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Research Article

The diagnostic value of systemic inflammation indices in pregnant women with acute appendicitis and their relationship with the duration of hospital stay

Gebe kadınlarda akut apandisitli hastalarda sistemik inflamasyon indekslerinin tanısal değeri ve hastanede kalış süresi ile korelasyonu

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ABSTRACT

Aim: Physiological and anatomical changes occurring during pregnancy can complicate the diagnosis of acute appendicitis (AA). This study aimed to evaluate the diagnostic performance of systemic inflammation indices in distinguishing AA in pregnant women and to assess their relationship with hospital stay duration.

Material and Methods: This retrospective study encompassed 32 pregnant patients who underwent appendectomy and 32 healthy pregnant (control group). Systemic inflammation indices were calculated based on neutrophil (N), platelet (P), and lymphocyte (L) levels as follows: The neutrophil-to-lymphocyte ratio (NLR) = N/L; the platelet-to-lymphocyte ratio (PLR) = P/L; systemic immune-inflammation index (SII) = (N×P)/L.

Results: The AA group had higher median levels of PLR (30.9 vs. 22.4, $p = 0.035$), NLR (6.1 vs. 3.5, $p < 0.001$), and SII (1370 vs. 807, $p < 0.001$) compared to the control group. Systemic inflammation indices showed a positive correlation with the Alvarado score and the length of hospital stay. SII values demonstrated superior diagnostic performance in predicting AA compared to NLR and PLR values. The threshold value for SII in predicting AA was identified as >1316, with a sensitivity of 85.8% and a specificity of 72.5%.

Conclusions: Systemic inflammation indices, particularly SII, demonstrate strong diagnostic value in distinguishing AA in pregnant women. SII demonstrated superior accuracy over NLR and PLR, correlating with both the Alvarado score and hospital stay, suggesting its utility as a diagnostic and prognostic marker.

Keywords: acute appendicitis, Alvarado score, pregnancy, systemic inflammation indices, systemic immune-inflammation index

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ÖZ

Amaç: Gebelik sırasında meydana gelen fizyolojik ve anatomik değişiklikler, akut apandisit (AA) tanısını zorlaştırabilir. Bu çalışmada gebe kadınlarda AA'yı ayırt etmede sistemik inflamasyon indekslerinin tanısal performansının değerlendirilmesi ve hastanede kalış süresi ile ilişkisinin değerlendirilmesi amaçlandı.

Gereç ve Yöntemler: Bu retrospektif çalışma, apendektomi uygulanan 32 gebe hasta ile 32 sağlıklı gebe (kontrol grubu) üzerinde gerçekleştirilmiştir. Sistemik inflamasyon indeksleri, nötrofil (N), trombosit (P) ve lenfosit (L) düzeylerine göre şu şekilde hesaplanmıştır: nötrofil-lenfosit oranı (NLR) = N/L; trombosit-lenfosit oranı (PLR) = P/L; sistemik immün-inflamasyon indeksi (SII) = (N×P)/L.

Bulgular: AA grubunda kontrol grubuna kıyasla PLR (30.9 vs. 22.4, p = 0.035), NLR (6.1 vs. 3.5, p < 0.001) ve SII (1370 vs. 807, p < 0.001) değerleri daha yüksek bulunmuştur. Sistemik inflamasyon indeksleri, Alvarado skoru ve hastanede kalış süresi ile pozitif korelasyon göstermiştir. SII, NLR ve PLR'ye göre AA'yı öngörmede daha yüksek tanısal performans sergilemiştir. AA'yı öngörmede SII için eşik değer >1316 olup, duyarlılık %85.8 ve özgüllük %72.5 olarak belirlenmiştir.

Sonuç: Sistemik inflamasyon indeksleri, özellikle SII, gebelerde AA'yı ayırt etmede güçlü tanısal bir değere sahiptir. SII'nin hem Alvarado skoru hem de hastanede kalış süresi ile korelasyon göstererek NLR ve PLR'ye göre üstün doğruluk gösterdiği ve tanı ve prognoz belirteci olarak yararlı olduğunu düşündürmektedir.

Anahtar Kelimeler: akut apandisit, Alvarado skoru, gebelik, sistemik inflamasyon indeksleri, sistemik immün-inflamasyon indeksi.

Introduction

Acute appendicitis (AA), often the primary surgical emergency in patients admitting to the emergency department with abdominal pain, also serves as the leading reason for non-obstetric surgeries during pregnancy. The reported incidence stands at 1 in 500 to 2000 pregnancies [1]. The diagnosis of AA becomes especially challenging during pregnancy due to the common occurrence of abdominal discomfort and gastrointestinal issues, alongside anatomical shifts owing to the enlarged uterus, and the typical leukocytosis seen in this period [2]. During pregnancy, the immediate diagnosis and treatment of AA are critically important due to its potential life-threatening complications for both the maternal and the fetus [3].

The diagnosis of AA necessitates integrating clinical assessments, laboratory findings, and radiological evaluations [4]. Recently, several studies involving pregnant women have demonstrated that inflammatory markers exhibit significant diagnostic capabilities in distinguishing patients with AA [5-7]. On the other hand, in pregnancy, physiological leukocytosis frequently occurs and is particularly linked with elevated neutrophil counts during the third trimester [8]. It has also been reported that in healthy pregnant women, there is an increase in inflammatory markers such as leukocytes and C-reactive protein (CRP) [3, 9]. This could also affect the diagnostic performance of inflammatory markers in pregnant women with AA. Additionally, conflicting results have been reported regarding the diagnostic role of comprehensive systemic inflammation indices in distinguishing these patients [5, 10-17].

We hypothesized that in pregnant women with AA, comprehensive new inflammation indices derived from different leukocyte parameters, such as the systemic immune-inflammation index (SII), as well as the neutrophil-to-lymphocyte ratio and the platelet-to-lymphocyte ratio, could be higher compared to healthy pregnant women. Therefore, this study aimed to investigate the diagnostic performance of systemic inflammation indices in distinguishing pregnant women with AA, as well as their correlation with the duration of hospital stay.

Material and Methods

This retrospective study was conducted on pregnant women between June 2018 and December 2023 in the Kutahya Health Sciences University General Surgery Clinic. All processes adhered to ethical guidelines and the principles outlined in the Declaration of Helsinki, as revised in Brazil in 2013. The study protocol received approval from the Kutahya Health Sciences University Faculty of Medicine Ethics Committee (Date: 05.03.2024 - No: 2024/03-21). Due to the retrospective design of the study, the local ethics committee waived the necessity for informed consent.

Previous studies have reported that the neutrophil-lymphocyte ratio (NLR) level in pregnant women with AA is approximately twice as high compared to healthy pregnant women (range of NLR for pregnant women with AA: 6.0-12.0; range of NLR for healthy pregnant women: 3.5-4.0) [10-15]. Accordingly, considering the mean NLR level to be 7.6±6.0 in pregnant women with AA and 3.8±3.0 in healthy pregnant women, it was determined that at least 31 patients are required for each group with a 5% margin of error and 90% power.

Study population

During the study period, a total of 176 pregnant women who were admitted to the emergency department due to abdominal pain were retrospectively evaluated. Patients with diabetes mellitus, hypertension, myocardial disorders, cancer or autoimmune diseases, hematological disorders, liver disease, kidney disease, chronic pulmonary diseases, infectious diseases, tobacco or alcohol use, prior antibiotic use, and those who underwent laparoscopic appendectomy, as well as those with incomplete records, were excluded from the study. After applying the exclusion criteria, the study included 32 pregnant women who were diagnosed with AA and received surgery, along with 32 patients identified as not having AA and who were not subjected to surgical intervention (control group). The control group was matched by age and gestational age to ensure comparability, enhancing the reliability of the study results.

Study protocol

Cases with suspected AA based on clinical findings underwent evaluation by ultrasound or magnetic resonance imaging (MRI) [18]. In cases of AA diagnosis, the appendectomy procedure was carried out using an open approach via a McBurney incision. Histopathological examinations confirmed the AA diagnosis. Patient electronic records were utilized to gather demographic and clinical information, including age, body mass index (BMI), gravida, parity, week of gestation, examinations findings, blood samples, and the duration of hospital stay.

The indices for inflammation were determined in the following manner: The platelet-to-lymphocyte ratio (PLR) = platelet count / lymphocyte count ratio; the NLR = neutrophil count / lymphocyte count; and SII = (platelet count × neutrophil count) / lymphocyte count [19, 20].

Statistical analysis

All analyses were conducted using IBM SPSS Statistics for Windows 20.0 (IBM Corp., Armonk, NY, USA) and Medcalc 11.4.2 (MedCalc Software, Mariakerke, Belgium) software. Categorical data were represented in terms of frequency and percentage. Group-wise comparisons were made utilizing the Chi-square test (with post-hoc cell-wise analysis) and the Fisher's Exact test. The normal distribution of numerical variables was assessed using the Kolmogorov-Smirnov test. Data exhibiting a normal distribution were presented as mean ± standard deviation, and comparisons between groups were made using the Student's T-test. Non-normally distributed data were displayed as median (interquartile range (IQR): 25-75 percentiles) and comparisons between groups were conducted using the Mann-Whitney U test. Stepwise multivariable logistic regression analysis was used to evaluate independent predictors of the AA. The evaluation of diagnostic performance was conducted through ROC analysis, and the cut-off values were determined using the Youden index method. Value of $p < 0.05$ were considered statistically significant.

Results

The study included 32 pregnant women with AA (mean age 27.2 ± 6.2 years) and a control group (mean age 26.9 ± 5.3 years). There were no significant demographic differences between the two groups. The mean leukocyte level (14.0 ± 4.7 vs. 10.0 ± 2.0 $x10^3$/µL; $p < 0.001$) and mean neutrophil level (11.3 ± 4.5 vs. 6.5 ± 1.4 $x10^3$/µL, $p < 0.001$) were higher in the AA group, while the median lymphocyte level was lower (1.4 vs. 1.8 $x10^3$/µL; $p < 0.001$). The AA group had higher median levels of PLR (30.9 vs. 22.4, $p = 0.035$), NLR (6.1 vs. 3.5, $p < 0.001$), and SII (1370 vs. 807, $p < 0.001$) compared to the control group (Table 1).

There was a positive correlation between the Alvarado score and PLR ($r = 0.291$, $p = 0.042$), NLR ($r = 0.326$, $p = 0.009$), and SII ($r = 0.397$, $p < 0.001$). Similarly, a positive correlation was observed between the length of hospital stay and PLR ($r = 0.295$, $p = 0.040$), NLR ($r = 0.315$, $p = 0.012$), and SII ($r = 0.374$, $p < 0.001$) (Table 2).

ROC Curve analysis, the SII demonstrated 85.8% sensitivity and 72.5% specificity for acute appendicitis diagnosis when a threshold of > 1316 was applied. SII values demonstrated superior diagnostic performance in predicting AA compared to NLR and PLR values (Table 3).

Table 1. Demographic and clinical findings

Variables	Acute Appendicitis n = 32	Control group n = 32	P-value
Age, years	27.2 ± 6.2	26.9 ± 5.3	0.658
Gravida	2 (1-3)	2 (1-3)	0.413
Parity	1 (0-2)	1.0 (0 -1)	0.322
Abortion	0	0	-
Trimester (%)			
First	14 (43.8)	15 (46.9)	0.864
Second	15 (46.9)	13 (40.6)	
Third	3 (9.4)	4 (12.5)	
Alvarado score	7 (6-9)	-	-
Laboratory findings			
Leukocytes, x103/µL	14.0 ± 4.7	10.0 ± 2.0	<0.001*
Lymphocytes, x103/µL	1.4 (1.3-2.3)	1.8 (1.6-2.1)	<0.001*
Neutrophils, x103/µL	11.3 ± 4.5	6.5 ± 1.4	<0.001*
Platelets, x103/µL	247.0 ± 56.6	233.4 ± 64.4	0.307
PLR	30.9 (20.7-40.1)	22.4 (17.6-35.0)	0.035*
NLR	6.1 (3.5-9.9)	3.5 (3.0-4.2)	<0.001*
SII	1370 (852-2251)	807 (639-953)	<0.001*
Hospital stay, day	3 (2-4)	-	-

Data are shown as mean ± SD or median (IQR) or number and percentage (%). *p<0.05 indicates statistical significance. Abbreviations: NLR, neutrophil to lymphocyte ratio; PLR, platelets to lymphocyte ratio; SII, systemic immune inflammation index.

Table 2. Parameters associated with Alvarado score and hospital stay.

Variables	Alvarado score		Hospital stay	
	r	p	r	p
Age	0.092	0.617	0.009	0.959
Trimester	-0.080	0.662	-0.001	0.996
Leukocytes	0.319	<0.001*	0.305	<0.001*
Lymphocytes	-0.314	<0.001*	-0.306	0.005*
Neutrophils	0.314	<0.001*	0.298	0.018*
Platelets	0.318	<0.001*	0.292	0.027*
PLR	0.321	<0.001*	0.305	<0.001*
NLR	0.336	<0.001*	0.315	<0.001*
SII	0.397	<0.001*	0.374	<0.001*
Hospital stay	0,337	<0,001*	-	-

*p<0.05 indicates statistical significance. Abbreviations: NLR, neutrophil to lymphocyte ratio; PLR, platelets to lymphocyte ratio; SII, systemic immune inflammation index.

Table 3. ROC analysis was performed to assess the predictive accuracy of preoperative laboratory findings in diagnosing appendicitis.

Results	PLR	NLR	SII
AUC ± SE	0.60 ± 0.05	0.75 ± 0.08	0.81 ± 0.04
Threshold value	> 150.5	> 4.8	> 1316
Sensitivity, %	61.7	74.6	85.8
Specificity, %	59.2	70.2	72.5

Abbreviations: AUC, area under the curve, NLR, neutrophil to lymphocyte ratio; PLR, platelets to lymphocyte ratio; SE, standart error; SII, systemic immune inflammation index.

Discussion

This study investigates the diagnostic utility of systemic inflammation indices, specifically NLR, PLR, and SII, in pregnant women with AA. The findings confirm that these hematologic markers, especially SII, exhibit strong correlations with clinical outcomes, such as hospital stay duration and disease severity. The results not only support their diagnostic value but also suggest that they may serve as valuable, accessible tools in settings where traditional imaging methods are either unavailable or present risks to the fetus [21]. Given the limitations of radiological diagnostics in pregnancy, these biomarkers offer an alternative or supplementary approach to enhance the diagnostic accuracy of AA, a condition where delayed treatment can have serious maternal and fetal consequences.

Various scoring systems have been developed to support the early diagnosis of acute appendicitis, typically relying on physical examination, laboratory results, and imaging. While these methods are simple and cost-effective, there is no scoring system specifically designed for pregnant women. Most studies focus on non-pregnant patients, with the Alvarado score being the most widely used. In pregnancy, its sensitivity and specificity have been reported to range between 69-86% and 61-77%, respectively [22, 23]. Pregnancy-related symptoms like nausea and abdominal pain can complicate diagnosis, requiring additional imaging, such as ultrasonography and MRI. Ultrasound is favoured for its accessibility and safety but is less reliable in later pregnancy stages [24, 25]. Weight gain related to pregnancy, differences in the anatomical location of the appendix, air in the intestinal loops, and operator experience affect the diagnostic accuracy of ultrasonography [26]. MRI, though more expensive and less accessible, offers higher diagnostic accuracy, with studies showing sensitivity and specificity rates of 91.8% and 97.9% [27]. Therefore, there is a need for easily accessible and inexpensive indicators that can predict AA in pregnant women.

Studies have examined the use of inflammatory markers in diagnosing inflammatory conditions in pregnant women with AA [5, 10-17]. In our study, NLR and PLR were significantly elevated in the AA group compared to controls, reflecting the heightened systemic inflammatory response associated with AA. These findings are consistent with the study of Çınar et al. and Güler et al., who both reported similar elevations in these markers among pregnant AA patients [10, 14]. The pathophysiological mechanism underlying this is likely due to the sharp increase in neutrophils in response to infection and tissue damage, alongside a relative decrease in lymphocyte counts, which contributes to the rise in these ratios. Importantly, the diagnostic utility of NLR and PLR in pregnant women is critical because these indices can help distinguish between normal pregnancy-related changes, such as physiological leukocytosis, and more severe inflammatory states like AA [21]. Yazar et al. conducted a retrospective analysis of 78 pregnant women suspected of having AA [11]. The study found that those with pathologically confirmed appendicitis exhibited significantly higher levels of CRP, white blood cell count, NLR, and PLR compared to both pregnant women without appendicitis and healthy control groups, including non-pregnant individuals. These markers were notably elevated in the appendicitis group, highlighting their potential diagnostic utility in distinguishing between healthy pregnancies and those complicated by appendicitis. The authors reported that the combination of WBC count, NLR, PLR, CRP levels, and lymphocyte count demonstrated 90% accuracy in predicting the diagnosis of AA [11].

The findings related to SII in this study are particularly noteworthy. SII, which integrates neutrophil, platelet, and lymphocyte counts into a single marker, was found to be superior to both NLR and PLR in predicting AA, with an AUC of 85.8% at a threshold of 1316. This result is in line with recent literature emphasizing SII's ability to provide a more comprehensive measure of the systemic inflammatory response. Telaferli et al. have demonstrated the utility of SII in complex inflammatory and infectious conditions, where it often surpasses traditional markers in sensitivity and specificity [17]. A study led by Güler et al. reported that SII levels demonstrated a lower accuracy rate in predicting acute appendicitis in pregnant women, compared to leukocyte and neutrophil levels [14]. The difference between the studies may be due to the inclusion criteria of the patients. The significantly higher SII levels observed in our AA group suggest that this index could serve as a powerful tool for early identification of AA in pregnant women, a population where timely diagnosis is often hampered by overlapping clinical symptoms with pregnancy, such as nausea, vomiting, and abdominal discomfort. Also, SII combines neutrophil, platelet, and lymphocyte counts into a single marker, providing a more comprehensive reflection of the systemic inflammatory response. This integration may explain its superior diagnostic and prognostic performance compared to NLR and PLR, which assess fewer components of the inflammatory response.

A another finding of our study is the positive correlation between SII and the Alvarado score, which underscores the potential benefit of combining systemic inflammatory indices with established clinical scoring systems. The Alvarado score is widely used in diagnosing AA, but its application in pregnancy has been less validated, as pregnancy-related physiological changes can obscure some of its clinical components, such as rebound tenderness or leukocytosis [28, 29]. By integrating SII

into the diagnostic process, clinicians may be able to refine the Alvarado score's predictive power, particularly in ambiguous cases where imaging is not conclusive. Furthermore, the significant correlation between SII and hospital stay duration reinforces the utility of this marker not only as a diagnostic tool but also as a prognostic indicator. Patients with higher SII values may be more prone to prolonged recovery times, which could guide decisions regarding postoperative monitoring and care. Studies suggest that higher SII values are associated with more severe cases of appendicitis, including complicated cases, and these values can help differentiate between uncomplicated and complicated appendicitis in pregnant patients [30]. In cases where appendicitis is complicated, pregnant women tend to have longer hospital stays, driven by the need for more intensive management, including possible surgical interventions like appendectomy [1, 30].

This study has several limitations. First, the relatively small sample size may limit the generalizability of the results. Larger, multicentre studies would be required to confirm the diagnostic thresholds and improve the robustness of the findings. Second, while systemic inflammation indices such as NLR, PLR, and SII are useful markers of inflammation, they are not specific to AA. These indices can also be elevated in other inflammatory conditions, such as urinary tract infections or cholecystitis, which are common in pregnancy [31]. Additionally, the retrospective nature of the study introduces potential biases, particularly in the collection and interpretation of clinical data. Moreover, the study did not account for the distinction between complicated and uncomplicated appendicitis, which may influence both clinical management and outcomes. Future prospective studies could help to minimize these biases and better control for confounding factors.

Conclusion

This study demonstrates that systemic inflammation indices, particularly SII, offer strong diagnostic value for acute appendicitis in pregnant women. The significant correlations between SII and both the Alvarado score and hospital stay duration highlight its potential as both a diagnostic and prognostic tool. In the context of pregnancy, where traditional imaging methods may pose risks or be less effective, incorporating systemic inflammation markers into clinical practice could improve the early detection and management of AA, ultimately leading to better maternal and fetal outcomes. Further research, particularly large-scale prospective studies, is needed to validate these findings and establish standardized diagnostic protocols for the use of systemic inflammation indices in pregnancy.

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Conflicts of Interest

The authors declare they have no conflicts of interest.

Ethics Approval

The study was approved by the Kutahya Health Sciences University Faculty of Medicine Ethics Committee (Date: 05.03.2024 - No: 2024/03-21).

Availability of Data and Material

The data that support the findings of this study are available on request from the corresponding author.

Authors' contribution

Concept – B.I.C., Design- B.I.C. and M.A.T.; Supervision - BIC; Data collection and/or processing – B.I.C. and M.A.T., Analysis and/or interpretation - B.I.C. and M.A.T. Writing – BIC; Critical review- MAT. All authors read and approved the final version of the manuscript.

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