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Neutrophil- to- Lymphocyte Ratio as a Predictor of acute Appendicitis and Its Severity

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Abstract:Background: The Neutrophil-to-Lymphocyte Ratio (NLR) is an emerging biomarker for the diagnosis and severity assessment of acute appendicitis. This study evaluates the predictive value of NLR in patients undergoing appendicectomy.

Patients and Methods: This cross-sectional retrospective study included 856 patients who underwent open appendicectomy for suspected acute appendicitis between 2015 and 2023. Preoperative clinical assessments, standard laboratory tests, and imaging techniques such as ultrasonography and CT were used for diagnosis. An automated hematology analyzer measured neutrophil and lymphocyte percentages to calculate NLR. Patients were divided into two groups: Group A (acute appendicitis) with subgroups A1 (non-complicated) and A2 (complicated), and Group B (normal appendix).

Results: Of the 856 patients, 821 (95.9%) had acute appendicitis (Group A) and 35 (4.1%) had a normal appendix (Group B). Group A had a significantly higher mean NLR (7.29 ± 6.30) compared to Group B (5.30 ± 4.70) ($p < 0.001$). The NLR cutoff value of 4.8 yielded a sensitivity of 66.63% and specificity of 51.43% for distinguishing acute appendicitis. Within Group A, non-complicated appendicitis (A1) had a mean NLR of 7.79 ± 8.68 , while complicated appendicitis (A2) had a mean NLR of 6.99 ± 5.92 . The cutoff value of 5.8 for subgroup differentiation resulted in a sensitivity of 73.13% and specificity of 49.05%.

Conclusions: The Neutrophil-to-Lymphocyte Ratio is a valuable predictor of acute appendicitis and its severity. An NLR cutoff of 4.8 effectively distinguishes between acute appendicitis and a normal appendix, while a cutoff of 5.8 differentiates between complicated and non-complicated appendicitis.

Keywords: Neutrophil-to-Lymphocyte Ratio, Acute Appendicitis, Biomarker, Appendicectomy, Diagnostic Tool

Introduction

Inflammation of the appendix is the most prevalent surgical emergency worldwide. It is the most frequent cause of abdominal pain requiring surgery, with a lifelong risk of 7% and perforation rates of 17-20%^{1, 2}. Preoperative detection of acute appendicitis remains difficult, particularly in the elderly and in females with gynecological or urinary disorders. This diagnosis largely depends on a detailed history and skilled clinical examination^{3, 4}.

Imaging tools such as pelvic-abdominal ultrasonography and computerized tomography (CT) scans can also diagnose acute appendicitis. However, their usage is limited, particularly in impoverished nations, due to high costs and scarcity^{5, 6}.

Even though the symptoms and signs of complicated appendicitis are well known, early detection can be challenging. According to the World Society of Emergency Surgery (WSES) 2020 recommendations, acute appendicitis includes gangrene, perforation, or abscess. The prevalence of perforated appendicitis ranges from 16% to 40% generally and is higher in younger age groups, ranging from 40% to 57%, often related to delayed diagnosis. Consequently, if acute appendicitis is not diagnosed quickly after presentation, there is a higher risk of morbidity and mortality^{7, 8}.

Numerous scoring approaches have been developed to aid in the rapid clinical detection and categorization of acute appendicitis, including the Alvarado score, Pediatric Appendicitis Score (PAS), Appendicitis Inflammatory Response (AIR), and Shera score⁹⁻¹¹. Although the clinical factors used by each of these scores differ, the PAS overdiagnoses appendicitis 32% of the time, and the Alvarado score 35%. Furthermore, these scoring methodologies do not accurately predict the severity of acute appendicitis. Neutrophilia and lymphocytopenia are cellular response components in systemic inflammation, and the rise in the difference between neutrophil and lymphocyte levels indicates the intensity of the inflammatory response. The NLR and Platelet-to-Lymphocyte Ratio (PLR) are simple, affordable, and easily obtainable indicators of inflammation^{7, 12, 13}.

In this retrospective study, the NLR was investigated for its capacity to predict acute appendicitis before surgery and distinguish between uncomplicated and severe appendicitis. Diagnosing appendicitis effectively can be challenging, especially in the elderly or in cases of atypical presentation. This may result in an increase in negative appendicectomies, as well as higher morbidity and mortality rates. This study aims to evaluate the NLR's ability to predict acute appendicitis before surgery and to distinguish between uncomplicated and severe appendicitis. The goal is to reduce the frequency of negative appendicectomies and missed diagnoses of appendicitis, thereby lowering morbidity and mortality.

Patients and methods

Study Design and Population

This cross-sectional retrospective study was conducted on patients who underwent open appendectomy for acute appendicitis between 2015 and 2023. Preoperative clinical history, physical examination, standard laboratory testing, and imaging techniques such as ultrasonography, and in certain cases, CT, were used to establish the clinical diagnosis of acute appendicitis. An automated hematology analyzer was used to measure the neutrophil and lymphocyte percentages.

Inclusion and Exclusion Criteria

This study included all patients diagnosed with acute appendicitis, including those whose intraoperative findings were acute appendicitis or a normal appendix. Patients who had another pathology other than acute appendicitis intraoperatively were excluded from the study. Complicated appendicitis was defined as gangrenous and/or perforated appendicitis.

Group Classification

The NLR of the patients was compared to their intraoperative findings, which were divided into two groups: Group A, which included positive appendicitis cases further subdivided into Group A1 (non-complicated

appendicitis) and Group A2 (complicated appendicitis), and Group B, which included negative appendicitis cases.

Sample Size and Technique

The sample size was at least 101 patients, determined using the Raosoft Sample Size Calculator (<http://www.raosoft.com/samplesize.html>), based on the prevalence of acute appendicitis in Saudi Arabia, which is 7%. A convenient sampling technique was used. Group A was subdivided into two subgroups: Group A1 (687 patients) and Group A2 (134 patients).

Statistical Analysis

Data were analyzed statistically using the SPSS software package version 20.0 (Prentice-Hall, Chicago, IL, USA). Numbers and percentages were used to describe qualitative data. The Student's t-test was used to compare quantitative data. The Chi-square (X^2) test was used to compare categorical variables between the two groups. When more than 20% of the cells had an expected count of less than 5, Chi-square adjustment was applied using the Fisher Exact test or Monte Carlo correlation (MC). ROC analysis was used to calculate the cutoff values for group discrimination parameters. The ROC curve was created by plotting the sensitivity and specificity for each outcome under investigation. A p-value of less than 0.05 was considered statistically significant.

Results

This study included records from 856 patients. There were 821 patients in Group A and 35 in Group B (**Table 1**). In terms of subgroups, Group A1 had 134 patients and Group A2 had 687 patients (**Table 2**).

Groups A and B had mean NLR values of 7.29 ± 6.30 and 5.30 ± 4.70 , respectively, showing a significant difference ($p < 0.001$). The NLR cutoff value was 4.8, resulting in a sensitivity of 66.63% and specificity of 51.43% (**Table 3**).

The mean NLR values for Groups A1 and A2 were 7.79 ± 8.68 (SD) and 6.99 ± 5.92 (SD), respectively. The cutoff value for this subgroup was 5.8, with 73.13% sensitivity and 49.05% specificity (**Table 3**).

Table 1. Patient distribution in the main groups based on NLR cutoff values

Cutoff value of NLR	Group (A) Acute appendicitis	Group (B) Normal appendix
<4.8	274	18
>4.8	547	17
Total	821	35

NLR: Neutrophil-to-lymphocyte ratio.

Table 2. Patient distribution in subgroups based on NLR cutoff value.

Cutoff value of NLR	Group (A1) Complicated AA	Group (A2) Non-Complicated AA
<5.8	36	337
>5.8	98	350
Total	134	687

AA: Acute appendicitis.

Table 3. Comparison both between groups and between subgroups

Group	Mean NLR	SD (\pm)	Cutoff value	P-value	Sensitivity	Specificity
A	7.29	6.3	4.8	<0.001	66.63 %	51.43 %
B	5.30	4.7				
A1	8.87	7.79	5.8	<0.001	73.13 %	49.05 %
A2	6.99	5.92				

A: Positive appendectomy group; B: Negative appendectomy group; A1: Complicated appendectomy group; A2: Non-complicated appendectomy group.

Discussion

Acute Appendicitis (AA) is a common occurrence in emergency rooms. It is not always possible to diagnose AA at an early stage. Surgeons face a difficult decision between waiting until the diagnosis is certain and operating early to avoid complications such as perforation and peritonitis. An early operation can remove a normal appendix with minimal risk of morbidity^{14,15}.

On the other hand, clinicians may not have access to imaging facilities, particularly in remote areas. Furthermore, ultrasonography and computed tomography imaging may not always provide an accurate diagnosis. Clinicians still require a reliable and simple test to determine the diagnosis.

In the present study, an NLR cutoff value of 4.80 could distinguish between a normal appendix and AA with a sensitivity of 66.63% and specificity of 51.43%, resulting in a high false positive rate. These results are in accordance with previous reports by Ishizuka et al., which also discriminated between a normal appendix and AA but with different cutoff values (NLR cutoff was >4.8 in Ishizuka et al. and <4.8 in other studies)¹⁶.

The study's low sensitivity and specificity may be due to the variation in the timing of the test (as some patients may come to the hospital early, while others may not come unless the condition is complicated). Additionally, the inclusion of solely operated patients leaves missing data on suspected cases that were not operated on or were treated medically. Machine calibration may also be a confounding factor.

The NLR cutoff value for complicated appendicitis in this study is 5.80, with a sensitivity of 73.13% and specificity of 49.05%. NLR appears to be more effective in distinguishing complicated cases, with higher sensitivity. This cutoff value is lower than the suggested value of 8.00 for detecting gangrenous appendicitis in the Ishizuka et al. study¹⁶. Kahramanca et al.¹⁷ reported an NLR cutoff for complicated appendicitis of 5.74% with a sensitivity of 70.8% and specificity of 48.5%. Yazici et al.¹⁸ found that sensitivity is highest at NLR >3.5, whereas specificity progressively rises with NLR. The highest values are achieved at NLR >5.0. The results of Ajeni et al.¹¹ report an NLR sensitivity of 70.3% and a specificity of 70% for distinguishing complicated from non-complicated appendicitis.

Some studies have demonstrated that NLR offers higher diagnostic accuracy than other laboratory tests, such as white blood cells or C-reactive protein. According to these studies, NLR upon hospital admission is a reliable predictor of positive appendicitis^{13,19}. Lymphocyte counts can decline during appendicitis, especially in gangrenous appendicitis¹⁷. This process may explain the increased cutoff value in complex appendicitis. In cases with non-severe appendicitis, the large rise in NLR could be attributable to a higher number of neutrophils than leukocytes during the acute phase of inflammation.

The present study found that an NLR of 4.8 is a reliable measure for diagnosing acute appendicitis, while an NLR of 5.8 can distinguish between complicated and non-complicated appendicitis. A normal reading for NLR does not rule out the diagnosis. Prospective randomized trials are necessary to determine the appropriate NLR and test its accuracy. The surgeon's clinical evaluation should remain the primary focus.

Conclusion

Preoperative NLR can help diagnose acute appendicitis and distinguish between simple and complicated cases. It can be used in conjunction with clinical examinations.

Acknowledgments

None.

Ethical Approvals

The article protocol was reviewed and approved by the institutional review board of Damietta Faculty of Medicine, Al-Azhar University, Damietta, Egypt (Registration number: DFM-IRB 0001267-20-09-012)

Conflict of Interests

No conflict of interest.

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