



The Change of Neutrophil Lymphocyte Ratio in Acute Appendicitis

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Abstract

Acute appendicitis is the most common indication for emergency abdominal surgery, although it remains difficult to diagnose. Aim of this study is to investigate the supporting role of neutrophil/lymphocyte ratio in diagnosis of acute appendicitis. The medical records of 241 patients who had undergone appendectomy between June 2013 and March 2014 were investigated retrospectively. Sixty patients who had undergone at least one complete blood count during preoperative hospital admission and who had no other active inflammatory conditions at the time the sample was taken were included in the study. Neutrophil/lymphocyte ratio and leukocyte count values were determined in each patient at hospital admission and during active acute appendicitis. Age, sex, neutrophil/lymphocyte ratio and leukocyte counts were recorded for each patient. The mean age of the patients was 33.15 ± 10.94 years; male to female ratio was 1.5:1. Mean leukocyte count was significantly higher in acute appendicitis group ($13.14 \pm 2.99 \times 10^3/\text{mm}^3$) than control group ($7.42 \pm 2.12 \times 10^3/\text{mm}^3$) ($p=0.01$). The best cutoff point for leukocyte count was $10.10 \times 10^3/\text{mm}^3$, with sensitivity of 94% and a specificity of 75%. Mean neutrophil/lymphocyte ratio was significantly higher in acute appendicitis group (5.47 ± 3.24) than control group (1.99 ± 1.11) ($p=0.02$). The best cutoff point for neutrophil/lymphocyte ratio was 1.73, with sensitivity of 97% and a specificity of 87%. Area under receiver operating characteristic curve was 0.67 for leukocyte count and 0.60 for neutrophil/lymphocyte ratio. Neutrophil/lymphocyte ratio was significantly higher in acute appendicitis and can be used as a supportive diagnostic parameter in the diagnosis of acute appendicitis.

Key Words: Acute appendicitis, neutrophil/lymphocyte ratio, diagnosis.

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Introduction

Acute appendicitis (AA) remains the most common indication for emergency abdominal surgery [1]. Acute appendicitis is most common between ages of 20-40 years, and more common in males than females [2]. Lumen occlusion and subsequent inflammation plays an important role in the pathogenesis of AA [3]. Acute appendicitis is still a difficult diagnosis based on clinical and laboratory data. In adult patients, appendicitis-mimicking conditions of gastrointestinal, urologic, or gynecologic origin make the diagnosis even more difficult [1]. There is not a single laboratory marker for discriminating AA from other causes of abdominal pain [4]. Laboratory indicators that have been associated with AA include leukocytosis, left shift, elevated C-reactive protein and elevated erythrocyte sedimentation rate [5].

Blood platelets, macrophages, mast cells, leukocytes and endothelial cells are major cellular players against to stress in circulation. Physiological response of the leukocytes against to inflammation, leads to increased number of neutrophils and decreased number of lymphocytes [6,7]. Therefore, ratios of these leukocyte subgroups (neutrophil/lymphocyte ratio) could be used as an important marker of inflammation. This marker is cheap, readily accessible and can be calculated quite easily. Recently, neutrophil/lymphocyte ratio (NLR) has been shown to reflect inflammatory burden in some acute inflammatory diseases like to AA [8-11]. Whitney and colleagues found a significant variability in gene expression in terms of leukocytes among healthy blood donors [12]. Gordon et al. were determined, patients had different responses to inflammatory stimuli [13]. There are some individual differences against to inflammation between patients, therefore NLR will vary from person to person in response to inflammatory stimuli.

Inflammation plays an important role in the pathology of AA [3]. Aim of this retrospective study is to investigate the supporting role of NLR in the diagnosis of AA. In the present study, to reduce individual differences of patients against to inflammation, each patient's previous leukocyte count (LC) and NLR values, collected under non-inflammatory conditions, were compared with laboratory values from samples taken at the time of AA.

Material Method

This study was designed and conducted at Sakarya University Education and Research Hospital. We retrospectively reviewed the medical records of 243 patients who had undergone appendectomy in General Surgery Unit between June 2013 and March 2014. In this study, laboratory and clinical data were obtained from the digital medical records database of the hospital. Only two patients' pathology reports could not be obtained within this time period. These two patients were excluded from study. The remaining 241 patients had confirmed AA noted in the surgical and pathology reports.

The primary analysis in this study was the comparison of the patient NLR and LC values that at the time of AA to data collected prior to the operation. Co-morbidities, medications, pregnancy are major factors that all affect the inflammatory response and wound healing [14,15]. According to medical records, patients under the age of 18, pregnant women, had a history of chronic drug use and additional disease (like diabetes mellitus, hypertension, heart disease, vascular diseases, and cancer), and also patients had no any hospital admission before operation were excluded. So a total of 103 patients were excluded from study. Records for remaining 138 patients were examined retrospectively using the computerized medical records database of the hospital. This evaluation included all records dated within the previous 6 years. In 78 patients no blood sample data prior to onset of AA were available. These patients were excluded from study. Exclusion criteria and number of excluded patients were listed in Table 1.

Table 1. Exclusion criteria and number of excluded patients.

Exclusion Criteria	Excluded Patients (n)
• Patients under the age of 18.	2
• Pregnant women.	9
• A history of additional diseases and chronic drug use.	19
• Patients that had no any hospital admission before operation.	73
• Patients that had no blood sample, that was taken during non-inflammatory state before operation	78

According to medical records 60 patients had provided least one blood sample was taken during a previous non-inflammatory state. These patients were included in the study. Table 2

show the clinic where each patient was admitted prior to onset of AA, the diagnosis at these clinics, gender and the number of patients.

Table 2. Referenced clinics, diagnoses, gender and number of patients.

Referenced Clinic	Diagnosis	Gender and Number of Patients
Cardiology	Nonspecific Chest Pain	Male; 8, Female; 10
Blood Bank	Blood Donation	Male; 9
Internal Medicine	Dyspepsia, Constipation	Male; 6, Female; 5
PT&R	Myalgia	Male; 2, Female; 2
Psychiatry	Depression and Anxiety	Male; 1, Female; 3
Neurology	Benign Positional Vertigo	Male; 3, Female; 1
Chest Diseases	Dyspnea	Male; 2, Female; 1
Urology	Infertility and BPH	Male; 2
Otorhinolaryngology	Tinnitus and NSD	Male; 2
Obstetrics	Infertility	Female; 1
Infectious Diseases	Tick Bite	Male; 1, Female; 1

PT&R; Physical Therapy and Rehabilitation, BPH; Benign Prostatic Hypertrophy, NSD; Nasal Septum Deviation.

Previous NLR and LC values corresponding to the non-inflammatory state were determined in all 60 patients (Group 1). Leukocyte count and NLR values of same patients at the time of AA were also determined (Group 2). These values were obtained from first blood samples collected after onset of AA. Age, sex, NLR and LC values were recorded.

The leukocyte, neutrophil and lymphocyte level analyses were performed using commercially available analyzer (CELL-DYN 3700, Abbott Diagnostics, Abbott Park, IL, USA) in laboratory.

Statistical analysis; Statistical analyses were performed using the Statistical Package for Social Sciences version 16.0. (SPSS: An IBM Company, version 16.0, IBM Corporation, and Armonk, New York, USA). All data were expressed as the mean $\pm$ standard deviation (SD). The Student t-test was used to compare continuous variables between the control and the patient groups. The Pearson correlation analysis was carried out to examine the linear relationships among the variables. The cut-off values of parameters for discrimination of the groups were determined using the Receiver Operating Characteristic (ROC) curve analysis. The areas under the ROC curves (AUC) were calculated and the specificity, sensitivity and accuracy of the LC and NLR for predicting AA were calculated for various cut-off points.

Results

A total of 60 patients were included in the final study group. The mean age of the patients was 33.15 ± 10.94 years (range: 19 to 70 years); 36 patients were male and 24 patients were female. Male to female ratio was 1.5:1. Distribution of LC and NLR values were listed in Table 3.

Table 3. Leukocyte count and neutrophil/lymphocyte ratio values of patients.

	Group 1 (n=60)	Group 2 (n=60)	p
LC	$7.42 \pm 2.12 (\times 10^3/\text{mm}^3)$	$13.14 \pm 2.99 (\times 10^3/\text{mm}^3)$	P=0.01
NLR	$1.99 \pm 1.11 (\times 10^3/\text{mm}^3)$	$5.47 \pm 3.24 (\times 10^3/\text{mm}^3)$	P=0.02

LC; Leukocyte count, NLR; Neutrophil/lymphocyte ratio.

Leukocyte count was significantly higher in group 2 according to group 1 ($p=0.01$). Receiver operating characteristic curve analysis indicated that the best cut-off point for LC in the diagnosis of AA was $10.10 \times 10^3/\text{mm}^3$, which had a sensitivity of 94% and a specificity of 75%. Area under curve for LC was 0.67.

Neutrophil/lymphocyte ratio value was significantly higher in group 2 compared with the group 1 ($p=0.02$). Receiver operating characteristic curve analysis suggested that the optimal cut-off point for NLR in the diagnosis of AA was 1.73, which had a sensitivity of 97% and a specificity of 87%. Area under curve for NLR was 0.60.

Receiver operating characteristic curve for NLR and LC was shown in Figure 1.

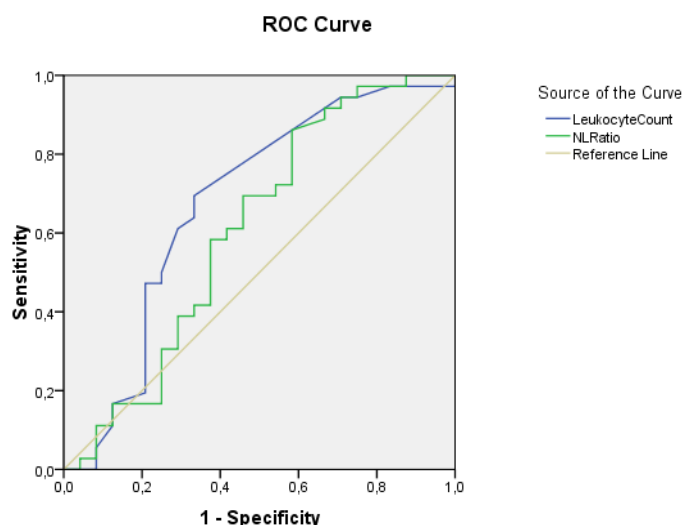


Figure 1. Receiver operating characteristic curve of neutrophil/lymphocyte ratio and leukocyte count.

Discussion

Acute appendicitis is one of the most common indication for emergency surgery. Diagnosis of this disease is quite difficult based on only examination and laboratory findings [1]. Acute appendicitis occurs in patients of all ages, although it is more common among patients 20 to 40 years old. Acute appendicitis more common in men, with a male to female ratio of 1.4:1 [2]. In our study group the mean age of patients was 33.15 ± 10.94 years (19-70) and the male to female ratio was 1.5:1, findings that are consistent with the current literature.

Several reports have suggested that elevated LC is typically the first laboratory measure to indicate inflammation of the appendix, and most patients present with AA present with leukocytosis. In several published studies, the sensitivity and specificity of LC in the diagnosis of AA has been reported as 67-97.8% and 31.9-80%, respectively [5,16,17]. The present study found that LC was significantly higher in AA and sensitivity and specificity of LC were 94% and 75%, respectively.

Recently, elevated NLR was found as a diagnostic parameter in some acute inflammatory diseases. De Jager and colleagues found elevated NLR value was predictor of bacteremia than routine parameters like C-reactive protein level, white blood cell count and neutrophil count. [8]. Ahsen and co-workers were sad; NLR might be used in the Familial Mediterranean Fever patient as an indicator of the subclinical inflammation [9]. Gunay and colleagues found an

elevated NLR value could be considered as a new inflammatory marker for assessment of inflammation in chronic obstructive pulmonary disease patients [10]. Like these studies, Gokmen et al. were sad, NLR may be seen as a useful marker for demonstrating inflammation together with acute phase reactants such as C-reactive protein in ankylosing spondylitis [11].

In the literature, there are some studies that investigated diagnostic role of NLR in AA. Kahramanca et al. were found a significantly higher values of NLR in positive appendectomy group according to negative appendectomy group. Neutrophil/lymphocyte ratio had a sensitivity of 65.3% and a specificity of 54.7% for the diagnosis of AA. Neutrophil/lymphocyte ratio was significantly higher in complicated appendicitis according to non-complicated appendicitis [18]. Ishizuka and colleagues found a significant association between NLR and severity of acute appendicitis. Neutrophil/lymphocyte ratio was significantly different between catarrhal, phlegmonous and gangrenous appendicitis groups [19]. Markar and colleagues were found a higher level of NLR in AA. In this study, they speculated that NLR had greater diagnostic accuracy than white blood cell and C-reactive protein [20]. Yazici and colleagues were investigated the diagnostic role of NLR in childhood AA. They found a higher level of NLR in AA group than non-specific abdominal pain group. In this study NLR had a sensitivity of 91% and a specificity of 72% [21]. Goodman et al. found elevated NLR value in AA. They suggested that NLR was more sensitive than the total leukocyte count in diagnosis of AA [22]. Like these studies, we found significantly elevated level of NLR in AA. Additionally NLR had a sensitivity of 97% and a specificity of 87% in our study. These values were higher than the other studies. In the present study, area under curve was 0.67 for LC and 0.60 for NLR. Unlike the studies of Markar [20] and Goodman [22], there was no advantage for NLR than LC in diagnosis of AA. In various inflammatory diseases, regular response of circulating leukocytes is increased level of neutrophil and reduced level of lymphocyte counts [23]. In AA as an inflammatory disease, elevated level of NLR is usual.

In all of these studies the control group was composed of distinct patients with no symptoms, including patients admitted to outpatient centers for routine exams. But patients shows different responses to inflammatory stimuli [12,13]. This may introduce bias into certain study designs. Our study is therefore more meaningful because control and AA group's data were obtained from the same patients and there was no intra-individual differences between patients in terms of NLR. The present study has excellent clinical applicability.

Limitations

In our study, we have tried to select previous blood samples when there was no an inflammatory condition of patients, but this situation could not be fully excluded. This was the most important limitation of this study.

Conclusion

Acute appendicitis is the most common cause of emergent abdominal surgery and remains difficult to diagnose. This study showed that neutrophil/lymphocyte ratio is increased in acute appendicitis. Neutrophil/lymphocyte ratio has lower diagnostic accuracy than leukocyte count, although it can be used as a supportive parameter in the diagnosis of acute appendicitis.

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