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Original Research Article

Neutrophil-lymphocyte ratio as a severity predictor in acute appendicitis

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ABSTRACT

Background: Acute appendicitis is a frequent surgical admission that requires timely diagnosis and swift treatment. While the gold-standard diagnostic modality is CT scan, some healthcare settings cannot offer imaging to all patients. Resource-limited hospitals have to make a diagnosis of acute appendicitis on a combination of physical exam and laboratory results. The neutrophil-to-lymphocyte ratio (NLR) is a simple and cost-effective marker of subclinical inflammation, easily calculated from white blood cell differential counts.
Methods: A retrospective analysis was conducted on medical records of patients diagnosed with acute appendicitis between 2021 and 2022 at a Tertiary Referral Center in Mexico. Leukocyte and lymphocyte counts were studied to establish the NLR and its association with the severity and stage of appendicitis with post-surgical pathology outcomes.
Results: The 362 patients were included for analysis. NLR was greater in patients with complicated acute appendicitis ($p<0.001$). Specificity and sensitivity for diagnosis of any severity of disease were 78% and 53% while for prediction of complicated cases was 81% in sensitivity and specificity of 48%.
Conclusions: The present study demonstrated that the NLR is a valuable marker for diagnosing acute appendicitis and predicting its severity. A simple complete blood count provides a cost-effective option for vulnerable populations and healthcare systems.

Keywords: Acute appendicitis, Severity predictor, Neutrophil-lymphocyte ratio

INTRODUCTION

Acute appendicitis remains one of the most common causes of emergency surgical admissions worldwide, necessitating prompt diagnosis and timely intervention to prevent adverse outcomes. The lifetime risk of developing appendicitis approaches 10%, and approximately 20% of these cases progress to a complicated form, associated with increased morbidity and prolonged hospitalization. Early identification and appropriate management of these severe cases are therefore imperative. Traditionally, the diagnosis has relied on a combination of clinical evaluation and imaging modalities.[1] Nevertheless, numerous studies

have explored the utility of adjunctive tools to enhance diagnostic accuracy, particularly in equivocal presentations.[2] These tools acquire greater relevance in resource-limited settings, where access to advanced imaging may be constrained or where healthcare systems experience episodic overload.

Several clinical scoring systems have been developed to aid in the diagnosis of acute appendicitis, including the Alvarado and RIPASA scores.[3] However, no single biochemical, hematological, or clinical parameter has demonstrated consistent reliability in predicting disease severity, length of hospital stay, or the likelihood of postoperative complications.[4,5] Current literature suggests that laboratory investigations primarily serve to reinforce clinical suspicion in typical cases rather than definitively exclude the diagnosis. Among the most frequently evaluated biomarkers are total leukocyte count, absolute neutrophil count, and C-reactive protein (CRP), given their widespread availability and established role in reflecting the systemic inflammatory response.[6]

NLR has emerged as a promising, cost-effective inflammatory marker, derived from routine differential leukocyte counts.[7] As index reflecting balance between innate immune activation (neutrophilia) and adaptive immune suppression (lymphopenia), NLR may provide more nuanced depiction of systemic inflammation.[8,9] This dual-pathway insight potentially enhances its utility not only in diagnosing acute appendicitis but also in stratifying disease severity. Nonetheless, generalizability and diagnostic performance of NLR across diverse populations remain under investigation.

In the present study, we report the findings of a one-year retrospective analysis of patients undergoing appendectomy at a low-resource, single-institution center in Latin America. Our objective was to evaluate the feasibility and diagnostic reliability of the NLR as a predictor of complicated acute appendicitis in this specific clinical and socioeconomic context.

METHODS

Following institutional ethics approval, a retrospective observational study was conducted at Hospital Metropolitano, a Tertiary Referral Center in Mexico. Adult patients (≥18 years) who underwent surgery for suspected acute appendicitis between August 2021 and August 2022 were included.

Patients were classified based on intraoperative and histopathological findings into five diagnostic categories: follicular lymphoid hyperplasia, edematous, suppurative, gangrenous, and perforated appendicitis. These were subsequently grouped into two broader categories: uncomplicated appendicitis (follicular lymphoid hyperplasia and edematous appendicitis) and complicated appendicitis (gangrenous and perforated appendicitis). The primary objective was to evaluate the correlation between the preoperative NLR the independent variable and the severity of appendicitis, as defined by the postoperative pathological diagnosis considered the dependent variable.

Electronic medical records were reviewed to extract demographic, clinical, laboratory, operative, and outcome data. Statistical analyses were performed using SPSS version 29.0 (SPSS Inc., Chicago, IL, USA) and R version 4.3.1 (R Core Team, Vienna, Austria). Continuous variables were expressed as means with standard deviations (SD) and compared using the student's t test for normally distributed data. For non-normally distributed variables, the Mann-Whitney U test was used, and results were reported as medians and ranges. Categorical variables were presented as frequencies and percentages and compared using the chi-square test. A two-tailed $p<0.05$ was considered statistically significant.

To assess the predictive value of NLR for complicated appendicitis, receiver operating characteristic (ROC) curves were constructed using the empirical model via the "ROCit" and "pROC" packages in R. The area under the curve (AUC), optimal cut-off values, sensitivity, and specificity were determined.

Postoperative complications including pneumonia, sepsis, intra-abdominal abscess, acute kidney injury, atelectasis, and mortality were documented and included in the analysis of clinical outcomes.

Inclusion and exclusion criteria, patients were included if they underwent appendectomy with a preoperative clinical diagnosis of acute appendicitis and had complete demographic, laboratory, and histopathological data available in their medical records. Exclusion criteria comprised patients with missing laboratory or histopathology reports, those with chronic inflammatory or hematologic diseases, immunosuppression, active malignancy, or ongoing corticosteroid or cytotoxic drug therapy, as these conditions could alter inflammatory markers such as the NLR. Patients who underwent incidental appendectomy during another surgical procedure were also excluded.

RESULTS

A total of 362 patients met the inclusion criteria and were included in the final analysis. No statistically significant differences were observed in baseline demographic or clinical characteristics between patients with uncomplicated versus complicated acute appendicitis. Variables assessed included age, sex, body mass index (BMI≥30), history of uncontrolled hypertension, active tobacco use, and alcohol consumption ($p>0.05$). Detailed demographic data are presented in Table 1.

The mean duration of symptoms prior to medical attention was 51.14 hours (± SD), equivalent to

approximately 2.13 days. Regarding diagnostic imaging, 47 patients (13.0%) underwent computed tomography (CT), 130 (35.9%) underwent ultrasonography, and 6 (1.7%) had plain abdominal radiographs. Notably, 179 patients (49.5%) were diagnosed clinically without the aid of imaging studies.

Surgical approach was laparoscopic in 120 cases (33.1%) and open in 242 cases (66.9%). Postoperative recovery was managed on an outpatient basis in 74 patients (20.4%), while the remaining 288 (79.6%) required hospitalization. The mean intraoperative blood loss was 30 mL, and the average postoperative length of hospital stay was 1.6 days.

Patients with histopathologically confirmed acute appendicitis exhibited significantly higher mean NLR levels than those without histological evidence of the disease ($p<0.001$). Furthermore, patients with complicated appendicitis had a mean NLR that was 4.33 units higher than those with uncomplicated disease ($p<0.001$). No statistically significant differences in NLR values were observed in relation to postoperative complications, need for reoperation, postoperative drainage, or hospital readmission ($p>0.05$) Complete results of the NLR comparisons are shown in Table 2.

ROC curve analysis was performed using histopathological diagnosis as the reference standard. For overall acute appendicitis, NLR yielded an AUC of 0.67 (95% CI: 0.59-0.74), with a Youden Index cut-off of 8.8 (specificity: 78%, sensitivity: 53%).

For complicated appendicitis, AUC was 0.68 (95% CI: 0.62–0.73), with a cut-off of 6.5 (sensitivity: 81%, specificity: 48%). The ROC curves with corresponding AUC values and optimal thresholds for both diagnostic scenarios are depicted in Figure 1 A and B, respectively.

Using histopathological findings as the gold standard, 316 patients (87.3%) were confirmed to have acute appendicitis. Among these, 85 cases (23.5%) were classified as perforated, 74 (20.4%) as gangrenous, 123 (34.0%) as suppurative, and 34 (9.4%) as edematous. There were 44 cases (12.2%) of follicular lymphoid hyperplasia and 2 cases (0.6%) of neoplasms.

A total of 44 patients (12.5%) developed postoperative complications. These included 11 surgical site infections (3.0%), 3 cases of healthcare-associated pneumonia (0.8%), 7 instances of postoperative sepsis (1.9%), 17 intra-abdominal abscesses (4.7%), 1 case of acute kidney injury (0.3%), and 5 cases of atelectasis (1.4%). Eleven patients (3.0%) required reoperation, 9 (2.5%) of which were for surgical drainage. Four additional patients (1.1%) underwent percutaneous drainage. Ten patients (2.8%) required hospital readmission, and no mortalities were recorded during the study period.

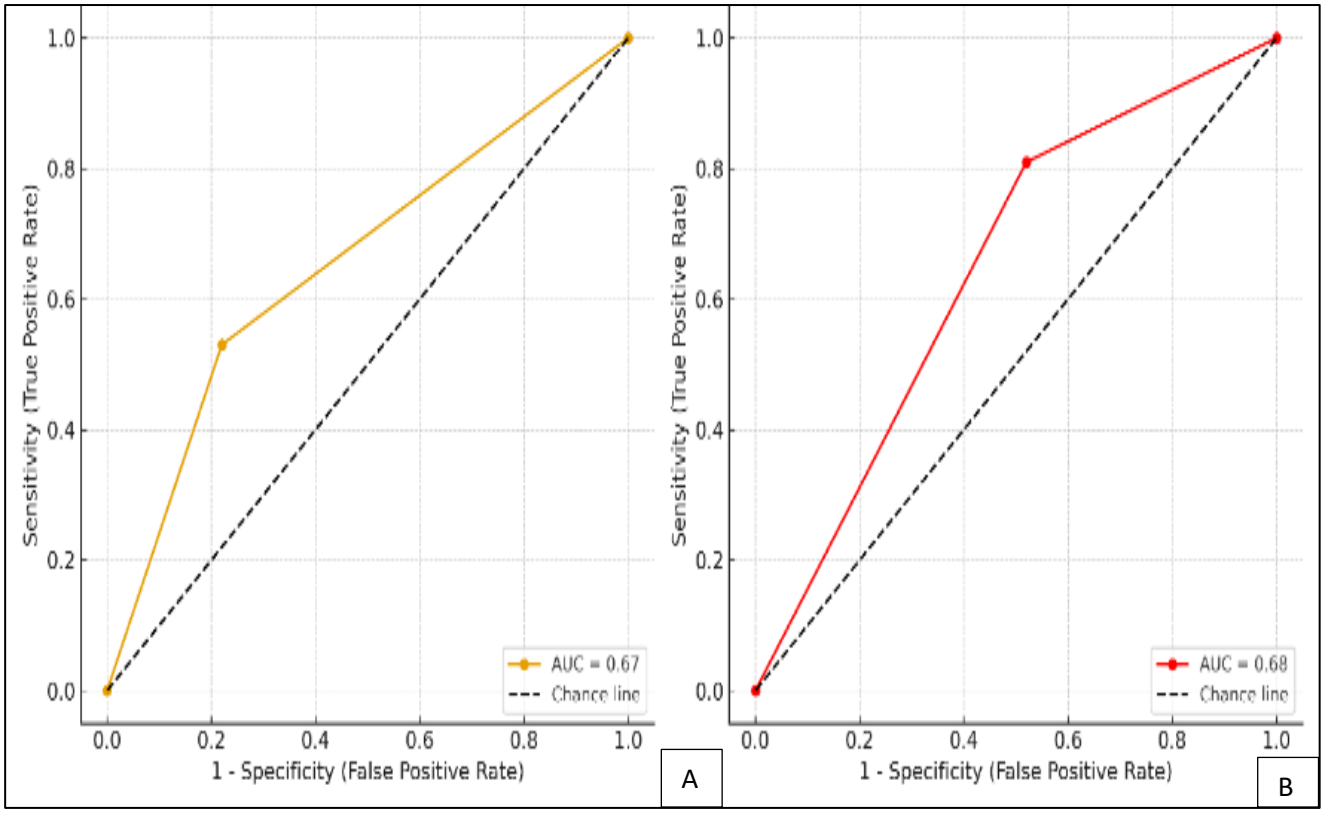

Figure 1 (A and B): A: ROC curve illustrating the diagnostic accuracy of NLR for acute appendicitis (any severity). B: ROC curve demonstrating the diagnostic performance of NLR for complicated acute appendicitis.

Table 1: Baseline demographic and clinical characteristics of patients with uncomplicated and complicated acute appendicitis.

Variables	Uncomplicated acute appendicitis, (n=203)	Complicated acute appendicitis, (n=159)	P value
Age, (in years), mean (±SD)	28.2 (±12.4)	28.5 (±12.6)	0.79
Sex-male	122 (60%)	90 (56%)	0.50
BMI ≥ 30	16 (8%)	15 (9%)	0.60
Uncontrolled HTN	5 (2%)	3 (2%)	1
T2DM	10 (5%)	10 (6%)	0.57
Active smoking	49 (24%)	42 (26%)	0.62
Alcohol abuse[a]	41 (20%)	38 (23%)	0.39

[a]Greater than the CDC recommended maximum of 2 drinks a day for males and 1 for females. T2DM=type 2 diabetes mellitus, HTN=hypertension, BMI = body-mass index.

Table 2. Comparison of mean neutrophil-to-lymphocyte ratio (NLR) according to clinical outcomes and histopathological findings in acute appendicitis.

Variables	Binary outcome of variable	Mean (±SD) NLR	Mean difference and 95% CI	P value
Postoperative complications	Yes	13.79 (±10.53)	-3.23 (-7.6 - 1)	0.05
	No	10.56 (±7.96)		
Acute appendicitis by histology	Yes	11.30 (±8.35)	-4.069 (-6.06- -2.07)	<0.001
	No	7.24 (±5.98)		
Complicated acute appendicitis	Yes	13.22 (±8.99)	-4.33 (-6.04- -2.62)	<0.001
	No	8.88 (±6.95)		
Readmission	Yes	15.07 (±13.30)	-4.4 (-9.5-0.74)	0.09
	No	10.66 (±7.99)		
Reoperation	Yes	14.95 (±7.7)	-4.2 (-9.1-0.654)	0.08
	No	10.65 (±8.1)		
Postop drain	Yes	22.49 (±18.25)	-11.95 (-40.96-17.04)	0.28
	No	10.54 (±7.9)		

DISCUSSION

Our findings demonstrate that the NLR is significantly elevated in patients with complicated acute appendicitis when compared to those with uncomplicated presentations. This association was also evident when evaluating NLR as a supportive tool for the diagnosis of acute appendicitis. While the ROC curve analysis revealed only moderate diagnostic performance, the practical value of NLR lies primarily in stratifying disease severity rather than establishing a definitive diagnosis.

This has particular relevance in resource-limited settings, where advanced imaging modalities such as computed tomography may not be readily accessible. Uncomplicated acute appendicitis has been shown to be amenable to conservative antibiotic management in selected cases.[10-12] In contrast, complicated appendicitis is associated with higher morbidity, increased risk of sepsis, and worse perioperative outcomes.[13] Thus, early identification of patients with complicated disease is paramount to guide timely surgical intervention. The higher sensitivity observed at a lower NLR cut-off point for complicated appendicitis suggests that NLR may help identify high-risk patients in such scenarios, albeit at the expense of specificity.

Contrary to some earlier studies, we did not find a significant association between NLR and postoperative complications, reoperations, or hospital readmissions.[4] This indicates that while NLR may be useful for preoperative risk stratification, it does not appear to predict postoperative outcomes reliably. For postoperative risk evaluation, tools such as the ACS NSQIP surgical risk calculator may provide greater prognostic accuracy.

Our findings are consistent with previous investigations into the diagnostic utility of NLR in appendicitis. Ishizuka et al reported a significant association between elevated NLR and gangrenous appendicitis, albeit using a narrower definition of complicated disease.[14] In our study, both gangrenous and perforated appendicitis were included, allowing for a broader clinical spectrum. Although our optimal threshold for complicated appendicitis (NLR=6.5) was lower than the value reported by Ishizuka et al (NLR=8.0), the overall

diagnostic performance was similar. This variation may reflect differences in patient populations, healthcare settings, or study design.

Some authors have reported correlations between elevated NLR and prolonged hospital stay.[2] However, in our cohort, no such relationship was observed. These discrepancies may stem from institutional differences in perioperative management, discharge criteria, or sample size variability.

While NLR offers a cost-effective and accessible adjunct in clinical decision-making, particularly in under-resourced environments, it should not supplant imaging-based diagnostics, which remain the gold standard. When imaging is unavailable or inconclusive, NLR may serve as a helpful biomarker within a broader clinical and laboratory framework.

Limitations

This study is subject to the limitations inherent to retrospective analyses. First, the observational and single-center design may affect generalizability. Second, only a single NLR value at presentation was considered, and no dynamic measurements were assessed. Third, although histopathological classification strengthens validity, variability in surgical and pathological interpretation may exist. Finally, despite statistically significant findings, the modest AUC and low specificity highlight the limitations of NLR as a standalone diagnostic tool.

CONCLUSION

The NLR is a simple, accessible adjunct that may aid in the diagnosis and severity stratification of acute appendicitis, especially in settings where advanced imaging is limited. However, it should be interpreted as part of a comprehensive clinical assessment and not as a replacement for imaging or expert judgment.

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