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PROGNOSTIC UTILITY OF THE NEUTROPHIL–LYMPHOCYTE RATIO IN PREDICTING SEVERITY AND COMPLICATIONS OF ACUTE APPENDICITIS: A HOSPITAL-BASED ANALYTICAL STUDY

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ABSTRACT
Background: Acute appendicitis remains one of the most common surgical emergencies worldwide, with disease severity ranging from mild inflammation to perforation and gangrene. Early identification of patients at risk for severe or complicated appendicitis is crucial to reduce morbidity and optimize surgical decision-making. Conventional laboratory parameters such as total leukocyte count have shown inconsistent prognostic performance, necessitating evaluation of derived inflammatory markers. The neutrophil–lymphocyte ratio (NLR), obtained from routine complete blood counts, reflects systemic inflammatory response and may offer prognostic value in acute appendicitis.
Objectives: To calculate the neutrophil–lymphocyte ratio manually from complete blood count parameters in patients with acute appendicitis and to assess its utility in predicting disease severity and complications based on histopathological outcomes.
Methods: A hospital-based analytical study was conducted in a tertiary care teaching hospital over one year, including 71 adult patients who underwent emergency appendectomy for clinically suspected acute appendicitis. Preoperative absolute neutrophil and lymphocyte counts were obtained at admission, and NLR was calculated manually. Histopathological examination served as the reference standard and categorized appendicitis into moderate and severe forms, with complicated appendicitis defined by perforation or gangrene. Receiver operating characteristic curve analysis was used to determine the prognostic performance of NLR, and sensitivity, specificity, and area under the curve were calculated.
Results: Histopathological confirmation of appendicitis was observed in 90.1% of cases, while 9.9% were early or non-diagnostic. Complicated appendicitis accounted for 23.94% of cases. An NLR cut-off ≥5.7 predicted severe appendicitis with an area under the curve of 0.998, sensitivity of 96.15%, and specificity of 100%. An NLR cut-off >11.6 predicted complicated appendicitis with an area under the curve of 0.991, sensitivity of 100%, and specificity of 98.18%. NLR showed limited discriminatory ability for early appendicitis.
Conclusion: The neutrophil–lymphocyte ratio is a highly reliable prognostic marker for predicting severity and complications in acute appendicitis, though it has limited value in identifying early disease. Given its simplicity, low cost, and universal availability, NLR can serve as a valuable adjunct to clinical and radiological assessment for early risk stratification, particularly in resource-limited settings.

KEYWORDS: Appendicitis, Neutrophil-Lymphocyte Ratio, Disease Severity, Inflammation, Prognosis, Appendectomy.

INTRODUCTION
PAcute appendicitis is one of the most common surgical emergencies encountered worldwide and continues to account for a substantial proportion of emergency abdominal surgeries. Standard surgical textbooks describe acute appendicitis as an inflammatory condition of the vermiform appendix, most commonly initiated by luminal obstruction that leads to bacterial overgrowth, ischemia, and progressive transmural inflammation [1]. Despite being a well-recognized clinical entity, appendicitis remains diagnostically challenging due to its variable presentation and unpredictable disease course.
Recent evidence suggests that clinical practice does not consistently adhere to established appendicitis management guidelines, contributing to heterogeneity in diagnostic and therapeutic approaches across institutions [2]. This inconsistency underscores the persistent uncertainty in accurately stratifying disease severity at initial presentation. Laboratory investigations have traditionally supported clinical decision-making; however, commonly used markers such as total leukocyte count and C-reactive protein demonstrate variable diagnostic performance, particularly when correlated

with symptom duration [3]. These limitations highlight the need for more reliable biomarkers that reflect the underlying inflammatory burden.

From an anatomical and developmental perspective, the appendix is derived from the midgut and is rich in lymphoid tissue, making it particularly susceptible to inflammatory responses [4,5]. Obstruction caused by lymphoid hyperplasia, fecaliths, or less commonly anatomical anomalies can trigger acute inflammation, which may either remain localized or progress to gangrene and perforation. The biological variability in disease progression complicates early risk stratification.

Epidemiologically, the global burden of acute appendicitis remains significant. Population-based data from the United States have demonstrated changing trends over time, with a relative decline in non-perforated appendicitis but persistent rates of perforated disease, suggesting that severe appendicitis continues to contribute substantially to morbidity [6]. Such findings imply that improvements in early diagnosis may not necessarily translate into proportional reductions in complicated disease.

In the Indian context, acute appendicitis predominantly affects adolescents and young adults, with a consistent male predominance. A retrospective study from North-East India demonstrated notable seasonal variation and highlighted delayed presentation as a major contributor to disease severity [7]. These observations are particularly relevant in low- and middle-income countries, where disparities in healthcare access, diagnostic facilities, and referral pathways remain common.

Modern understanding recognizes appendicitis as a spectrum rather than a binary condition. Contemporary literature emphasizes that uncomplicated and complicated appendicitis represent biologically distinct entities with different prognostic implications [8]. Histopathological correlation studies have shown that laboratory parameters often overlap between uncomplicated appendicitis, complicated appendicitis, and reactive lymphoid hyperplasia, thereby limiting the discriminatory value of conventional blood tests [9]. Additionally, structural abnormalities such as appendiceal diverticula, intussusception, and fecaliths have been associated with increased risk of inflammation and complications [10].

Management strategies for acute appendicitis have evolved substantially over the past decade. Meta-analyses have demonstrated that selected cases of non-perforated appendicitis can be managed conservatively with antibiotics, challenging the long-standing paradigm of mandatory appendectomy [11]. Large randomized trials have further supported non-operative management in carefully selected patients, although recurrence and failure rates remain concerns [12]. These evolving strategies place even greater emphasis on accurate prognostic assessment at presentation.

Notably, the natural history of appendicitis is heterogeneous. Earlier observational studies suggested that some cases may resolve spontaneously without surgical intervention, reinforcing the concept that not all appendicitis follows a uniform progressive course [13,14]. However, the inability to reliably predict which patients will progress to perforation remains a major limitation in conservative management strategies.

Randomized clinical trials evaluating antibiotic therapy for uncomplicated appendicitis have demonstrated acceptable short-term outcomes but have also emphasized the critical importance of excluding complicated disease prior to non-operative management [15]. Misclassification of disease severity can result in delayed surgery and increased morbidity, particularly in resource-limited settings.

In this context, there is a clear need for simple, cost-effective, and universally available prognostic markers that can assist in early risk stratification. Conventional laboratory parameters alone are insufficient to reliably predict disease severity or outcomes. Derived inflammatory indices, particularly those reflecting systemic immune response, offer potential advantages over isolated cell counts.

The neutrophil-to-lymphocyte ratio has emerged as a promising biomarker that integrates innate immune activation and stress-related lymphocyte suppression. Given its availability from routine complete blood counts, it represents a practical tool in emergency surgical settings. However, despite increasing interest, there remains limited high-quality evidence correlating neutrophil-to-lymphocyte ratio values with histopathological severity and operative outcomes, especially within the Indian population.

Therefore, the present study was undertaken to evaluate the prognostic utility of the neutrophil-to-lymphocyte ratio in patients with acute appendicitis. By correlating NLR values with histopathological severity and intraoperative findings, this study aims to determine whether NLR can serve as a reliable predictor of disease outcome. Establishing such a marker could aid early decision-making, optimize surgical timing, and potentially reduce morbidity associated with complicated appendicitis, particularly in settings where advanced imaging may not be readily available.

METHODOLOGY

This hospital-based analytical study was conducted in the Department of General Surgery at a tertiary care teaching hospital over a period of one year, from January 2024 to January 2025, after obtaining approval from the Institutional Ethics Committee. A total of 71 consecutive adult patients aged 18–80 years who presented with clinically suspected acute appendicitis and subsequently underwent emergency appendectomy were included in the study after obtaining informed written consent. Patients with other concurrent acute inflammatory or infectious conditions, chronic inflammatory disorders, immunosuppressive illnesses, malignancy, or those below 18 years and above 80 years of age were excluded to avoid confounding of inflammatory markers. The sample size was determined based on feasibility and case load during the study period, and was considered adequate for prognostic accuracy analysis using receiver operating characteristic (ROC) curves, as similar diagnostic accuracy studies evaluating neutrophil–lymphocyte ratio in acute appendicitis have reported reliable estimates with sample sizes ranging from 50 to 100 patients. Demographic details, duration of symptoms, clinical findings, and ultrasonography reports were recorded prospectively. Preoperative laboratory parameters were retrieved from electronic medical records, including total leukocyte count, absolute neutrophil count, and absolute lymphocyte count obtained at the time of admission prior to surgical intervention. The neutrophil-to-lymphocyte ratio (NLR) was manually calculated by dividing the absolute neutrophil count by the absolute lymphocyte count. All patients underwent appendectomy, and intraoperative findings were documented by the operating surgeon, with specific note of perforation or gangrenous changes. Resected appendiceal specimens were subjected to histopathological examination, which served as the reference standard for diagnosis and severity assessment. Based on histopathological findings, appendicitis was categorized into moderate disease, defined by inflammation confined up to the subserosal layer, and severe disease, defined by transmural inflammation extending to the serosa; complicated appendicitis was defined by the presence of perforation or gangrene. Statistical analysis was performed using IBM SPSS version 23. Continuous variables were summarized using mean with standard deviation or median with interquartile range as appropriate, while categorical variables were expressed as frequencies and percentages. Receiver operating characteristic curve analysis was employed to evaluate the prognostic performance of NLR in differentiating moderate versus severe appendicitis and complicated versus uncomplicated appendicitis, and optimal cut-off values were derived based on maximum Youden index. Sensitivity, specificity, and area under the curve (AUC) with 95% confidence intervals were calculated, and a p value of <0.05 was considered statistically significant.

Results :

Table 1. Demographic Profile of the Study Population (n = 71)

Variable	Frequency	Percentage (%)
Age group (years)		
≤18	3	4.2
19–30	29	40.8
31–40	24	33.8
>40	15	21.1
Sex		
Male	45	63.4
Female	26	36.6

Table 2. Disease Outcome and Prognostic Categories

Outcome variable	Frequency (n = 71)	Percentage (%)
Histopathologically confirmed appendicitis	64	90.1
Early / non-diagnostic appendicitis	7	9.9
Uncomplicated appendicitis	54	76.06
Complicated appendicitis (overall)	17	23.94
• Perforated appendix	16	22.53
• Gangrenous appendix	1	1.40

Table 3. Histopathological Severity Distribution (Prognostic Stratification)

Histopathological severity (n = 64)	Frequency	Percentage (%)
Moderate appendicitis	38	53.52
Severe appendicitis	26	36.62
Total	64	100

Table 4. Prognostic Performance of N:L Ratio for Severity Prediction

Prognostic comparison	N:L ratio cut-off	AUC	95% CI	Sensitivity (%)	Specificity (%)	p value
Moderate vs Severe appendicitis	≥5.7	0.998	0.946–1.000	96.15	100	<0.001

Table 5. Prognostic Performance of N:L Ratio for Complicated Appendicitis

Prognostic outcome	N:L ratio cut-off	AUC	95% CI	Sensitivity (%)	Specificity (%)	p value
Complicated vs Uncomplicated appendicitis	>11.6	0.991	0.932–1.000	100	98.18	<0.001

Table 6. Summary of N:L Ratio Cut-offs and Prognostic Utility

Clinical outcome predicted	N:L ratio cut-off	AUC	Sensitivity (%)	Specificity (%)
Early appendicitis vs appendicitis	>3.12	0.563	53.13	83.33
Moderate vs severe appendicitis	>5.7	0.998	96.15	100

Complicated vs uncomplicated appendicitis	>11.6	0.991	100	98.18

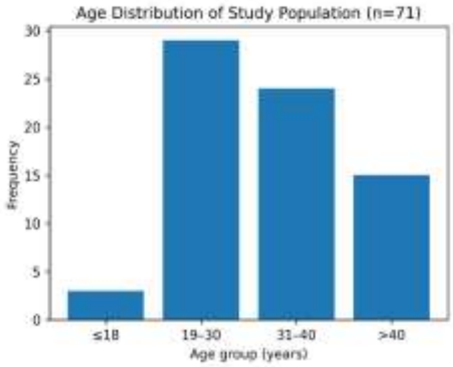

Figure 1 : Age Distribution of the Study Population (n = 71)

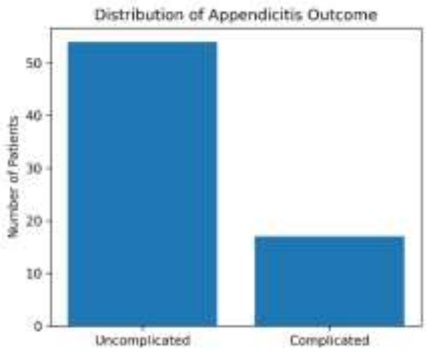

Figure 2 : Distribution of Complicated vs Uncomplicated Appendicitis

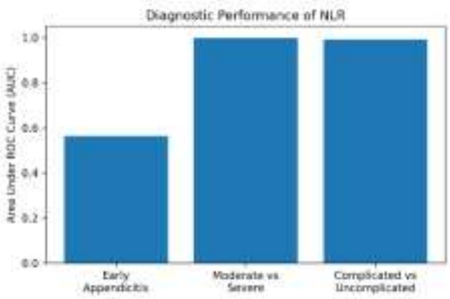

Figure 3 : Diagnostic Performance of NLR (AUC Comparison)

DISCUSSION

The present study evaluated the prognostic utility of the neutrophil–lymphocyte ratio (NLR) in acute appendicitis and demonstrated that NLR is a highly reliable marker for predicting disease severity and complications, though it showed limited discriminatory ability for early appendicitis. According to the 2020 update of the World Society of Emergency Surgery (WSES) Jerusalem guidelines, early identification of complicated appendicitis is critical, as perforation and gangrene are associated with increased postoperative morbidity and prolonged hospital stay [16]. In the current study, complicated appendicitis constituted 23.94% of cases, with 22.53% perforated and 1.40% gangrenous appendicitis, figures that fall within the complication range acknowledged by WSES but highlight the continued burden of advanced disease at presentation.

Delay in surgical intervention is a major determinant of appendiceal complications. A meta-analysis by van Dijk et al. involving over 37,000 patients reported that in-hospital delays beyond 24 hours were associated with a significant increase in perforation risk, with pooled odds ratios ranging from 1.6 to 2.3, depending on delay duration [17]. While the present study did not formally quantify in-hospital delay, the proportion of severe appendicitis (36.62%) and complicated appendicitis (23.94%) suggests that delayed presentation and progression remain clinically relevant. The excellent prognostic performance of NLR in this study provides a potential tool to mitigate the impact of such delays by enabling early identification of high-risk patients.

Negative appendectomy remains an important quality indicator in appendicitis management. Seetahal et al., in a 10-year national review, reported a negative appendectomy rate of 11.83%, with higher rates in females [18]. In comparison, the present study reported histopathological confirmation of appendicitis in 90.1% of cases, with 9.9% classified as early or non-diagnostic appendicitis, indicating a slightly lower negative appendectomy rate than that reported by Seetahal et al.

However, the NLR in the present study showed poor performance for early appendicitis (AUC 0.563, sensitivity 53.13%, specificity 83.33%), confirming that NLR alone cannot be used to reduce negative appendectomy rates and aligning with the conclusions of Seetahal et al. that no single parameter is sufficient for diagnosis.

The limited prognostic value of conventional laboratory tests has been well documented. Chen et al. demonstrated that total leukocyte count and imaging findings showed considerable overlap between uncomplicated and complicated appendicitis, limiting their predictive accuracy for disease severity [19]. While Chen et al. did not report NLR-specific cut-offs, their findings support the present observation that isolated laboratory values lack discriminatory power. In contrast, the present study showed that a derived inflammatory index, NLR, could clearly differentiate disease severity, with an AUC of 0.998 for moderate versus severe appendicitis, highlighting a key advantage over traditional parameters.

Imaging-based diagnostic approaches have also shown limitations in severity prediction. Al-Faouri et al. reported that CT had higher diagnostic accuracy than the Alvarado score, with diagnostic accuracy exceeding 90%, but did not reliably differentiate uncomplicated from complicated appendicitis [20]. This limitation mirrors the present study, where imaging contributed to diagnosis but prognostic stratification was achieved primarily through NLR, particularly at higher cut-offs. The inability of CT to predict biological severity reinforces the relevance of inflammatory biomarkers.

Probabilistic diagnostic models comparing CT and ultrasonography have further highlighted contextual variability. Cochon et al. demonstrated that imaging accuracy was highly dependent on pre-test probability, with Bayesian modeling showing fluctuating post-test probabilities across clinical scenarios [21]. These findings contrast with the present study, where NLR demonstrated consistent prognostic accuracy independent of imaging modality, particularly for severe and complicated disease.

Concerns regarding imaging-related adverse effects also influence diagnostic strategies. Sonhaye et al. reported that contrast-induced nephropathy occurred in up to 11% of emergency CT scans in high-risk patients [22]. While the present study did not assess imaging-related complications, the availability of NLR as a non-invasive, cost-effective prognostic marker provides a clinically valuable alternative, especially in patients where contrast-enhanced CT is contraindicated.

Global observational data from the POSAW study reported complicated appendicitis rates ranging between 20% and 30%, with higher rates in low- and middle-income countries [23]. The 23.94% complication rate observed in the present study lies squarely within this range, supporting the external validity of the cohort. Importantly, the POSAW study did not evaluate NLR-based prognostication, whereas the present study demonstrated that an NLR >11.6 predicted complicated appendicitis with 100% sensitivity and 98.18% specificity, providing novel prognostic insight beyond epidemiological reporting.

Clinical scoring systems have been extensively studied but show variable performance. A systematic review by Bai et al. reported pooled sensitivity of approximately 85% and specificity as low as 43% for the Alvarado score in children, limiting its utility for severity prediction [24]. Although pediatric populations differ from adults, these findings parallel adult studies where Alvarado scoring performs poorly in prognostic discrimination. In contrast, the present study achieved near-perfect specificity (100%) for severe appendicitis using NLR ≥5.7.

Similarly, Kanumba et al. reported that the modified Alvarado score had a sensitivity of 91% but specificity of only 50% for appendicitis diagnosis in Tanzania, with limited ability to identify complicated disease [25]. This contrasts sharply with the present study, where NLR demonstrated 98.18% specificity for complicated appendicitis, highlighting its superiority as a prognostic marker in resource-limited settings.

The Appendicitis Inflammatory Response (AIR) score was developed to improve severity prediction. Von-Mühlen et al. reported sensitivity of 90% and specificity of 85% for severe appendicitis using AIR score thresholds [26]. While these values are clinically acceptable, they remain inferior to the 96.15% sensitivity and 100% specificity achieved by NLR for severe appendicitis in the present study. This comparison underscores the incremental value of NLR over composite scoring systems.

Earlier WSES guidelines cautioned against reliance on scoring systems alone due to inconsistent performance across populations [27]. Subsequent accuracy studies confirmed that while scoring systems aid diagnosis, their prognostic value is limited [28]. The present study supports these conclusions by demonstrating that NLR, a single derived marker, outperforms multi-parameter scores in prognostic stratification.

RIPASA scoring has been advocated for Asian populations. Mumtaz et al. reported sensitivity of 96.7% and specificity of 82.3% for appendicitis diagnosis but did not demonstrate reliable differentiation between uncomplicated and complicated disease [29]. A meta-analysis by Frountzas et al. further confirmed that while RIPASA improves diagnostic sensitivity compared to Alvarado scoring, neither score provides robust prognostic discrimination for complications [30]. In contrast, the present study demonstrated that NLR >11.6 achieved AUC 0.991, with 100% sensitivity for complicated appendicitis, clearly outperforming existing scoring systems.

LIMITATIONS

The present study has certain limitations that should be considered while interpreting the findings. First, this was a single-center hospital-based study conducted in a tertiary care setting, which may limit the generalizability of the results to primary or secondary care centers, where patient profiles, disease severity at presentation, and diagnostic resources may differ. Second, the sample size, although adequate for receiver operating characteristic (ROC) curve analysis and comparable to similar prognostic accuracy studies, remains relatively modest, particularly for subgroup analyses such as gangrenous appendicitis, which was observed in a small number of patients. This may have influenced the precision of estimates for rare outcomes.

Third, the study included only patients who underwent appendectomy, and therefore findings may not be applicable to patients managed conservatively with antibiotics. Biochemical or pre-clinical appendicitis cases that resolved without surgery were not included, potentially introducing selection bias toward more clinically evident disease. Fourth, the neutrophil–lymphocyte ratio was measured only at the time of admission, and serial changes in NLR during the disease course were not evaluated, which could have provided additional prognostic insight.
Fifth, although histopathological examination was used as the reference standard for severity classification, interobserver variability in pathological interpretation could not be entirely excluded. Finally, multivariate analysis adjusting for potential confounders such as symptom duration and comorbidities was limited by sample size, and residual confounding cannot be ruled out. Despite these limitations, the study provides robust preliminary evidence supporting the prognostic value of NLR in acute appendicitis.

CONCLUSION

The present study demonstrates that the neutrophil–lymphocyte ratio is a highly effective prognostic marker for predicting disease severity and complications in patients with acute appendicitis. While NLR showed limited utility in identifying early or non-diagnostic appendicitis, it exhibited excellent discriminatory performance in differentiating moderate from severe appendicitis and in predicting complicated appendicitis, including perforation and gangrene. The derived cut-off values showed high sensitivity and specificity, indicating that NLR reliably reflects the underlying inflammatory burden and disease progression.
These findings have important clinical implications, particularly in emergency surgical settings where rapid decision-making is essential. Given that NLR is inexpensive, readily available from routine blood investigations, and does not require additional resources, it can serve as a valuable adjunct to clinical assessment and imaging. Incorporation of NLR into initial evaluation protocols may aid early risk stratification, facilitate timely surgical intervention for high-risk patients, and potentially reduce morbidity associated with delayed treatment.
Importantly, the study reinforces that NLR should not be used as a standalone diagnostic tool for acute appendicitis but rather as a prognostic marker to complement existing diagnostic modalities. In resource-limited settings, where access to advanced imaging may be constrained, NLR may provide critical support in identifying patients at risk for severe or complicated disease.
In conclusion, the neutrophil–lymphocyte ratio represents a simple, reliable, and clinically meaningful prognostic marker in acute appendicitis. Further multicenter studies with larger sample sizes and inclusion of conservatively managed patients are warranted to validate these findings and to refine standardized cut-off values for broader clinical application.

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