were studied. Women were defined as having infection if they developed fever or clinical signs of infection during their postpartum hospitalization or were readmitted for fever or clinical signs of infection up to forty-two days after delivery (CS). In the control group, the first three patients who had a cesarean section in the first week of the month were randomly selected until the same number of patients as in the study group was reached. Inclusion criteria for the study were singleton pregnancy and delivery by cesarean section. Exclusion criteria were multiple pregnancy, fetal anomalies, intrauterine exitus, and placental abnormalities. Accordingly, 110 patients were included in the study group. The total number of patients was 220, and data were obtained from patients' medical records. The data included various demographic, obstetric, and neonatal variables.

Laboratory tests, including DNI, leukocyte count, and neutrophil percentage, were measured within 12 hours before surgery (day 0) and 24 hours after surgery (day 1). DNI level is routinely determined at our institution during complete blood count examination. Delta DNI and NLR were calculated by subtracting day 1 from day 0. Blood samples were brought to the hematology laboratory in tubes containing ethylenediaminetetraacetic acid. These samples were centrifuged at 1500 g rpm for 10 minutes, and the DNI value (%) was calculated using the automated hematology instrument (Mindray BC-6000) available in our laboratory. The neutrophil-to-lymphocyte ratio (NLR) was calculated by dividing the neutrophil count by the lymphocyte count.

Analysis was performed using SPSS version 23.0 (Statistical Package for the Social Sciences, IBM, New York). The Kolmogorov-Smirnov test was used for the normal distribution and the Student t test for the data analysis. For data that did not conform to the normal distribution, the Mann-Whitney U test was used. Receiver operating characteristic analysis was performed to determine the appropriate cut-off point for the independent markers and to calculate the sensitivity and specificity values. A statistically significant p value was considered to be less than 0.05.

RESULTS

In this study, 110 patients were hospitalized for wound infection after cesarean section, and the same number of patients were included in the control group. The demographic characteristics of these patients are shown in

Table 1. Clinical and disease characteristics of patients and control group.

Patients	Study Population (n: 110)	Control Group (n: 110)	p
Age (mean (min-max))	26.5 (19-42)	34.7 (17-55)	0.06
Parity			
0	3 (2.7 %)	8 (7.2 %)	0.85
1-2	7 (6.3 %)	16 (14.5 %)	
> 2	100 (90.9%)	86 (78.1%)	
Body Mass Index (kg/m^2)	29.3 ± 4	27.5 ± 3.9	**0.001**
Smoking	18(25.7%)	9(12.9%)	0.067
Gestational Diabetes	20 (18.2 %)	10 (9 %)	0.052
Emergent Cesarean Delivery	14 (12.7%)	10(9 %)	0.396
Number of previous cesarean delivery			**0.018**
1	38(34.5%)	37(33.3%)	
2	23(20.9%)	17(15.3%)	
3	7(6.3%)	3(2.7%)	
4	3(2.7%)	1(0.9%)	
Operative time (minutes)	49 ± 17	55 ± 15	**0.009**
>50 minutes (n)	40	56	**0.035**
< 30 minutes (n)	17	7	**0.029**

The mean age of the patients included in the study was 30.6 (17-55) years, and the body mass index was 28.4±3.95 kg/m2. The number of patients diagnosed with gestational diabetes mellitus in the study group was 20 (18.2%). As the number of cesarean sections increased, the likelihood of wound infection increased (p=0.018). The duration of cesarean section was shorter in the study group (49±17min, 55±15 min, p=0.018). DNI and NLR values, obtained from complete blood count parameters in the study group and control group, are summarized in

Table 2. Characteristics of DNI and NLR values of participants.

Patients	Study Group (n: 110)	Control Group (n: 111)	p
DNI day 0	2.46±3.07	2.62±3.12	0.054
DNI day 1	1.28±2.37	1.37±2.97	0.771
Δ DNI	1.17±3.60	1.25±3.60	0.67
NLR day 0	6.75±5.11	6.21±4.68	0.62
NLR day 1	10.08±6.08	8.38±5.63	0.98
Δ NLR	3.32±6.91	2.17±7.30	0.54

There was no significant difference between the two groups with respect to these values.

The NLR values for predicting postcesarean wound infection were shown in

Table 3. ROC analysis for NLR in postceserean wound infection.

	Preoperative NLR	Postoperative NLR	Delta NLR
Area under Curve	0.606	0.772	0.655
Cut-off *	4	9	3.2
Sensitivity (95 % CI)	80 (71.3- 87.2 %)	84.6 (76.4- 90.7 %)	76 (67.3- 83.9 %)
Specifity (95 % CI)	38.7 (29.6 – 48.5)	62 (52.5 – 71.2)	49.6 (39.9 – 59.2)
Positive likelihood ratio	1.31 (1.1-1.56)	2.23 (1.74 – 2.87)	1.51 (1.22-1.87)
Negative likelihood ratio	0.52 (0.33- 0.8)	0.25 (0.16 -0.39 %)	0.48 (0.32- 0.7)

The optimal cut-off value for NLR day 0 was 4.00, with a sensitivity of 80% (71.3-87.2), a specificity of 38.7% (29.6-48.5), a positive likelihood ratio of 1.31 (1.1-1.56), a negative likelihood ratio of 0.52 (0.33-0.80), and an area under the receiver operating characteristic curve of 0.606. The optimal cut-off value for NLR day 1 was 9.00, with a sensitivity of 84.6% (76.4-90.7), a specificity of 62% (52.5-71.2), a positive likelihood ratio of 2.23 (1.74-2.87), a negative likelihood ratio of 0.25 (0.16-0.39), and an area under the ROC curve of 0.772. The optimal cut-off value for delta NLR was 3.2, with a sensitivity of 76% (67.3-83.9), a specificity of 49.6% (39.9-59.2), a positive likelihood ratio of 1.51 (1.22-1.87), a negative likelihood ratio of 0.48 (0.32-0.70), and an area under the ROC curve of 0.655

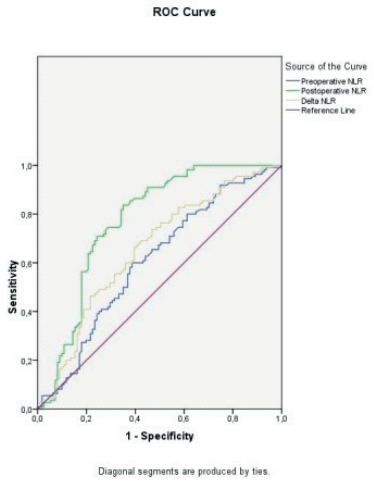

Figure 1: ROC curve for NLR in postceserean wound infection.

Factors that were effective for the development of wound infection were NLR at day zero, day one, and delta NLR. It was found that the body mass index above 27, the frequency of cesarean sections over 1, and the length of the operation (more than 50 minutes or less than 30 minutes) all had an impact on the development of wound infection.
Multivariate analysis of these data is summarized in Table 4.

Table 4. Multivariable logistic regression analysis of the risk factors for postcesartean wound infection.

	Odds Ratio	95 % confidence interval	P value
Preoperative NLR	2.58	1.12 – 5.96	**0.026**
Postoperative NLR	7.8	3.53 – 17.3	**0.001**
Delta NLR	2.28	1.03 – 5.03	**0.041**
BMI > 27	2.94	1.47 – 5.92	**0.002**
Previous cesarean > 1	3.88	1.56 – 9.66	**0.004**
Smoking	2.17	0.69 – 6.79	0.181
Gestational Diabetes	1.59	0.58 – 4.38	0.367
Emergent Cesarean Delivery	0.87	0.28 - 2.74	0.816
Operative time > 50 minutes	0.34	0.16 – 0.72	**0.005**
Operative time < 30 minutes	3.91	1.25 – 12.2	**0.019**

DISCUSSION

In this retrospective study, 110 patients who developed wound infection after cesarean section were compared with the control group. Specifically, postoperative NLR score, number of previous cesarean sections, and duration of surgery were found to be effective risk factors for wound infection.
There are several methods to define surgical site infection based on objective criteria.[14] There are many risk factors including presence of infection, advanced age, smoking and immobilization.[15] Biomarkers available for the diagnosis of sepsis or infection include white blood cell (WBC) count, lactic acid, procalcitonin, and C-reactive protein (CRP).[16] A "left shift" results from the release of immature neutrophils into the circulation during infection and an increase in the ratio of immature to total granulocytes.[17] However, it is difficult to accurately measure immature granulocytes, and their diagnostic value is controversial.[18]
Previous studies have shown that there is an association between DNI and morbidity and mortality, particularly in non-surgical sepsis patients.[19,20] It has been highlighted that DNI levels at day 3 were found to be particularly significant in studies that did not include obstetric procedures and measured each day before and after surgery.[21] Some studies have investigated whether DNI levels during hospitalization can be used for prediction. For example, one study reported that the optimal DNI threshold for predicting mortality in patients with gram negative bacteremia was 7.6%.22 Park et al. reported that a DNI value above 6.5% was a good indicator of severe sepsis and septic shock.[23] Lee et al. reported that a DNI value of 2% 72 hours after the onset of neonatal sepsis was associated with 7-day mortality. In our study, the effect of DNI levels in blood samples from pregnant patients before and after cesarean section on wound infections was investigated and no conclusive results were obtained.
NLR is a proinflammatory marker and has been shown to be a reliable marker of systemic inflammation.[12] It is controversial whether NLR is a predictive parameter for infections associated with abdominal surgery. On the other hand, a study examining complete blood count parameters in wound infections after cesarean section found that NLR and PLR were independently associated with infection control after CS.[25] It is well known that prolonged hospitalization is required as a result of these infections, which may affect the bond between mother and child. The use of antibiotics results in increased costs. For these reasons, it is important to be prepared for these infections and take appropriate precautions. Known risk factors for infections after CS include maternal age, obesity, diabetes mellitus, fewer prenatal care visits, chorioamnionitis, repetitive cesarean section, emergency cesarean section, operation time longer than 60 minutes, clamp closure, and high blood loss.26 Similar to the literature, NLR values before and after cesarean section were found to have predictive value for wound infection in our study. In addition, high body mass index, increased number of previous cesarean sections, and duration of operation time were found to be effective. In addition, the center where this study was conducted is a branch hospital where the same routine procedures are used

for every cesarean section, the same suture materials are used, and the same procedures are performed regardless of the individual. Review of patient records confirmed that no blood transfusion was performed and that no additional complications appeared in the operative reports. We found that shortened surgical time independently increased the risk of wound infection after CS. This could be due to the emergency CS in which the aseptic technique cannot be followed because of the rapid delivery of the baby.

The small sample size and retrospective design are the main limitations of our study. In addition, the sample size had to be kept smaller in this study because we had to take the values before the pandemic Covid-19 and it was not known whether the pandemic would affect the complete blood count parameters. Now that the impact of the pandemic is diminishing, it is appropriate to conduct prospective studies on this topic.

CONCLUSION

We have shown that NLR levels during cesarean section can predict the development of infections after cesarean section. This is the first study in which DNI and NLR values were evaluated together in wound infections after cesarean section. Further studies are needed in this regard.

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Disclosures

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Authorship Contributions: Conception and design of the study: MCI, CI
Acquisition of data: MCI, SYE, ESC, HNO
Analysis and/or interpretation of data: MCI, CP, YEU, CI
Drafting the manuscript: MCI, ESC, HNO, CI

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