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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 (AA). This study evaluates the predictive value
of NLR in cases 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 hematologyanalyzer measured neutrophil and lymphocyte percentages to calculate NLR. The cases were divided into two groups: Group A (AA) with subgroups A1 (non-complicated) and A2 (complicated), and Group B (normal appendix).

Results: Of the 856 patients, 821 (95.9%) had AA (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 toGroup 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 NLR is a valuable predictor of AA and its severity. An NLR cutoff of 4.8 effectively distinguishes between AA 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

Appendix Inflammation 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 (AA) remains difficult, particularly in the elderly and in females withgynecological 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].

Despite the well-established clinical manifestations of complicated appendicitis, achieving early diagnosis remains challenging. According to the 2020 guidelines from the World Society of Emergency Surgery (WSES), acute appendicitis encompasses conditions such as gangrene, perforation, and abscess formation. Perforated appendicitis occurs in approximately 16% to 40% of cases, with a higher incidence—between 40% and 57%—in younger populations, often attributed to delayed diagnosis. Consequently, failure to promptly diagnose acute appendicitis increases the likelihood of both morbidity and mortality [7, 8].

Various scoring systems have been developed to enhance the swift clinical diagnosis and classification of acute appendicitis. These include the Alvarado score, Pediatric Appendicitis Score (PAS), Appendicitis Inflammatory Response (AIR), and Shera score [9-11]. While these tools differ in the clinical criteria they assess, the PAS has been shown to overdiagnose appendicitis in 32% of cases, while the Alvarado score overestimates it 35% of the time. Importantly, these scoring mechanisms are insufficient in accurately predicting the severity of the condition. Neutrophilia and lymphocytopenia, key indicators of systemic inflammation, reflect the intensity of the body's inflammatory response, with an elevated neutrophil-to-lymphocyte ratio (NLR) serving as a useful marker. Similarly, the platelet-to-lymphocyte ratio (PLR) is a simple, cost-effective, and accessible measure 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 AA before surgery and to distinguish between uncomplicated andsevere 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 AA 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 clinical diagnosis of AA. An automated hematology analyzer was used to measure the NLR percentages.

Inclusion and Exclusion Criteria

This study included all patients diagnosed with AA, including those whose intraoperative findings were acute appendicitis or a normal appendix. Patients who had another pathology other than acuteappendicitis intraoperatively were excluded from our study. Complicated appendicitis is characterized by the presence of gangrene and/or perforation.

Group Classification

The NLR of 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 cases determined using the Raosoft Sample Size Calculator (http://www.raosoft.com/samplesize.html), based on the prevalence of AA 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

The statistical analyses of the data were conducted using SPSS software program version 20.0 (Prentice-Hall, Chicago, IL, USA). Qualitative data was characterized using percentages and numerical values. The Student's t-test was used to compare quantitative data. The categorical variables were analyzed between two groups using the Chi-square (X2) test. When the anticipated count of less than 5 occurred in over 20% of the cells, the Fisher Exact test or Monte Carlo correlation (MC) was used to implement a Chi-square correction. ROC analysis was used to ascertain the cutoff values for group discrimination parameters. The sensitivity and specificity of each examined outcome were plotted to create the ROC curve. Statistical significance was established as a p-value of under 0.05.

Results

This study included records from 856 cases. There were ients 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 ($p<0.001$). NLR cutoff value was 4.8, resulting in 66.63% sensitivity and 51.43% specificity **(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 (±)	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

AA is a common phenomenon in emergency departments. Diagnosing AA at an early stage is not always practicable. The choice for surgeons to proceed with early intervention to avert complications including perforation and peritonitis, or to postpone until a definitive diagnosis is established, presents a significant challenge. An unremarkable appendix may be excised with low morbidity with an early surgical intervention [14, 15].

Conversely, healthcare professionals may lack access to imaging facilities, especially in distant areas. Moreover, computed tomography and ultrasonography may not consistently provide a correct diagnosis. A clear and reliable test is essential for physicians to establish a diagnosis. The present study demonstrated that an NLR cutoff of 4.80 could differentiate between a normal appendix and acute appendicitis, with a sensitivity of 66.63% and a specificity of 51.43%, resulting in a notable false positive rate. These findings align with those of Ishizuka et al., who used a similar NLR threshold (>4.8) to distinguish normal appendices from acute appendicitis, although other studies have employed lower cutoff values (<4.8)[16].

The study's reduced sensitivity and specificity may be attributed to the variability in test scheduling, as some individuals may present to the hospital early, while others may only seek care after the problem becomes complex. The absence of data regarding suspected instances that were either untreated surgically or managed medically is the consequence of the inclusion of only operated patients. Machine calibration has the potential to be a confounding variable.

In this study, the NLR cutoff value for complicated appendicitis was 5.80, yielding a sensitivity of 73.13% and a specificity of 49.05%. NLR proved to be more effective in identifying complicated cases, demonstrating higher sensitivity. This cutoff is lower than the 8.00 threshold suggested by Ishizuka et al. for detecting gangrenous appendicitis [16]. Kahramanca et al. [17] reported a similar NLR cutoff of 5.74%, with a sensitivity of 70.8% and a specificity of 48.5%. Yazici et al. [18] found that sensitivity peaks when NLR exceeds 3.5, while specificity progressively increases with higher NLR values, reaching its maximum at NLR >5.0. The results of Ayeni et al. [11] reported an NLR sensitivity of 70.3% and a specificity of 70% for distinguishing between complicated and non-complicated appendicitis.

Some research has shown that NLR provides greater diagnostic accuracy compared to other lab tests like WBCs or CRP [13, 19]. Studies suggest that NLR at hospital admission serves as a reliable predictor of appendicitis [13, 19]. Lymphocyte counts tend to decrease, particularly in cases of gangrenous appendicitis [17], which may account for the elevated NLR cutoff in complex cases. In non-severe appendicitis, the marked increase in NLR may be due to a higher neutrophil count relative to leukocytes during the acute inflammatory phase.

The current research demonstrated that an NLR of 4.8 is a valid metric for identifying acute appendicitis, whereas an NLR of 5.8 may discriminate between difficult and non-complicated appendicitis. A normal NLR result does not exclude the diagnosis. Randomized studies are essential to ascertain the suitable NLR and evaluate its precision. The surgeon's clinical assessment should be the primary emphasis.

Conclusion

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

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None.

Ethical Approvals

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

Conflict of Interests

No conflict of interest.

References:

1. Kong VY, Sartorius B, Clarke DL. Acute appendicitis in the developing world is a morbid disease. Ann R Coll Surg Engl. 2015;97:390-395.
2. Louw J, McCaul M, English R, et al. Factors Contributing to Delays to Accessing Appendectomy in Low- and Middle-Income Countries: A Scoping Review. World J Surg. 2023;47:3060-3069.
3. Gaitini D, Beck-Razi N, Mor-Yosef D, et al. Diagnosing Acute Appendicitis in Adults: Accuracy of Color Doppler Sonography and MDCT Compared with Surgery and Clinical Follow-Up. American Journal of Roentgenology. 2008;190:1300-1306.
4. Drake FT, Flum DR. Improvement in the diagnosis of appendicitis. Adv Surg. 2013;47:299-328.
5. Moussa BS, Ali MA, Mohamed DAR, Shahhat AME. Comparing the diagnostic accuracy of modified RIPASA and MASS in patients diagnosed with acute appendicitis in Suez Canal University Hospital Emergency Department: a cross-sectional study. BMC Emerg Med. 2022;22:142.
6. Bahrami M, Mirgaloyebayat H, Mohajeri Z, et al. The diagnostic value of the computed tomography scan and ultrasonography in acute appendicitis. Am J Nucl Med Mol Imaging. 2023;13:11-17.
7. Di Saverio S, Podda M, De Simone B, et al. Diagnosis and treatment of acute appendicitis: 2020 update of the WSES Jerusalem guidelines. World J Emerg Surg. 2020;15:27.
8. Bhangu A, Søreide K, Di Saverio S, Assarsson JH, Drake FT. Acute appendicitis: modern understanding of pathogenesis, diagnosis, and management. Lancet. 2015;386:1278-1287.
9. Iftikhar MA, Dar SH, Rahman UA, et al. Comparison of Alvarado score and pediatric appendicitis score for clinical diagnosis of acute appendicitis in children—a prospective study. Annals of Pediatric Surgery. 2021;17: 17:10.
10. Jose T, Rajesh PS. Appendicitis Inflammatory Response Score in Comparison to Alvarado Score in Acute Appendicitis. Surg J (N Y). 2021;7:e127-e131.
11. Ayeni A, Mahmood F, Mustafa A, et al. Predicting the Severity of Acute Appendicitis in Children Using Neutrophil-to-Lymphocyte Ratio (NLR) and Platelet-to-Lymphocyte Ratio (PLR). Cureus. 2022;14:e28619.
12. Fuhrer AE, Sukhotnik I, Ben-Shahar Y, Weinberg M, Koppelmann T. Predictive Value of Alvarado Score and Pediatric Appendicitis Score in the Success of Nonoperative Management for Simple Acute Appendicitis in Children. Eur J Pediatr Surg. 2021;31:95-101.
13. Von-Mühlen B, Franzon O, Beduschi MG, Kruel N, Lupselo D. AIR score assessment for acute appendicitis. Arq Bras Cir Dig. 2015;28:171-173.
14. Mostafa R, El-Atawi K. Misdiagnosis of Acute Appendicitis Cases in the Emergency Room. Cureus. 2024;16:e57141.
15. Mostbeck G, Adam EJ, Nielsen MB, et al. How to diagnose acute appendicitis: ultrasound first. Insights Imaging. 2016;7:255-263.
16. Ishizuka M, Shimizu T, Kubota K. Neutrophil-to-lymphocyte ratio has a close association with gangrenous appendicitis in patients undergoing appendectomy. Int Surg. 2012;97:299-304.
17. Kahramanca S, Ozgehan G, Seker D, et al. Neutrophil-to-lymphocyte ratio as a predictor of acute appendicitis. Ulus Travma Acil CerrahiDerg. 2014;20:19-22.
18. Yazici M, Ozkisacik S, Oztan MO, Gürsoy H. Neutrophil/lymphocyte ratio in the diagnosis of childhood appendicitis. Turk J Pediatr. 2010;52:400-403.
19. Prasetya D, Rochadi, Gunadi. Accuracy of neutrophil lymphocyte ratio for diagnosis of acute appendicitis in children: A diagnostic study. Annals of Medicine and Surgery. 2019;48:35-38.