

DIAGNOSING CASES OF COMPLICATED APPENDICITIS USING NEUTROPHIL-LYMPHOCYTE RATIO: A PROSPECTIVE STUDY

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Abstract: *This study aimed to investigate the significance of the neutrophil-lymphocyte ratio (NLR) in the diagnosis of complicated appendicitis and distinguish it from uncomplicated appendicitis. Acute appendicitis is a typical surgical emergency, with a lifetime probability of 8.6% for males and 6.7% for females. It is crucial to diagnose and treat this condition promptly to prevent complications such as perforation, peritonitis, and fluid collection, which can lead to extended hospital stays, morbidity, and mortality. The prospective observational study lasted for three months at Ruth K.M. Pfau Civil Hospital, Karachi. Patients between the ages of 16 and 40 who were diagnosed with acute appendicitis using clinical and/or radiological evidence and underwent appendectomy were included in the study. Pre-operative assessments and laboratory results, including NLR, were recorded and compared to operative findings. The study found that NLR values greater than 8.0 were indicative of complicated appendicitis, with a sensitivity of 90.9% and a specificity of 100%. Therefore, NLR has a high predictive value for identifying complicated appendicitis in our local population.*

Keywords: Neutrophil-lymphocyte, ratio, appendicitis, NLR, complicated

Introduction

Acute appendicitis represents the prevailing surgical emergency, exhibiting a lifetime probability of 8.6% in males and 6.7% in females (Calis, 2018). It is a clinical diagnosis based on history and physical examination. However, the typical presentation only accounts for 60 to 70% of cases requiring further evaluation with the help of laboratory and radiological investigations like WBC, neutrophils, U/S, and CT scans (Alvarado, 2016).

Prompt diagnosis and surgical management are essential to prevent complications like perforation, peritonitis, and fluid collection, leading to a prolonged hospital stay, morbidity, and mortality (Balogun et al., 2019). Although improvements have been made with imaging, diagnosing complicated appendicitis still poses a challenge in resource-limited areas where health care setup lacks such costly diagnostic facilities (Behairy et al., 2019).

Even in this modern era of advanced investigations, researchers still focus on easily accessible and cost-effective diagnostic markers for complicated appendicitis pre-operatively—several scoring systems and parameters, such as CRP and WBC. ESR, neutrophil count, bilirubin, etc., have been studied for early detection of complicated cases, but none have proven to be an accurate marker for diagnosis. No biomarker currently exists with optimal performance that may reliably and independently identify acute appendicitis or foretell the condition's severity or consequences. Most patients with appendicitis have elevated white blood cell (WBC) counts, although an elevated WBC count is not a reliable indicator of whether the appendicitis is simple or complex (Rajalingam et al., 2022).

Recently, neutrophil-lymphocyte ratio NLR has been studied as a good marker of inflammation, and several studies prove that it is of greater importance in diagnosing

acute appendicitis than standard WBC count. The calculation is derived by taking the ratio of the neutrophil and lymphocyte counts observed in the peripheral blood (Buonacera et al., 2022). The physiological response to inflammation increases neutrophils and decreases lymphocytes, thus making it possible to use NLR as an essential marker of inflammation (Berridge, 2014).

Several studies have shown an NLR of more than 3.5 to be a reliable indicator of acute appendicitis, and studies also reveal that increasing NLR > 8.0 can be associated with an increasing risk of complications (Sipra et al., 2021).

In this study, we propose determining the diagnostic value of NLR in the diagnosis of complicated appendicitis and differentiating it from uncomplicated appendicitis pre-operatively. This may have significance for prioritizing surgical cases, monitoring patients receiving conservative treatment, and treating patients unable to get CT scans often (such as pregnant or pediatric patients). Thus, this study was designed to assess the utility of the Neutrophil-lymphocyte ratio in diagnosis complicated appendicitis and to differentiate it from simple appendicitis.

Methodology

After getting approval from the Institutional Review Board by DUHS (IRB-3056/DUHS/Approval2023/290), we conducted a Prospective Observational Study for three months from June 2023 to August 2023 at the surgical department of Dr Ruth PFau Civil Hospital, DUHS Karachi. The sample size was estimated based on the study by Sengul et al. via OpenEpi sample size calculator for comparing two means (Zarog et al., 2023). The mean NLR for uncomplicated appendicitis was 6.2 +/- 3.4, while that for complicated appendicitis was 13.8 +/- 6.7. The ratio of

difficult to uncomplicated cases was 0.2. Keeping the power at 95%, confidence interval at 95%, and significance level of 5%, we estimated a total sample size of 65.

We included Patients between the ages of more than 16 years and less than 40 years undergoing appendectomy after clinical and radiological evidence of acute appendicitis. We excluded pregnant females, patients with histopathological diagnosis of Appendicular Malignancy or with comorbidities like Cardiac diseases, Diabetes Mellitus, lymphoproliferative disorders, and patients on steroid therapy. Patients diagnosed with appendicular mass were excluded from this study and managed as per the Oschner-Scheren Regimen.

All the participants were briefed about the study and its benefits before being inducted. Consent was taken from all participants. In cases where participants could not give consent, their first-degree relatives were sought for consent procedure. Parental or guardian consent was required for participants who were under the age of 18. Patients arriving in the ER with Signs and symptoms of appendicitis were evaluated and investigated as per routine. CBC, CRP, and Ultrasound of the abdomen were carried out. The neutrophil-lymphocyte ratio was calculated. Appendectomies were performed in those who needed operative intervention. Operative Findings were noted down, and appendix biopsies were sent for histopathology. Patient's progress was followed till their discharge. Histopathology reports were retrieved to detect histological types of appendicitis in relation to the NLR ratio.

Data was entered and analyzed via SPSS v26. For continuous variables such as age and leukocyte count, the mean and standard deviation were determined, while

frequencies and percentages will be reported for categorical variables. The cut-off values for NLR were calculated via the receiver operating characteristic curve (ROC), and sensitivity and specificity were estimated for the respective cut-off values with their corresponding 95% confidence intervals. Comparisons were drawn via Chi square's test of independence for categorical variables. Fischer's Exact test is used if the Chi-square assumptions are unmet. When analyzing continuous data, the Mann-Whitney U test was used for non-normally distributed data, and the independent sample t-test for normally distributed data. Results were stratified based on age, gender, and other potential confounding variables, and post-stratification analyses were performed. A significant p-value is less than 0.05.

Results

Table 1 shows the clinical and demographic attributes of the study participants in the study groups. The majority of the participants in all three study groups were males. Mean ± S. D of the participants' neutrophil levels in both study groups were 42.8±5.1, 119.27±8.5, and 59.9±6.61 (%) (P value <0.0001). Mean ± S. D of the participants' neutrophil to leucocyte ratio in all three study groups were 4.8±0.7, 10.42±1.32, and 5.36±0.49 (P value <0.0001). The majority of the participants in both groups underwent an appendectomy to treat complicated and uncomplicated acute appendicitis. Figures 1-3 and Table 2 show the ROC curve of WBC and NLR for distinguishing between acute and complicated appendicitis, with the AUC of 0.599 and 1.000, respectively.

Table 1: Comparison of clinical and demographic characteristics of the study participants in the study groups. :

Parameters	Negative appendectomy (n=6)	Complicated (N=11)	Uncomplicated (n=48)	P-Value
Age (years)	31.3±6.4	28.18±5.19	27.7±4.7	0.251
Gender				0.006
Male	4 (67%)	6 (55%)	27 (56%)	
Female	2 (33%)	5 (45%)	21 (35%)	
HB (g/dL)	12±0.89	12.09±1.04	11.9±1.2	0.9116
WBCs (x10 ³ /μL)	9±0.8	11.54±1.43	11.2±1.28	<0.0001
Neutrophils (%)	42.8±5.1	119.27±8.5	59.9±6.61	<0.0001
NLR	4.8±0.7	10.42±1.32	5.36±0.49	<0.0001
Thrombocyte (x10 ³ /μL)	224±11.0	328.9±17.21	257.7±27.28	<0.0001
CRP (mg/L)	0.81±0.09	6.9±1.04	4±1.07	<0.0001
Abdominal Ultrasound				0.341
Visualized	4 (66%)	10 (91%)	29 (60%)	
Not Visualized	2 (34%)	1 (9%)	19 (40%)	
Surgical Approach				0.096
Appendectomy (Grid iron)	5 (83%)	8 (73%)	26 (54%)	
Laparoscopy	1(16%)	1 (9%)	7 (14%)	
Laparotomy	0	2 (18%)	15 (31%)	

Table 2: ROC curve for the diagnosis of complicated appendicitis

Parameters	AUC	95% CL		Cut off	Sensitivity	Specificity	P value
		Upper limit	Lower limit				
NLR	1.000	99.8	58.7	>8	90.91	100	<0.0001
WBCs	0.599	0.719	0.470	>9.9	100	16.7	0.256

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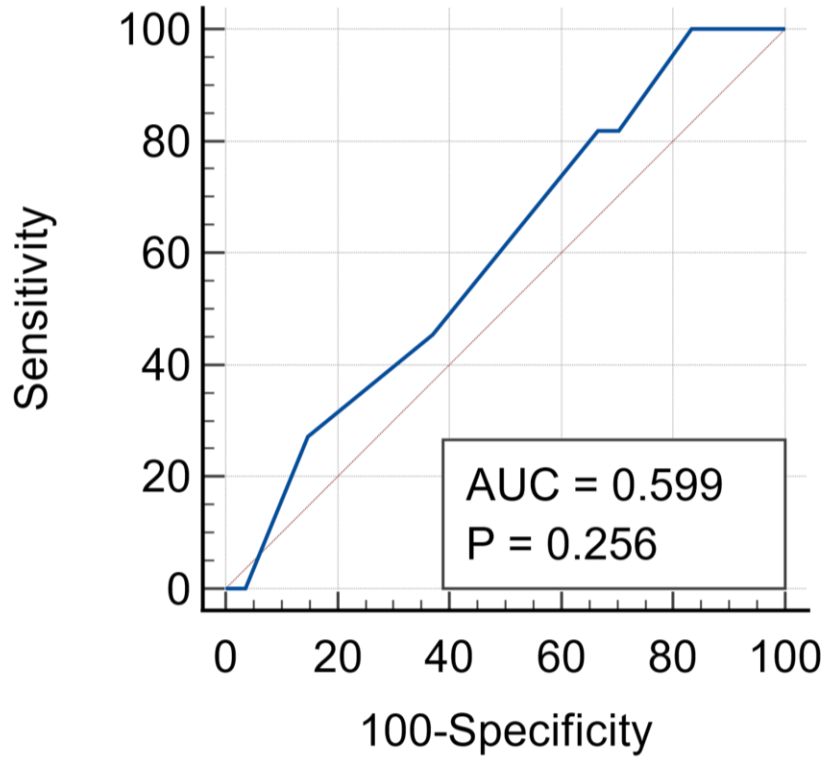


Figure 1: ROC analysis of WBC for differentiating simple from complicated appendicitis, with the AUC of 0.599.

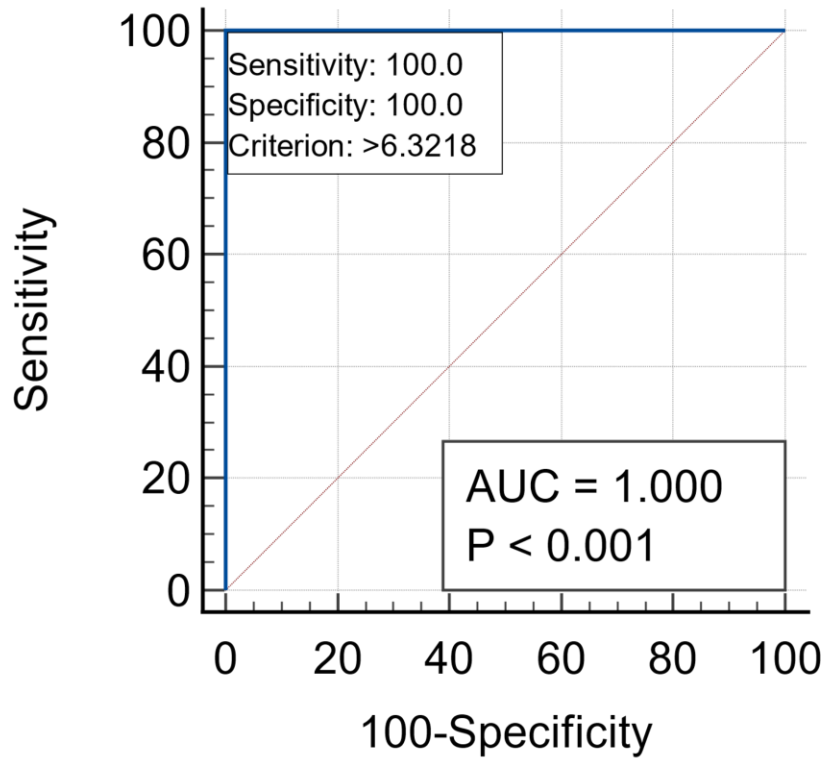


Figure 2: ROC curve of NLR for differentiating superficial from complicated appendicitis, with the AUC of 1.000.

Discussion

Acute appendicitis is a widely recognized cause of acute abdomen (Hajibandeh et al., 2020) and necessitates urgent surgical intervention (Boshnak et al., 2018). The diagnosis of acute appendicitis is made using imaging techniques and scoring systems for laboratory tests, although it is essential to acknowledge that some instances may encounter complications due to the challenges and delays in diagnosis (Ünal, 2018; Yılmaz et al., 2017).¹ This study was conducted to establish the predictive value of NLR in diagnosing cases of complicated appendicitis and to differentiate between simple and complex appendicitis in our local population.

Multiple studies have shown raised levels of NLR in acute appendicitis as a reliable marker in diagnosing cases of acute appendicitis (Ahmed et al., 2019; Akyüz et al., 2020; Hajibandeh et al., 2020; Zarog et al., 2023). We analyzed the importance of NLR in differentiating between simple and complicated appendicitis in our study and found that patients with complicated appendicitis had NLR of >8.0 with a sensitivity of 90.1% and specificity of 100%, which is comparable with other studies (Bălănescu et al., 2022; Sengul et al., 2020). Sengul et al. showed higher sensitivity of NLR than WBC, CRP, and NEU for diagnosing complicated appendicitis in adolescents (Sengul et al., 2020). NLR is not only raised in adolescents with complicated appendicitis but in the pediatric groups also, as proved by many studies (Ayeeni et al., 2022; Bălănescu et al., 2022).

The leukocyte count has been extensively investigated as a laboratory measurement and early indicator in individuals with AA, while the rise in leukocyte levels in non-complicated appendicitis (NCA) is a fact (Ayeeni et al., 2022). However, its role in diagnosing cases of complicated appendicitis (CA) has been debatable. In a retrospective analysis by Oymaci et al., a WBC count of >13.6 was associated with the risk of complicated appendicitis with the sensitivity of 63.4% and specificity of 81.1% (Oymaci et al., 2023). However, in a recent cross-sectional study by Mekrugsakit et al., WBC failed to show an association with CA with the sensitivity of 62% and specificity of 50% (Mekrugsakit and Tullavardhana, 2023). Similarly, Yokoyama et al. have documented that the count of white blood cells (WBCs) and the determination of neutrophil percentage lack utility in surgical indication in cases of appendicitis (Yokoyama et al., 2009). In their study, the values of WBCs were almost the same in complicated and uncomplicated appendicitis. In our research, WBC count did not show a significant correlation with cases of complicated appendicitis (p value= 0.26). These findings further support the significance of NLR as probably the most important indicator in diagnosing patients of CA.

Appendicitis is primarily diagnosed on clinical assessment. Over the last few decades, the use of Ultrasonography and various biochemistry markers have been assessed for aiding in correct diagnosis. Nowadays, CT is also widely used for pre-operative imaging in atypical cases. Lastly, the advent of Diagnostic laparoscopy ± Appendectomies greatly enhances the surgeon's ability to minimize rates of negative appendectomies. As in our study, the rate of negative appendectomy is 9.2%. According to some studies, the use of all these resources can reduce the rate of negative appendectomies. However, using these resources can pose a

significant financial burden on the general population. In a developing country like ours, the availability of CT and adequate laparoscopic exposure is also concerning. In such cases, bio-markers like that of NLR can aid in accurate and timely diagnoses.

Another area of concern is patients in whom the use of imaging techniques is limited, for example, pregnant patients, patients with psychosocial issues, etc. Appendicitis is one of the most typical cause of non-obstetrical emergency surgery (Mukherjee and Samanta, 2019)¹. However, diagnoses of appendicitis in such cases is challenging due to unusual deviation of the appendix due to growing uterus and risk of radiation exposure in the pregnant female. Studies have shown that the use of NLR in pregnant females can effectively diagnose cases of appendicitis and reduce the incidence of misdiagnosis and associated worse outcomes (Peksöz et al., 2022).

The interest in treating uncomplicated appendicitis conservatively is also growing. Various authors have reported promising hospital-based conservative treatment results for uncomplicated cases (Iftikhar et al., 2021; Naik, 2021; Yang et al., 2019). This paradigm is importance in reducing surgery and anesthesia-induced morbidity to patients and reducing surgical burden in an overly-packed surgical theatres like those in our country. This issue can be addressed with a high sensitivity and specificity of NLR for diagnosing simple and particularly complicated appendicitis as reported in our study. Patients with NLR values raised > 8.0 with a risk of complicated appendicitis can be operated on earlier.

One of the most significant limitation of our study is that it was carried out at a single Centre with a small sample size. We also did not include the population of <16 and >40 years old, so it cannot tell about the effects of age on NLR's ability to diagnose complicated appendicitis. Also, we eliminated people with co-morbidities and pregnancy in our study population. These are potential areas where further studies with a much bigger sample size could be carried out.

Conclusion

This study found that NLR has a very strong predictive value for diagnosing cases of complicated appendicitis in our local population.

Declarations

Data Availability statement

All data generated or analyzed during the study are included in the manuscript.

Ethics approval and consent to participate.

Approved by the department Concerned. (IRB-3056/DUHS/Approval2023/290).

Consent for publication

Approved

Funding

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Conflict of interest

The authors declared an absence of conflict of interest.

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