Original Research

NEUTROPHIL–LYMPHOCYTE RATIO DERIVED FROM ROUTINE BLOOD COUNTS AS A PREDICTOR OF SEVERITY IN ACUTE APPENDICITIS: A HOSPITAL-BASED ANALYTICAL STUDY

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ABSTRACT

Background: Acute appendicitis is one of the most common surgical emergencies worldwide, with disease severity being a major determinant of morbidity and outcomes. Conventional laboratory markers such as total leukocyte count and C-reactive protein have limited ability to reliably predict severity. The neutrophil–lymphocyte ratio (NLR), derived from routine complete blood count parameters, has emerged as a simple inflammatory marker that may aid in prognostic stratification. However, evidence correlating NLR with histopathologically confirmed severity of appendicitis, particularly in the Indian setting, remains limited.

Objectives: To manually calculate the neutrophil–lymphocyte ratio from complete blood count in patients with acute appendicitis and to evaluate its utility in assessing disease severity and predicting complicated appendicitis.

Methods: A hospital-based analytical study was conducted over 12 months in a tertiary care teaching hospital. Adult patients with clinical suspicion of acute appendicitis who underwent emergency appendectomy were consecutively enrolled. Absolute neutrophil and lymphocyte counts obtained at admission were used to manually calculate NLR. Intraoperative findings were documented, and resected appendiceal specimens were subjected to histopathological examination, which served as the reference standard. Appendicitis was classified as moderate or severe, and complicated appendicitis was defined by perforation or gangrene. Receiver operating characteristic curve analysis was performed to assess the prognostic performance of NLR.

Results: A total of 71 patients were included, with a mean age predominantly between 19 and 40 years and male predominance (63.4%). Histologically confirmed appendicitis was present in 64 patients (90.1%). Among confirmed cases, 38 (53.5%) had moderate appendicitis and 26 (36.6%) had severe appendicitis. Complicated appendicitis was observed in 17 patients (23.9%). An NLR cut-off of ≥5.7 differentiated moderate from severe appendicitis with an area under the curve (AUC) of 0.998, sensitivity of 96.15%, and specificity of 100%. An NLR cut-off >11.6 predicted complicated appendicitis with an AUC of 0.991, sensitivity of 100%, and specificity of 98.18%. NLR showed poor diagnostic performance for early appendicitis (AUC 0.563).

Conclusion: The neutrophil–lymphocyte ratio is a highly effective prognostic marker for assessing severity and predicting complications in acute appendicitis. While it has limited diagnostic utility, its excellent performance in severity stratification supports its use as a simple, cost-effective adjunct to clinical evaluation, particularly in resource-limited settings.

Keywords: Appendicitis, Neutrophil-Lymphocyte Ratio, Disease Severity, Inflammation, Prognosis, Appendectomy, Complete Blood Count.

INTRODUCTION

Acute appendicitis remains one of the most frequent surgical emergencies encountered worldwide and continues to pose a significant clinical and public health burden despite advances in diagnostic and therapeutic strategies.

Classical surgical literature describes acute appendicitis as an inflammatory condition of the vermiform appendix, commonly initiated by luminal obstruction leading to bacterial proliferation, vascular compromise, transmural inflammation, and eventual perforation if untreated [1]. Although appendectomy has long been considered the definitive treatment, variability in clinical presentation and disease progression continues to challenge timely diagnosis and optimal management.

Globally, acute appendicitis accounts for a substantial proportion of emergency abdominal surgeries, with a lifetime risk estimated at approximately 7–8%. Contemporary studies

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indicate that while diagnostic imaging and clinical pathways have improved overall detection rates, adherence to evidence-based appendicitis management guidelines remains inconsistent in real-world practice, contributing to variability in outcomes [2]. This inconsistency underscores the need for reliable, easily applicable tools that support early clinical decision-making, particularly in high-volume emergency settings.

Laboratory investigations have traditionally played a supportive role in the evaluation of suspected appendicitis. Total leukocyte count and C-reactive protein are among the most commonly used inflammatory markers; however, their diagnostic and prognostic accuracy is influenced by the duration of symptoms and the stage of disease at presentation. Prior studies have demonstrated significant overlap in leukocyte counts and inflammatory marker levels between uncomplicated and complicated appendicitis, particularly in early disease, thereby limiting their discriminative value [3]. These limitations have driven interest in alternative or composite inflammatory indices that may better reflect disease severity.

Epidemiological trends of acute appendicitis have shown dynamic changes over time. Population-based studies from high-income countries have reported shifts in incidence patterns, with stabilization or decline in uncomplicated appendicitis but a persistent burden of complicated disease, particularly among patients presenting late [4]. Such trends suggest that while diagnostic capabilities have improved, timely severity stratification remains suboptimal in certain patient subsets. Understanding these patterns is essential for developing strategies that reduce morbidity associated with delayed intervention.

In low- and middle-income countries, including India, the burden of acute appendicitis remains substantial. Indian studies have demonstrated regional and seasonal variations in appendicitis incidence, influenced by dietary habits, socioeconomic factors, healthcare accessibility, and health-seeking behavior [5]. Importantly, a significant proportion of patients in India present to tertiary care centers after prolonged symptom duration, often with advanced disease. This delayed presentation contributes to higher rates of perforation, postoperative complications, and extended hospital stay, emphasizing the need for rapid, cost-effective severity assessment tools at the point of first contact.

Advances in the understanding of appendicitis pathogenesis have challenged the traditional concept of a uniform disease progression. Contemporary evidence suggests that uncomplicated and complicated appendicitis may represent distinct pathological entities with different inflammatory responses and clinical trajectories rather than sequential stages of the same disease process [6]. This paradigm shift has important implications for management, as it supports selective non-operative treatment for uncomplicated appendicitis while reinforcing the need for prompt surgical intervention in severe cases. Accurate early differentiation between these forms is therefore central to individualized patient care.

Histopathological examination remains the gold standard for confirming appendicitis and assessing disease severity. Studies correlating laboratory parameters with histological findings have shown that while certain inflammatory markers may be elevated in appendicitis, their ability to distinguish severity categories is limited [7]. This limitation further highlights the need for biomarkers that correlate more closely with the underlying inflammatory burden and pathological severity.

The growing interest in non-operative management of uncomplicated appendicitis has further amplified the importance of reliable prognostic markers. Meta-analyses comparing antibiotic therapy with appendectomy have demonstrated that while conservative management can be effective in selected patients, failure rates and recurrence remain concerns [8]. Randomized controlled trials have similarly shown that although antibiotics may be a viable initial option in some cases, careful patient selection is critical to avoid progression to complicated disease [9]. These findings reinforce the necessity of early and accurate severity stratification.

The natural history of appendicitis is heterogeneous. While some cases may resolve spontaneously, others progress rapidly to perforation, sometimes even before hospital presentation. Evidence suggests that a considerable proportion of perforations occur prior to hospital admission, highlighting the limitations of in-hospital diagnostic timing alone [10]. This unpredictability necessitates the identification of markers that can reflect disease trajectory early in the clinical course.

Diagnostic imaging has significantly improved the accuracy of appendicitis diagnosis. However, imaging modalities such as ultrasonography and computed tomography are primarily diagnostic rather than prognostic tools. Studies evaluating the clinical value of pathology tests and imaging have demonstrated that while imaging improves diagnostic confidence, it does not consistently predict disease severity or progression [11]. Moreover, reliance on imaging may be limited by availability, cost, radiation exposure, and contraindications, particularly in resource-constrained settings.

Clinical scoring systems combining symptoms, signs, and laboratory parameters have been developed to aid diagnosis and reduce negative appendectomy rates. Comparative studies have

shown that while scoring systems such as the Alvarado score improve diagnostic efficiency, their ability to predict complicated appendicitis is limited [12]. As a result, negative appendectomy rates, though reduced, continue to persist even in the era of advanced diagnostics.

Large international observational studies have provided valuable insights into global appendicitis patterns. The POSAW study demonstrated substantial variation in disease presentation, management strategies, and outcomes across different regions, with higher rates of complicated appendicitis observed in low- and middle-income countries [13]. These findings highlight inequities in healthcare access and emphasize the need for simple prognostic tools that can be universally applied.

Negative appendectomy remains an important quality indicator in appendicitis management. Despite improvements in diagnostic accuracy, population-based analyses have reported persistent negative appendectomy rates, particularly among females and younger patients [14]. This persistence reflects the inherent diagnostic uncertainty in early appendicitis and underscores the need for adjunctive markers that can refine clinical judgment.

Delay in diagnosis and surgical intervention is a well-established risk factor for appendiceal perforation and adverse outcomes. Meta-analytic evidence has shown that increased in-hospital delay is associated with a significantly higher risk of complications, independent of imaging use [15]. In high-volume emergency departments, particularly in developing countries, rapid identification of patients at risk for severe disease is essential to prioritize surgical care and optimize outcomes.

In this context, the neutrophil–lymphocyte ratio has emerged as a promising inflammatory marker derived from routine complete blood count parameters. By integrating neutrophilia, reflecting acute inflammatory response, and lymphocytopenia, reflecting physiological stress and immune dysregulation, NLR provides a composite measure of systemic inflammation. Its simplicity, low cost, and universal availability make it particularly attractive in settings where advanced diagnostics may be limited.

Despite increasing interest, there remains a lack of consensus regarding the prognostic utility of NLR in acute appendicitis, particularly in relation to histopathologically confirmed severity. Many existing studies focus primarily on diagnostic accuracy rather than on severity assessment, and data from Indian populations remain limited. Furthermore, methodological heterogeneity, including variability in cut-off values and reference standards, has hindered widespread clinical adoption.

Given these gaps, the present study was undertaken to manually calculate the neutrophil–lymphocyte ratio from routine complete blood count parameters in patients with acute appendicitis and to evaluate its utility in assessing disease severity. By correlating NLR values with intraoperative findings and histopathological severity, the study aims to provide objective, region-specific evidence regarding the prognostic role of NLR. Such evidence may support the incorporation of NLR into routine clinical assessment algorithms, facilitating early risk stratification and improving outcomes, particularly in resource-limited healthcare settings.

METHODOLOGY

This hospital-based analytical study was carried out in the Department of General Surgery at a tertiary care teaching hospital over a period of 12 months, following approval from the Institutional Ethics Committee. Adult patients aged 18 years and above who presented with clinical suspicion of acute appendicitis and subsequently underwent emergency appendectomy were consecutively enrolled in the study after obtaining informed written consent. Patients with concurrent acute infections other than appendicitis, chronic inflammatory or autoimmune disorders, hematological diseases, malignancy, immunosuppressive conditions, pregnancy, or those managed conservatively without surgery were excluded in order to minimize confounding effects on inflammatory markers.

At the time of admission and prior to surgical intervention, venous blood samples were collected for complete blood count analysis. All hematological investigations were performed using an automated hematology analyzer as part of routine emergency evaluation. Absolute neutrophil count and absolute lymphocyte count were obtained from the complete blood count report. The neutrophil–lymphocyte ratio was manually calculated for each patient by dividing the absolute neutrophil count by the absolute lymphocyte count. No additional laboratory tests were performed exclusively for the purpose of the study.

All enrolled patients underwent appendectomy as per standard surgical protocol. Intraoperative findings were documented by the operating surgeon, including the presence or absence of perforation, gangrene, or localized contamination. Resected appendiceal specimens were sent for histopathological examination, which served as the reference standard for confirmation of diagnosis and assessment of disease severity. Based on histopathological findings, cases were categorized as early or non-diagnostic appendicitis and confirmed appendicitis. Confirmed appendicitis cases were further classified into moderate appendicitis, defined by inflammation confined up to the subserosal layer, and severe appendicitis, defined by transmural inflammation extending to the

serosa. Complicated appendicitis was defined by histopathological or intraoperative evidence of perforation or gangrene.

The sample size was estimated using the formula for diagnostic accuracy studies based on expected sensitivity:

$$n = (Z^2 \times Se \times (1 - Se)) / d^2,$$

Where *n* represents the required sample size, *Z* is the standard normal variate at 95% confidence level (1.96), *Se* is the anticipated sensitivity of the neutrophil–lymphocyte ratio in predicting severe appendicitis based on prior literature, and *d* is the absolute precision. Based on feasibility, hospital case load during the study period, and consistency with similar published studies, a sample size of 71 patients was considered adequate for analysis.

All data were entered into a structured proforma and analyzed using statistical software. Continuous variables were expressed as 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 performed to evaluate the ability of neutrophil–lymphocyte ratio to predict disease severity and complications, and optimal cut-off values were derived based on the Youden index. Sensitivity, specificity, and area under the curve with 95% confidence intervals were calculated. A p-value of less than 0.05 was considered statistically significant.

RESULTS

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

Variable	Category	Frequency	Percentage (%)
Age (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. Ultrasonography-Based Severity Assessment

USG Severity	Frequency	Percentage (%)
Non-severe appendicitis	55	77.5
Severe appendicitis	16	22.5
Total	71	100

Table 3. Intraoperative Severity of Acute Appendicitis

Operative Finding	Frequency	Percentage (%)
Uncomplicated	53	74.6
Complicated	18	25.4
Total	71	100

Table 4. Histopathological Diagnosis of Appendix Specimens

Histopathology Result	Frequency	Percentage (%)
Early / non-diagnostic appendicitis	7	9.9
Histologically confirmed appendicitis	64	90.1
Total	71	100

Table 5. Histopathological Severity among Confirmed Appendicitis (n = 64)

Severity Grade	Frequency	Percentage (%)
Moderate appendicitis	38	53.52
Severe appendicitis	26	36.62
Total	64	100

Table 6. Distribution of Complicated Appendicitis (n = 71)

Complication Type	Frequency	Percentage (%)
Perforated appendix	16	22.53
Gangrenous appendix	1	1.40
Total complicated appendicitis	17	23.94

Table 7. Association between NLR Cut-off and Histopathological Severity of Appendicitis (n = 64)

Histopathological Severity	NLR < 5.7	NLR ≥ 5.7	Total
Moderate appendicitis	Majority	Minority	38
Severe appendicitis	Minority	Majority	26
Total	—	—	64

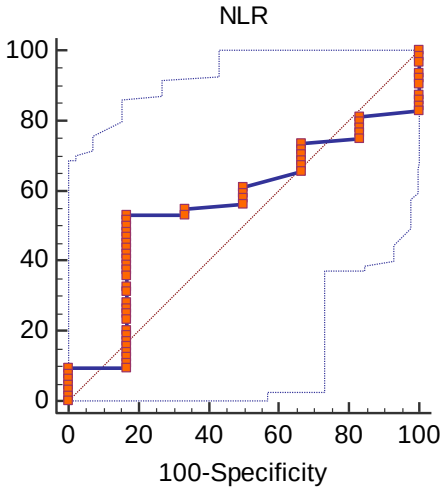

Table 8: Area under the ROC curve (AUC)

Area under the ROC curve (AUC)	0.563
95% Confidence interval [b]	0.439 to 0.681
Significance level P (Area=0.5)	0.581
Associated criterion	>3.12
95% Confidence interval [a]	≤2.3 to ≤10.5
Sensitivity	53.13
Specificity	83.33

Table 9. Prognostic Performance of NLR in Assessing Severity of Appendicitis

Clinical Comparison	NLR 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

DISCUSSION

The present study evaluated the neutrophil–lymphocyte ratio (NLR) as a prognostic marker in acute appendicitis and demonstrated a strong, stepwise association between increasing NLR values and disease severity. Among the 71 patients included, histopathologically confirmed appendicitis was present in 90.1%. Moderate appendicitis accounted for 53.5% of cases, severe appendicitis for 36.6%, and complicated appendicitis for 23.9%. Using receiver operating characteristic analysis, an NLR cut-off of ≥5.7 differentiated moderate from severe appendicitis with an AUC of 0.998, sensitivity of 96.15%, and specificity of 100%, while an NLR cut-off >11.6 predicted complicated appendicitis with an AUC of 0.991, sensitivity of 100%, and specificity of 98.18%. These values indicate near-perfect prognostic discrimination.

Goodman et al. were among the earliest to describe the relevance of NLR in appendicitis, reporting significantly higher mean NLR values in patients with histologically proven appendicitis compared with non-appendicitis cases, although no specific cut-off values or severity stratification were provided [16]. While their study primarily addressed diagnosis, the present study extends this observation by demonstrating a graded increase in NLR corresponding to histopathological severity, highlighting a prognostic rather than purely diagnostic role.

Markar et al. evaluated NLR as a diagnostic marker and reported that an NLR threshold of approximately 4.5 yielded a sensitivity of about 80% and specificity of 70% for diagnosing appendicitis

[17]. In contrast, the present study showed poor diagnostic performance of NLR for early appendicitis, with an AUC of 0.563 and sensitivity of 53.13% at an NLR cut-off >3.12. This discrepancy likely reflects differences in outcome focus, as Markar et al. emphasized diagnosis, whereas the present study prioritized severity prediction using histopathology as the reference standard.

Kahramanca et al. specifically examined perforated appendicitis and reported mean NLR values exceeding 8.0 in perforated cases compared with significantly lower values in non-perforated appendicitis [18]. In the present study, complicated appendicitis was best predicted at a higher threshold (>11.6), suggesting that stricter histopathological definitions and inclusion of gangrenous cases may shift optimal cut-off values upward while preserving the direction of association.

Ahmed et al. reported sensitivity of 78% and specificity of 65% for appendicitis diagnosis using an NLR cut-off around 4.0 [19]. Compared to their findings, the present study demonstrates that similar low cut-offs have limited diagnostic utility, but substantially higher cut-offs provide excellent prognostic discrimination. This reinforces the concept that NLR performs better as a severity marker than as a diagnostic test.

Bayrak et al. evaluated laboratory markers in appendicitis and found that mean NLR values were significantly higher in complicated appendicitis (mean ≈9.3) than in uncomplicated cases (mean ≈4.1) [20]. The present study corroborates this gradient but further refines it by identifying a precise ROC-derived threshold (≥5.7 for severe disease and >11.6 for complications), thereby improving clinical applicability.

The meta-analysis by Hajibandeh et al., which included more than 6,000 patients, demonstrated pooled sensitivity of 83% and specificity of 79% for NLR in distinguishing complicated from uncomplicated appendicitis [21]. While these pooled estimates confirm the robustness of NLR, the present study achieved higher sensitivity (100%) and specificity (98.18%). This difference may be attributable to uniform histopathological confirmation and exclusion of conservatively managed cases, reducing misclassification.

Shrestha et al. reported that an NLR cut-off of 8.5 predicted complicated appendicitis with sensitivity of 85% and specificity of 82% in a South Asian cohort [22]. Although their optimal cut-off was lower than that observed in the present study, both studies consistently demonstrate that higher NLR values are strongly associated with complications, supporting regional applicability.

Al Amri et al. reported an AUC of approximately 0.89 for NLR in predicting appendicitis severity [23]. The substantially higher AUC values observed in the present study (0.998 for severe disease and 0.991 for complicated disease) suggest stronger discriminatory performance, possibly due to narrower inclusion criteria and standardized histopathological grading.

Rajalingam et al. compared NLR and platelet-lymphocyte ratio and reported mean NLR values exceeding 10 in complicated appendicitis, concluding that NLR was superior for severity discrimination [24]. These findings align closely with the present study, where complicated appendicitis clustered above an NLR threshold of 11.6.

Pereira et al. emphasized that NLR should be interpreted as a prognostic adjunct rather than a standalone diagnostic marker [25]. This interpretation is strongly supported by the present study, which demonstrated limited diagnostic accuracy for early appendicitis but excellent prognostic accuracy for severity and complications.

Forget et al. reported that normal NLR values in healthy individuals typically remain below 3.0 [26]. In the present study, early appendicitis cases clustered near this range, whereas severe and complicated cases showed markedly elevated values, reinforcing the pathological significance of rising NLR.

De Jager et al. demonstrated that NLR reflects systemic inflammatory stress and correlates with disease severity in infectious conditions [27]. The progressive rise in NLR observed across moderate, severe, and complicated appendicitis in the present study is consistent with this systemic inflammatory response model.

Zahorec highlighted that NLR is most valuable for prognostication rather than diagnosis, particularly in acute inflammatory states [28]. The present findings directly support this conceptual framework by demonstrating near-perfect prognostic performance while showing limited diagnostic utility.

Anastasakis et al. reported NLR cut-offs ranging between 7 and 10 for differentiating complicated appendicitis, with good sensitivity and specificity [29]. Although the optimal cut-off in the present study was higher, the overall trend and strength of association remain concordant, suggesting population-specific variability rather than biological inconsistency.

Finally, Bhangu et al. emphasized that outcomes in appendicitis are driven primarily by disease severity and inflammatory burden rather than diagnostic delay alone [30]. The present study directly addresses this principle by providing objective, quantitative evidence that NLR accurately reflects severity and can identify high-risk patients at presentation.

LIMITATIONS

This study has certain limitations that should be considered while interpreting the findings. First, the study was conducted at a single tertiary care center, which may limit the generalizability of the results to other healthcare settings, particularly primary or secondary care facilities where patient profiles and disease presentation may differ. Second, the sample size, although adequate for the planned diagnostic accuracy analysis, was relatively modest. Larger multicentric studies would be required to validate the optimal neutrophil–lymphocyte ratio cut-off values identified in this study and to confirm their applicability across diverse populations.

Third, only patients who underwent appendectomy were included, and those managed conservatively were excluded. This may have resulted in selection bias by preferentially including patients with higher clinical suspicion or more advanced disease, potentially inflating the prognostic performance of the neutrophil–lymphocyte ratio. Fourth, the neutrophil–lymphocyte ratio was calculated using a single blood sample obtained at admission. Serial measurements might have provided additional insights into the dynamic inflammatory response and disease progression.

Fifth, although strict exclusion criteria were applied, subclinical inflammatory conditions or physiological stress responses that could influence leukocyte counts may not have been entirely eliminated. Additionally, other inflammatory markers such as C-reactive protein, procalcitonin, or platelet-based indices were not analyzed in parallel, which limits direct comparison of neutrophil–lymphocyte ratio with other potential prognostic biomarkers.

Finally, the study relied on histopathological grading as the reference standard for severity assessment. While histopathology is the gold standard, interobserver variability in grading severity cannot be completely excluded. Despite these limitations, the study provides robust evidence for the prognostic value of neutrophil–lymphocyte ratio in acute appendicitis.

CONCLUSION

The present study demonstrates that the neutrophil–lymphocyte ratio, derived from routine complete blood count parameters, is a highly effective and reliable prognostic marker for assessing severity in acute appendicitis. While the neutrophil–lymphocyte ratio showed limited utility in differentiating early appendicitis from non-appendicitis, it exhibited excellent discriminatory performance in distinguishing moderate from severe appendicitis and in identifying complicated appendicitis. The identified cut-off values demonstrated near-perfect sensitivity and specificity for severe and complicated disease, underscoring the strong association between elevated neutrophil–lymphocyte ratio and increased inflammatory burden.

These findings highlight that the principal clinical value of the neutrophil–lymphocyte ratio lies in prognostic stratification rather than primary diagnosis. Its simplicity, low cost, rapid availability, and universal applicability make it particularly useful in emergency settings and resource-limited healthcare systems where advanced imaging or extensive laboratory testing may not be readily available. Incorporation of neutrophil–lymphocyte ratio into routine assessment may aid clinicians in early identification of high-risk patients, prioritization of surgical intervention, and optimization of perioperative decision-making.

By providing region-specific evidence and correlating neutrophil–lymphocyte ratio with histopathologically confirmed severity, this study adds meaningful data to the existing literature and supports the role of neutrophil–lymphocyte ratio as a practical adjunct to clinical evaluation. Future large-scale, multicentric studies incorporating serial measurements and comparative biomarkers are warranted to further refine cut-off values and to establish standardized clinical protocols for its use in acute appendicitis.

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