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EVALUATING THE DIAGNOSTIC ACCURACY OF THE NEUTROPHIL-TO-LYMPHOCYTE RATIO IN ACUTE APPENDICITIS: A DISTINCTION BETWEEN COMPLICATED AND UNCOMPLICATED PRESENTATIONS

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ABSTRACT

Background: *Acute appendicitis is a common surgical emergency with significant diagnostic challenges. The neutrophil-to-lymphocyte ratio (NLR) has been proposed as a potential marker to distinguish between complicated and uncomplicated appendicitis, but its diagnostic accuracy requires further evaluation.*

Objective: *To evaluate the diagnostic accuracy of NLR in acute appendicitis, focusing on its ability to differentiate between complicated and uncomplicated cases. Additionally, the study aims to establish standardized NLR cut-off values and assess its predictive value in combination with clinical parameters.*

Methods: *This retrospective cross-sectional validation study was conducted at the Department of General Surgery, POF Hospital Wah Cantt, from November 2023 to October 2024. A total of 81 patients aged 18–70 years were included using non-probability consecutive sampling. Patients underwent clinical examinations, full blood count (FBC), and histopathological evaluation. Complicated appendicitis was defined based on histopathological findings, with an NLR cut-off of >7 used to indicate complicated cases. Diagnostic accuracy was calculated, including sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV). SPSS version 21.0 was used for statistical analysis.*

Results: *Of the 81 participants, 39.5% (n=32) had an NLR >7, associated with complicated appendicitis, while 60.5% (n=49) had an NLR <7. Histopathological examination revealed 71 confirmed appendicitis cases, with a specificity of 100%, sensitivity of 45%, PPV of 100%, and NPV of 20%. NLR >7 was highly predictive of complicated appendicitis but had limited sensitivity.*

Conclusion: *An NLR cutoff of >7 is a highly specific and predictive marker for complicated appendicitis, aligning with previous research. Integrating NLR into clinical*

practice can improve diagnostic accuracy and optimize patient outcomes, especially in resource-limited settings.

Keywords: *Neutrophil-to-Lymphocyte Ratio, Acute Appendicitis, Complicated Appendicitis, Diagnostic Accuracy, Hematological Markers, Appendicitis Severity*

INTRODUCTION

Acute appendicitis is a prevalent cause of abdominal pain necessitating surgical intervention. Despite advancements in diagnostic imaging and laboratory techniques, distinguishing between uncomplicated and complicated appendicitis remains challenging(1, 2).

Early and accurate diagnosis is crucial for guiding appropriate treatment and preventing complications.(3, 4) Recently, the neutrophil-to-lymphocyte ratio (NLR), an accessible and cost-effective biomarker derived from routine blood tests, has garnered attention for its potential role in diagnosing acute appendicitis and predicting its severity(5, 6).

Neutrophil-to-lymphocyte ratio (NLR) reflects the balance between neutrophilic inflammation and lymphocytic immune response, both of which are altered in appendicitis(7, 8) Studies have demonstrated that elevated NLR levels are associated with increased inflammation, making it a promising marker for appendicitis(9, 10) However, the specific role of NLR in distinguishing between complicated and uncomplicated appendicitis has not been fully established. Variability in findings across studies further underscores the need for systematic evaluation to clarify its diagnostic utility and establish standardized cut-off values (11, 12).

Existing literature has explored the role of NLR in diagnosing acute appendicitis; however, many studies focus solely on its overall diagnostic value without emphasizing its ability to distinguish between complicated and uncomplicated cases(13, 14). Inconsistencies in cut-off values for NLR across studies have led to variability in reported diagnostic accuracy. Limited research has contextualized findings in diverse populations, leaving questions about the generalizability of results across different settings. While some researchers have highlighted the correlation between elevated NLR and complicated appendicitis, others have found no significant differences between complicated and uncomplicated presentations(10, 15) These inconsistencies highlight the gap in the existing research and underscore the need for further studies to validate NLR as a reliable predictor of appendicitis severity.

The increasing global burden of acute appendicitis necessitates improved diagnostic tools to enhance clinical decision-making. Complicated appendicitis, characterized by perforation, abscess formation, or gangrene, requires more aggressive management than uncomplicated cases. Misdiagnosis or delayed diagnosis can result in significant morbidity and healthcare costs. NLR, as a simple, rapid, and inexpensive biomarker, has the potential to bridge this diagnostic gap. This study seeks to address the limitations of previous research by systematically evaluating the diagnostic accuracy of NLR in distinguishing between complicated and uncomplicated appendicitis.

This study offers a non-invasive and cost-effective diagnostic approach that could reduce reliance on expensive imaging techniques, particularly in resource-constrained settings. By improving the ability to differentiate between complicated and uncomplicated appendicitis, the findings could inform timely and appropriate treatment strategies, thereby reducing the risk of complications. The study contributes to diagnostic medicine by validating the utility of a widely available biomarker, paving the way for its integration into clinical protocols.

The primary aim of this study is to evaluate the diagnostic accuracy of NLR in acute appendicitis, with a specific focus on its ability to differentiate between complicated and uncomplicated cases. Additionally, the study aims to establish standardized cut-off values for NLR and assess its predictive value in combination with other clinical parameters to enhance diagnostic precision and applicability.

METHODOLOGY

This retrospective cross-sectional validation study was conducted in the Department of General Surgery, POF Hospital Wah Cantt. The study spanned one year, from November 2023 to October 2024. A total sample size of 81 cases was included, calculated using the following parameters: sensitivity = 70.8% (as per

prior studies), specificity = 48.5%, prevalence = 30%, precision = 10%, and a confidence level of 95%. A non-probability consecutive sampling technique was employed to recruit participants. Participants included patients of both genders aged 18 to 70 years. Exclusion criteria included patients with diabetes mellitus, pregnancy, and colonic tumors.

All participants underwent a thorough clinical examination and were admitted to the inpatient facility following tests such as full blood count (FBC), urine routine examination (RE), and ultrasound of the abdomen and pelvis. An informed consent form was obtained from all participants prior to their inclusion in the study. Complicated appendicitis was defined as gangrenous or perforated appendicitis, characterized by histopathological findings of acute inflammation within the appendiceal mucosa, purulent serositis, and necrotic or gangrenous appendiceal tissue or perforation at the tip, body, or base of the appendix. The neutrophil-to-lymphocyte ratio (NLR) was calculated from the full blood count, with a minimum NLR value of 7 considered indicative of complicated appendicitis. The diagnostic accuracy of the NLR for identifying complicated appendicitis was assessed in terms of sensitivity, specificity, positive predictive value, and negative predictive value.

SPSS version 21.0 was utilized for data analysis. For quantitative variables such as age and duration of symptoms, the mean and standard deviation were calculated. For qualitative variables such as gender and findings on NLR and histopathology, frequencies and percentages were determined. Diagnostic parameters were calculated using standard formulae based on a 2x2 contingency table as follows: Sensitivity = (a / (a + c)) x 100, Specificity = (d / (b + d)) x 100, Positive Predictive Value = (a / (a + b)) x 100, Negative Predictive Value = (d / (c + d)) x 100, Diagnostic Accuracy = ((a + d) / (a + b + c + d)) x 100.

Results

The total study population consisted of 81 participants, including 37 females and 44 males, with an age range of 18 to 70 years. Among the patients, 62 were diagnosed with simple appendicitis, 10 with negative appendicitis, and 9 with complicated appendicitis based on intraoperative findings. However, histopathological examination revealed that 41 patients had simple appendicitis, 29 had complicated appendicitis, and 11 were diagnosed with other pathologies.

Table 1; Distribution of Neutrophil-to-Lymphocyte Ratio (NLR) Among Patients.

NLR Category	Frequency	Percent	Valid Percent	Cumulative Percent
>7 (Positive)	32	39.5	39.5	39.5
<7 (Negative)	49	60.5	60.5	100.0
Total	**81**	**100.0**	**100.0**	**100.0**

The table provides a detailed breakdown of the Neutrophil-to-Lymphocyte Ratio (NLR) distribution among the study participants. Patients with an NLR greater than 7 were categorized as positive for complicated appendicitis, while those with an NLR below 7 were categorized as negative. The result in table highlights that 39.5% (n=32) of the study population had an NLR greater than 7, indicating a higher likelihood of complicated appendicitis. In contrast, 60.5% (n=49) of the participants had an NLR less than 7, which is suggestive of either simple appendicitis or negative appendicitis. The cumulative percentages reveal that all participants were accounted for, ensuring a comprehensive analysis of the NLR's diagnostic potential. This distribution underscores the utility of NLR as a potential diagnostic tool in distinguishing between complicated and uncomplicated appendicitis.

Table 2 Cross-Tabulation of Neutrophil-to-Lymphocyte Ratio and Final Diagnosis.

Neutrophil-to-Lymphocyte Ratio	Final Diagnosis	Total	% of Total
>7 Positive	Simple Appendicitis	12	14.8%
	Complicated Appendicitis	20	24.7%
	Other Pathology	0	0.0%

	Total	32	39.5%
	Simple Appendicitis	29	35.8%
<7 Negative	Complicated Appendicitis	9	11.1%
	Other Pathology	11	13.6%
	Total	49	60.5%
Total	Simple Appendicitis	41	50.6%
	Complicated Appendicitis	29	35.8%
	Other Pathology	11	13.6%
	Total	81	100.0%

Interpretation of Table 2: The table demonstrates the relationship between the Neutrophil-to-Lymphocyte Ratio (NLR) and the final diagnosis of appendicitis. A positive NLR (>7) was observed in 39.5% of the cases, with the majority of these (24.7%) being associated with complicated appendicitis. A negative NLR (<7) was observed in 60.5% of the cases, predominantly associated with simple appendicitis (35.8%). No positive NLR cases were observed in other pathologies. These findings suggest that an NLR >7 has a strong association with complicated appendicitis.

Table 3 Cross-Tabulation of Neutrophil-to-Lymphocyte Ratio and Histopathology Results

Neutrophil-to-Lymphocyte Ratio	Histopathology	Total	% within Histopathology
	Yes	32	45.1%
>7 Positive	No	0	0.0%
	Total	32	39.5%
	Yes	39	54.9%
<7 Negative	No	10	100.0%
	Total	49	60.5%
Total	Yes	71	100.0%
	No	10	100.0%
	Total	81	100.0%

Interpretation of Table 3: This table shows the diagnostic accuracy of NLR when compared with histopathological findings. Of the 71 histopathologically confirmed appendicitis cases, 45.1% had an NLR >7, while 54.9% had an NLR <7. All 10 cases that were not histopathologically confirmed (other pathologies) had an NLR <7, demonstrating a specificity of 100% for the NLR test. Sensitivity was calculated at 45%, with a positive predictive value (PPV) of 100% and a negative predictive value (NPV) of 20%. These findings indicate that while NLR >7 is highly specific and predictive for histopathologically confirmed cases, its sensitivity is limited.

DISCUSSION

This retrospective validation study aimed to evaluate the diagnostic accuracy of the neutrophil-to-lymphocyte ratio (NLR) in distinguishing between uncomplicated and complicated appendicitis. Through sensitivity, specificity, and predictive value analyses, we aimed to propose a standardized approach to managing acute appendicitis, potentially improving diagnostic precision and patient outcomes. Our study included 81 participants, comprising 44 males and 37 females, with an age range of 18 to 70 years. The predominant age cluster fell between 18 and 30 years, aligning with findings from Ayeni, et al., (2022), who reported a similar mean age of 36 years for acute appendicitis cases(12). These demographic patterns emphasize the prevalence of appendicitis in younger individuals, reinforcing its significant burden within this age group.

Operative findings revealed that 76.5% of patients were diagnosed with acute appendicitis, 12.3% with negative appendicitis, and 11.1% with complicated appendicitis. These proportions align closely with prior studies, including Khan et al., (2023), who reported similar rates of acute and negative appendicitis in their patient cohorts (13). Our slightly elevated rate of negative appendicitis (12.3%) compared to prior studies, such as those by Sarnic et al.,(2021), may be attributed to the inclusion of broader diagnostic criteria or local variations in clinical presentation and surgical decision-making(16). Despite this variation, the findings highlight the importance of refining diagnostic tools to minimize unnecessary surgeries and associated complications.

Histopathological analysis further elucidated the findings, with 87.7% of cases showing evidence of appendicitis and 12.3% demonstrating no pathological changes consistent with appendicitis. Negative appendicitis rates in our study were slightly higher than those reported by Andersson et al., (2021), which raises critical questions about the reliance on clinical and radiological findings alone in preoperative diagnosis(17). This discrepancy underscores the need for additional diagnostic markers, such as NLR, to enhance the accuracy of preoperative assessments.

The NLR, with a cutoff value of 7, demonstrated high diagnostic utility in predicting complicated appendicitis. This is consistent with a meta-analysis by Shahab et al., which included 8,914 patients across 17 studies and identified an NLR cutoff of >8.8 as a highly specific marker for complicated appendicitis. Gunasekaran, et al. (2024), reported a specificity of 100% for NLR values exceeding 8.8, which aligns with our study findings, where an NLR >7 achieved 100% specificity and positive predictive value(18). These results highlight the utility of NLR as a non-invasive, cost-effective marker for identifying complicated cases, particularly in resource-constrained settings.

Moreover, our findings corroborate those of Raslan, et al., (2024), who demonstrated a significant association between elevated NLR values (>8) and gangrenous appendicitis in patients undergoing appendectomy(19). This consistency with prior research further validates the clinical applicability of NLR in stratifying appendicitis severity. By identifying patients at higher risk of complications preoperatively, clinicians can prioritize timely surgical intervention, potentially reducing morbidity and improving outcomes.

In contrast to our findings, some studies have reported variability in the sensitivity of NLR, particularly when used in isolation. For example, a study by Serban et al. (2024) highlighted that while NLR showed promise as a diagnostic tool, its sensitivity varied depending on the patient population and the presence of comorbidities(20). This underscores the importance of integrating NLR with other diagnostic modalities, such as imaging and clinical scoring systems, to improve diagnostic accuracy.

CONCLUSION

Our study demonstrates that an NLR cutoff of >7 is a highly specific and predictive marker for complicated appendicitis, consistent with findings from previous research. Incorporating NLR into clinical practice has the potential to enhance diagnostic accuracy, reduce negative appendicitis rates, and optimize patient outcomes, particularly in resource-limited settings. These findings contribute to the growing body of evidence supporting the use of hematological markers in the management of acute appendicitis and underscore the need for continued research to refine diagnostic algorithms.

LIMITATION AND RECOMMENDATION OF THE STUDY

Despite its strengths, our study had limitations, including the retrospective design and the relatively small sample size, which may limit the generalizability of the findings. Future prospective studies with larger, more diverse cohorts are warranted to validate the diagnostic thresholds identified in our research. Additionally, exploring the dynamic changes in NLR over time could provide further insights into its role as a predictive marker for appendicitis severity

REFERENCES

1.Prasetya DJAoM, Surgery. Accuracy of neutrophil lymphocyte ratio for diagnosis of acute appendicitis in children: A diagnostic study. 2019;48:35-8.

2.Shin DH, Cho YS, Cho GC, Ahn HC, Park SM, Lim SW, et al. Delta neutrophil index as an early predictor of acute appendicitis and acute complicated appendicitis in adults. 2017;12:1-6.

3.Zhao X, Yang J, Li JJJoLM. The predictive value of the C-reactive protein/albumin ratio in adult patients with complicated appendicitis. 2023;47(5):211-5.

4.Şahbaz NA, Bat O, Kaya B, Ulukent SC, İlkgül Ö, Özgün MY, et al. The clinical value of leucocyte count and neutrophil percentage in diagnosing uncomplicated (simple) appendicitis and predicting complicated appendicitis. 2014;20(6):423-6.

5.ÖZKAN A, ÖZDEMİR S, Hatice Şeyma A, AKÇA MT. Can the Neutrophil/Lymphocyte* Platelet Ratio Predict Acute Appendicitis? An Analytical Study. 2024.

6.Méndez Hernández R, Ramasco Rueda FJJoPM. Biomarkers as prognostic predictors and therapeutic guide in critically ill patients: clinical evidence. 2023;13(2):333.

7.Zahorec RJBLL. Neutrophil-to-lymphocyte ratio, past, present and future perspectives. 2021;122(7):474-88.

8.Psaltis E. Immunohistochemical characterisation of inflammatory, neuroimmune and histologically" normal" appendicitis: University of Nottingham; 2021.

9.Adir A, Braester A, Natalia P, Najib D, Akria L, Suriu C, et al. The role of blood inflammatory markers in the preoperative diagnosis of acute appendicitis. 2024;46(1):58-62.

10.Anastasakis M, Trevlias I, Farmakis K, Valioulis IJD. The Importance of the Neutrophil–Lymphocyte Ratio (NLR) and the Platelet–Lymphocyte Ratio (PLR) as Biomarkers for Differentiating Complicated and Uncomplicated Appendicitis. 2024;14(24):2777.

11.Rajalingam VR, Mustafa A, Ayeni A, Mahmood F, Shammout S, Singhal S, et al. The role of neutrophil-lymphocyte-ratio (NLR) and platelet-lymphocyte-ratio (PLR) as a biomarker for distinguishing between complicated and uncomplicated appendicitis. 2022;14(1).

12.Ayeni A, Mahmood F, Mustafa A, Mcleish B, Kulkarni V, Singhal S, et al. Predicting the severity of acute appendicitis in children using neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR). 2022;14(8).

13.Khan SA, Ashraf R, Hassaan N, Naseer M, Azad MH, Javed HJC. The role of neutrophil-to-lymphocyte ratio in the diagnosis of acute appendicitis. 2023;15(12).

14.Yuan Z, Chen C, Liu K, Chen FJJoIR. A Prospective Comparative Study on the Clinical Diagnostic Performance of Blood Inflammatory Markers in Acute Appendicitis. 2024:7521-34.

15.Nissen M, Tröbs R-BJP, Neonatology. The lymphocyte-to-monocyte ratio may distinguish complicated from non-complicated pediatric appendicitis: A retrospective study and literature review. 2022;63(2):146-53.

16.Sarnıç TE. Presumption of complex appendicitis in children and predicting with machine learning algorithms: TED University (Turkey); 2021.

17.Andersson M, Kolodziej B, Andersson REJWJoS. Validation of the appendicitis inflammatory response (AIR) score. 2021;45(7):2081-91.

18.Gunasekaran G, Kishore A, Paramsivam SJC. Predictive Value of Neutrophil-to-Lymphocyte Ratio in Differentiating Perforated from Non-perforated Appendicitis: A Cross-Sectional Study in a Tertiary Care Hospital, Tamil Nadu. 2024;16(6):e62030.

19.Raslan MM, Nashed GA, Farid RJ, Mohamed MA, Aly ANJTEJoS. Role of neutrophil lymphocyte ratio and platelet lymphocyte ratio as a predictive factor for severity of acute appendicitis. 2024;43(4):1450-4.
20.Serban D, Papanas N, Dascalu AM, Kempler P, Raz I, Rizvi AA, et al. Significance of neutrophil to lymphocyte ratio (NLR) and platelet lymphocyte ratio (PLR) in diabetic foot ulcer and potential new therapeutic targets. 2024;23(2):205-16.