



# Neutrophil/Lymphocyte Ratio in Acute Appendicitis: A State Hospital Experience

## Akut Apandisitte Nötrofil/Lenfosit Oranı: Bir Devlet Hastanesi Deneyimi

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### ABSTRACT

**Aim:** The aim of this study was to assert the diagnostic value of neutrophil/lymphocyte ratio (NLR) in cases diagnosed as acute appendicitis.

**Method:** The data of 112 patients diagnosed with acute appendicitis who were operated on by the same surgical team between January 2014 and December 2014 were retrospectively reviewed. Acute appendicitis patients included in the study were divided into two groups as uncomplicated (group 1) and complicated appendicitis (group 2) based on histopathology results. Group 3 consisted of healthy control subjects (n=50) who applied to the general surgery clinic.

**Results:** There were 71 patients in group 1, 34 patients in group 2 and 50 patients in the control group (group 3). There were no significant differences between groups in terms of age or gender. Significant differences emerged in leukocyte and NLR. There was a significant difference between group 1 and group 2 in terms of radiological appendix diameter and contamination around the appendix and fluid accumulation (p=0.001). However, a significant difference was not detected between NLR increase and contamination around the appendix, fluid accumulation, or appendix diameter.

**Conclusion:** We think that NLR, which can be taken from whole blood count in the diagnosis of acute appendicitis, is a parameter that can be easily used because of its low cost and easy accessibility.

**Keywords:** Appendicitis, complicated appendicitis, lymphocyte, neutrophil

### ÖZ

**Amaç:** Bu çalışmada akut apandisit tanısı alan olgularda nötrofil/lenfosit oranının (NLO) tanısal değerini ortaya koymayı amaçladık.

**Yöntem:** Ocak 2014-Aralık 2014 yılları arasında kliniğimizde aynı cerrahi ekip tarafından opere edilen akut apandisit tanılı 112 hastanın verileri geriye yönelik incelendi. Çalışmaya dahil edilen akut apandisit hastaları histopatoloji sonuçları esas alınarak komplike olmayan (grup 1) ve komplike apandisit (grup 2) olmak üzere iki gruba ayrıldı. Grup 3'ü ise genel cerrahi polikliniğine başvuran sağlıklı bireyler (n=50) kontrol grubunu oluşturdu.

**Bulgular:** Grup 1'de 71 hasta, grup 2'de 34 ve kontrol grubunda (grup 3) ise 50 hasta bulunmakta idi. Gruplar arasında yaş ve cinsiyet açısından anlamlı farklılık saptanmadı. Lökosit ve NLO'ya bakıldığında ise anlamlı farklılık mevcuttu. Grup 1 ve grup 2 arasında radyolojik apendiks çapı ve çevresel kirlenme açısından anlamlı farklılık izlendi (p=0,001). Ancak NLO'nun artışı ile apendiks çevresinde kirlenme, sıvı birikimi ve apendiks çapı arasında anlamlı fark saptanmadı.

**Sonuç:** Akut apandisit tanısında tam kan sayımından bakılabilen NLO, gerek düşük maliyetli gerekse de kolay ulaşılabilir olması nedeniyle rahatlıkla kullanılabilir parametre olduğunu düşünmekteyiz.

**Anahtar Kelimeler:** Apandisit, komplike apandisit, lenfosit, nötrofil

## Introduction

Acute appendicitis is one of the most common emergency conditions encountered in general surgery clinics.<sup>1</sup> Despite advances in medical technology and growing experience, acute appendicitis is still diagnosed based on clinical findings.

A detailed history and thorough physical examination are the first step in the evaluation of acute appendicitis patients.<sup>2</sup>

Most patients present with pain starting from the epigastric region and localizing to the lower right quadrant, nausea, vomiting and loss of appetite, though atypical presentations are also common. Delayed diagnosis increases rates of



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perforation and subsequent morbidity, while early surgical decisions to avoid complications increase the negative appendectomy rate.<sup>3</sup> The considerably high rates of perforation (15-45%) and negative appendectomy (7-25%) reported in the literature show that despite technological advances and clinical experience, we have yet to establish a foolproof diagnostic approach.<sup>2</sup>

The use of various diagnostic tools may reduce perforation rates, duration of hospital stays, and unnecessary surgeries in patients without acute appendicitis. These diagnostic tests include scoring systems, ultrasonography (USG), computed tomography (CT), magnetic resonance imaging and laparoscopy.<sup>4</sup>

Despite these options, this area remains the subject of intense study for many researchers hoping to develop a more effective diagnostic procedure for acute appendicitis. Their studies have primarily focused on laboratory tests and imaging modalities. To further this aim, in the current study we evaluated the role of the neutrophil-to-lymphocyte ratio (NLR)-a less investigated parameter-in the diagnosis of acute appendicitis, its association with radiologic diameter, and whether it can be used to differentiate complicated appendicitis.

## Materials and Methods

The medical records of 112 patients over 18 years old who were operated for presumed appendicitis by the same surgical team in our clinic between January 2014 and December 2014 were analyzed retrospectively. After surgery, the appendix tissue obtained was classified pathologically as normal or acute appendicitis. Gangrenous and perforated appendices were further separated into a complicated appendicitis group.

In 7 cases, the appendix was determined normal intraoperatively and appendectomy was performed. The pathology results confirmed normal appendix and these patients were excluded from the study.

The remaining acute appendicitis patients were divided based on histopathologic reports into an uncomplicated appendicitis group (group 1) and a complicated appendicitis group (group 2). Group 3 consisted of healthy individuals presenting to the general surgery clinic (n=50). None of the control subjects had malignancy or recent history of local/systemic inflammation. The controls were age- and gender-matched to the patient groups.

Demographic data such as age and gender, preoperative radiologic appendix diameter, presence of periappendiceal contamination/fluid, operative diagnoses and pathologic results were recorded for all patients.

Patients' leukocyte, neutrophil and lymphocyte counts were determined from values obtained from peripheral venous blood samples. The NLR was calculated by dividing the neutrophil count by the lymphocyte count.

Preoperative appendix diameter determined by USG and CT was measured in millimeters and recorded. The appendix was determined radiologically normal in 6 of the operated patients and could not be evaluated in 6 other patients. NLR and radiologic diameter measurements obtained from these 12 patients were excluded in the statistical analysis.

## Statistical Analysis

The Statistical Package for the Social Sciences (SPSS version 21.0, SPSS Inc., Chicago, IL, USA) software was used for biostatistical analyses. Data obtained from the study subjects was expressed as mean and standard deviation, and percentages when appropriate. Data distributions were evaluated for normality using Kolmogorov-Smirnov test. For normally distributed data, ANOVA was used for multiple group comparisons and Student's t-test was used for two-group comparisons. Relationships between statistically significant results were determined using post hoc Tukey test. Categorical variables were compared using chi-square test. Results were evaluated within a 95% confidence interval and level of significance was accepted as  $p < 0.05$ .

## Results

Of the 112 patients, 98 (87.5%) underwent surgery for presumed appendicitis and 14 (12.5%) for acute abdomen. After excluding 7 patients whose pathology report indicated normal appendix, the study included 105 patients. There were 71 patients in group 1, 34 patients in group 2, and 50 subjects in the control group (group 3).

There were no significant differences in age or gender distribution between the groups. Significant differences were observed in leukocyte counts and NLR. Post hoc Tukey test of significance revealed that there were significant differences in leukocyte count between the 3 groups, while the difference in NLR was not significant between groups 1 and 2 but was significant in all other group comparisons (Table 1).

Appendectomy was performed using open (McBurney) technique in 93 patients (88.5%), laparoscopic in 10 patients (9.5%) and umbilical minilaparotomy in 2 patients (1.9%). No significant differences emerged between the groups in terms of surgical method. The relatively low rate of laparoscopic appendectomy (9.5%) is due to the fact that the laparoscopy instruments in our hospital are not always functional. The laparotomic approach was used in cases where findings of acute abdomen and generalized peritonitis led to suspicion of complicated appendicitis.

Including the patients with normal appendix excluded from the study, the rate of complicated appendicitis was 32.9%. We believe this rate is high because people in the region have difficulty reaching the hospital. The rate of negative appendectomy in our study was 6.25%, consistent with the literature.

Although 56 of the 112 patients in our study exhibited contamination or fluid around the cecum and appendix on USG or CT, no contamination or fluid was reported for the other 56. There were significant differences between the groups in radiologic appendix diameter and periappendiceal contamination ( $p=0.001$ ). However, elevated NLR was not correlated with periappendiceal contamination or fluid. There was also no correlation between NLR elevation and appendix diameter ( $p>0.05$ ). Comparison of the appendectomy groups is summarized in Table 2.

## Discussion

Acute appendicitis is the most common cause of acute abdomen among all age groups. The timely and accurate diagnosis of patients presenting to emergency departments with presumed acute appendicitis continues to be a challenge. The patient's reported medical history and a physical examination are the foundation of diagnosis.<sup>5</sup> As a rule, when investigating the etiology of sudden abdominal pain in a previously healthy individual, appendicitis is the first condition that must be excluded.<sup>6</sup>

The principle symptom of acute appendicitis is abdominal pain. Classically, it starts as obtuse, moderate periumbilical pain arising from the activation of visceral afferent neurons, then generally localizes to the right lower quadrant (parietal pain) within 4 to 6 hours. This localizing pain is the most reliable diagnostic sign of appendicitis.<sup>1,7</sup>

Anorexia is the first and most constant symptom of appendicitis. If anorexia is absent, the diagnosis of appendicitis should be reconsidered. The order in which symptoms appear is important in the differential diagnosis. Anorexia is the first symptom in 95% of acute appendicitis patients, followed by abdominal pain and nausea/vomiting. If vomiting occurs before abdominal pain, this is also grounds for questioning an appendicitis diagnosis.<sup>8</sup>

Rebound in the right lower quadrant is one of the cardinal signs, and may be sufficient on its own for a diagnosis, especially in male patients.

White cell count is elevated in cases of acute, uncomplicated appendicitis. Leukocyte count ranges from 10.000-18.000/ $\text{mm}^3$  and the neutrophil ratio is greater than 75%. In about 10% of patients, leukocyte count may be normal. A white cell count over 20.000/ $\text{mm}^3$  suggests gangrenous, perforated appendicitis.<sup>9</sup>

USG is another method that can be used to facilitate diagnosis. The rate of accurate diagnosis by USG is 71-97%. An anterior-posterior appendix diameter greater than 6 mm is considered indicative of appendicitis. Diagnosis can also be based on a USG finding of appendicolith.<sup>4,10</sup> With CT, the

Table 1. Demographic data and laboratory values of the patient groups

Variable		Group 1 (n=71)	Group 2 (n=34)	Group 3 (n=50)	p value
Gender	Male	38 (53.5%)	18 (52.9%)	25 (50%)	0.926
	Female	33 (46.5%)	16 (47.1%)	25 (50%)	
Age (years)		31±13	31±11	27±10	0.234
Leukocyte count (per $\text{mm}^3$ )		11755±3227	13532±3791	7622±1864	0.01 <sup>a</sup>
Neutrophil/lymphocyte ratio		4.8±3.6	6.5±5.2	2.2±0.6	0.01 <sup>b</sup>

Post hoc Tukey test;

<sup>a</sup>Significant differences between all 3 groups

<sup>b</sup>Nonsignificant difference between group 1 and 2

Table 2. Comparison of the appendectomy groups

		Group 1 (n=71)	Group 2 (n=34)	p value
Surgical method	McBurney	62 (66.7%)	31 (91.2%)	0.600
	Laparoscopic	8 (11.3%)	2 (5.9%)	
	Median incision	1 (1.4%)	1 (2.9%)	
Radiologic contamination/fluid	(+)	27 (38%)	8 (23.5%)	0.001
	(-)	44 (62%)	26 (76.5%)	
Radiologic appendix diameter (mm)		8.35±1.9	10.1±2.1	0.001

rate of accurate acute appendicitis diagnosis in patients with abdominal pain is around 95%. CT can also reveal increased appendix diameter (>6 mm) due to distention, circular wall thickening and inflammation of periappendiceal fatty tissue.<sup>1,7</sup> Delayed diagnosis of patients presenting to emergency departments with abdominal pain results in increased morbidity and mortality. On the other hand, early surgical decisions lead to negative laparotomies. For this reason, various scales have been developed and several biomarkers are being investigated to aid in the diagnosis of acute appendicitis, which is the most common emergent pathology encountered in general surgery. Studies on how to reduce rates of negative appendectomy are ongoing. Whole blood count is a test that can be easily performed in all emergency departments. Several studies have examined the utility of NLR in reducing the negative appendectomy rate.

In a study including 75.000 patients, the negative appendectomy rate was 6% for males and 13.4% for females.<sup>9</sup> This rate varies from 4.7% to 17.2% in published studies from Turkey.<sup>3,11,12,13</sup> In the present study, the negative appendectomy rate was 6.3%, which is consistent with other series from Turkey.

Among whole blood markers, NLR has begun to receive more scrutiny recently, and it has been stressed that NLR may be a better marker for acute appendicitis than C-reactive protein, leukocyte or neutrophil count alone.<sup>14,15</sup> Considering that the primary agent in appendicitis is bacteria, it has been predicted that neutrophil count, which has greater sensitivity in bacterial infections, and its ratio to lymphocyte count would provide more valuable information.<sup>16</sup>

In the present study, we found statistically significant differences in NLR measured from initial whole blood samples taken from acute appendicitis and perforated appendicitis patients compared to the control group.

Goodman et al.<sup>15</sup> and Kahramanca et al.<sup>17</sup> reported that upper limits of 3.5 and 4.68, respectively, were suitable for NLR in acute appendicitis.

## Conclusion

NLR, which can be calculated from whole blood counts, is a low-cost and easily accessible parameter that can be easily utilized in the diagnosis of acute appendicitis.

## Ethics

Ethics Committee Approval: This study were retrospective study, Informed Consent: This study were retrospective study.

Peer-review: Internally peer-reviewed.

## Authorship Contributions

Surgical and Medical Practices: Nedim Akgül, Ebubekir Gündeş, Concept: Nedim Akgül, Ebubekir Gündeş, Design:

Nedim Akgül, Ebubekir Gündeş, Data Collection or Processing: Nedim Akgül, Ebubekir Gündeş, Analysis or Interpretation: Ebubekir Gündeş, Literature Search: Nedim Akgül, Ebubekir Gündeş, Writing: Nedim Akgül.

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