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Comparison of Cut-Off Value of Neutrophil to Lymphocyte Ratio in the Diagnosis of Non-Perforated Versus Perforated Appendix

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ABSTRACT

Neutrophil-To-Lymphocyte Ratio (NLR) gives diagnostic clue about non-perforated and perforated appendixes. However, there are many variations in its cut-off values in diagnosis of non-perforated and perforated appendixes, and there is no single value to differentiate severity of appendicitis. **Objective:** To determine the optimal NLR cutoff value for diagnosing perforated vs. non-perforated appendicitis in patients presenting with acute appendicitis. **Methods:** This comparative cross-sectional study was carried out at Surgical Department of Mayo Hospital, Lahore from July 2022 to January 2023. Total 105 patients with acute appendicitis undergoing open appendectomy were enrolled after written informed consent. The patients were grouped according to perforated and non-perforated appendicitis, and NLR value was compared in both groups. Continuous and categorical variables were presented as mean ± SD and frequency (%). **Results:** Non-perforated appendix group comprised 84 (80%) patients, whereas perforated appendix group comprised 21 (20%) patients. Mean NLR in perforated appendicitis group was higher as compared to non-perforated group (14.7 ± 12.6 vs. 7.36 ± 8.93, p = 0.01). Cut-off point for NLR was obtained at 5.71, with sensitivity and specificity noted was 66.7 % and 62%, respectively. **Conclusions:** The study highlighted the potential of NLR as predictive marker for distinguishing between perforated and non-perforated appendicitis. Its clinical utility is supported by identified cut-off value of 5.71, suggesting its role in aiding timely intervention and reducing complications.The findings reinforce the importance of NLR, particularly in identifying patients at higher risk of appendiceal perforation.

INTRODUCTION

Appendicitis, an acute inflammation of the appendix, most commonly occurs between ages 10 and 20 but can affect all age groups [1]. It has higher prevalence in males, with a male-to-female ratio of 1.4:1 [2]. It presents with periumbilical colicky pain that intensifies over 24 hours. As inflammation progresses, visceral pain transitions to somatic pain, leading to localized tenderness and peritoneal signs [3]. Classic symptoms occur in only 50% of cases, with vomiting (61–92%) and anorexia (74–78%) being common [4]. Acute appendicitis is linked to multiple factors, including obstruction, infection, diet, and socioeconomic status, with varying epidemiology between Western and Eastern societies [5]. Diagnosis is primarily clinical, with pain migration being a key indicator [3]. Surgery remains the standard treatment. In most cases of acute appendicitis, WBC count is elevated; however, its diagnostic specificity is limited, as many other conditions causing right lower quadrant pain can also lead to increased WBC levels [6]. Repeated WBC assessments over time may improve specificity, except in cases of perforation, where an initial drop may occur [7]. Neutrophilia is commonly observed and has predictive

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value, particularly in severe cases [8]. However, due to their limited specificity, WBC and differential leukocyte counts alone are not highly reliable for confirming appendicitis. NLR has emerged as a useful biomarker in distinguishing perforated from non-perforated appendicitis, aiding in early diagnosis and management decisions [9].

Recent studies have shown promising results for NLR in diagnosing and predicting complicated appendicitis in both pediatric and adult patients, but no consensus exists on its optimal cut-off value [10]. Thus, this study aims to determine the optimal NLR cut-off for predicting perforated versus non-perforated appendicitis. This study will be valuable to surgeons by aiding in early diagnosis and timely intervention, thereby improving patient outcomes and minimizing the risks of complications, morbidity, and mortality associated with appendicitis.

METHODS

This comparative cross-sectional study was conducted after taking ethical approval from IRB (No.18/RC/KEMU) at Department of General Surgery, Mayo Hospital, Lahore for duration of 6 months July 2022 to January 2023. Sample size of 105 patients was estimated using 95% confidence level and 30% absolute precision with expected sensitivity of Neutrophil to Lymphocyte ratio of 97.1%, expected specificity of 25.2%, expected sensitivity=97.1% and expected prevalence of acute appendicitis of 30% [11]. Patients were enrolled using non-probability convenient sampling. Before enrolment written consent was obtained from all patients or guardians. Patients of either gender aged between 13 to 60 years diagnosed having acute appendicitis (Alvarado score >7) were included. All patients having diagnosis of appendicitis with some other conditions like pregnancy, chronic liver or kidney disease, history of abdominal TB, or typhoid fever were excluded. Biodata and duration of symptoms was noted. The study incorporated detailed assessment of clinical presentation, laboratory parameters, and imaging findings. Clinical evaluation included symptoms such as abdominal pain, nausea, vomiting, fever, and localized tenderness. Laboratory parameters analyzed included complete blood count, and NLR was calculated from CBC report before undergoing appendectomy. All patients had open appendectomy under general anaesthesia using 5cm skin incision given at McBurney's point. The appendix was surgically removed and sent to the histopathology laboratory, where it was classified as perforated (showing perforation or gangrene at the tip, body, or base) or non-perforated (exhibiting hyperemic, edematous, or swollen wall without signs of perforation or gangrene). Data were analyzed using SPSS version 26.0. Quantitative variables were expressed as mean ± standard deviation, while qualitative variables were reported as frequencies and percentages. Diagnostic value of NLR was assessed through ROC analysis, and optimal cut-off value for predicting disease was determined based on highest accuracy of classification. Categorical variables were compared using chi-square test, whereas continuous variables using independent t-test, p-value of 0.050 was considered statistically significant. Prior to applying the independent t-test, normality of the data was assessed using the Shapiro-Wilk test and expected cell counts for all categories were greater than 5, satisfying the assumptions for the chi-square test.

RESULTS

As per findings of histopathology, division of the patients was done in two groups: where the group, having non-perforated appendix comprised of 84 patients (80%) whereas group having perforated appendix comprised of 21 patients (20%). Table 1 illustrates the comparison of sex and age between perforated and non-perforated appendicitis groups. Age was found to be comparable between perforated and non-perforated groups, 24.6 ± 10.7 years and 22.1 ± 7.8 years, respectively. Males comprised 57.1% of perforated appendicitis group, compared to 48.8% in non-perforated group. Females accounted for 49.2% in perforated group and 57.2% in non-perforated group (p = 0.490). Mean duration of symptoms was prolonged in perforated appendicitis patients 3.05 ± 2.08 days' vs 1.98 ± 2.25 days in non-perforated appendicitis patients, (p = 0.050). Abdominal pain was reported in 67% of patients with non-perforated appendicitis (n = 56), compared to 81% in perforated appendicitis group (n = 17) (p = 0.203). Nausea/vomiting occurred in 83% of on-perforated appendicitis group (n = 70), and 86% in perforated appendicitis group (n = 18) (p = 0.791).

Table 1: Comparison of Patients Related Characteristics between the Perforated and Non-Perforated Group (n = 105)

Variables	(Non-Perforated Appendix) Mean ± SD/ Frequency (%)	(Perforated Appendix) Mean ± SD/ Frequency (%)	p-Value
Age (Years)	22.1 ± 7.8	24.6 ± 10.7	0.310
Male	41 (48.8)	12 (57.1)	0.490
Female	43 (51.2)	9 (42.9)	
Duration of symptoms (Days)	1.98 ± 2.25	3.05 ± 2.08	0.050
Abdominal Pain	56 (67)	17 (81)	0.203
Nausea/Vomiting	70 (83)	18 (86)	0.791

As shown in table 2, mean NLR value was significantly higher in perforated appendicitis group (14.7 ± 12.6) compared to non-perforated group (7.36 ± 8.93) (p = 0.010). Significantly greater proportion of patients with perforated appendicitis (66.7%) had NLR values above predicted cut-off (5.71), whereas significantly larger number of patients with non-perforated appendicitis (61.9%) had NLR values below cut-off (p = 0.010).

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Table 2: Comparison of Neutrophil-to-Lymphocyte Ratio (NLR) in Patients with Non-Perforated and Perforated Appendicitis (n = 105)

NLR	Non-Perforated Appendix Frequency (%) /Mean ± SD	Perforated Appendix Frequency (%) /Mean ± SD	p-Value
>5.71	32 (38.1)	14 (66.7)	0.010
≤5.71	52 (61.9)	7 (33.3)	
Mean ± SD	7.36 ± 8.93	14.7 ± 12.6	0.010

Based on ROC curve (Figure 1), cut-off point for NLR was obtained at 5.71 with sensitivity of 66.7 % and specificity of 62 %. The area under the curve (AUC) for NLR was 73.1% (p = 0.001)(Table 3).

Table 3: ROC Analysis of Neutrophil-to-Lymphocyte Ratio (NLR) in Differentiating Perforated and Non-Perforated Appendicitis

Area	Standard Error[a]	Asymptotic Significant[b]	Asymptotic 95% Confidence Interval		Sensitivity	Specificity
			Lower Bound	Upper Bound		
0.731	0.056	0.001	0.622	0.840	66.7% (95% CI: 46.5% - 86.9%)	62% (95% CI: 51.6% - 72.4%)

[a] Under the nonparametric assumption; [b] Null hypothesis: true area = 0.5

In figure 1 ROC curve showed the diagnostic performance of NLR in distinguishing perforated from non-perforated appendicitis.

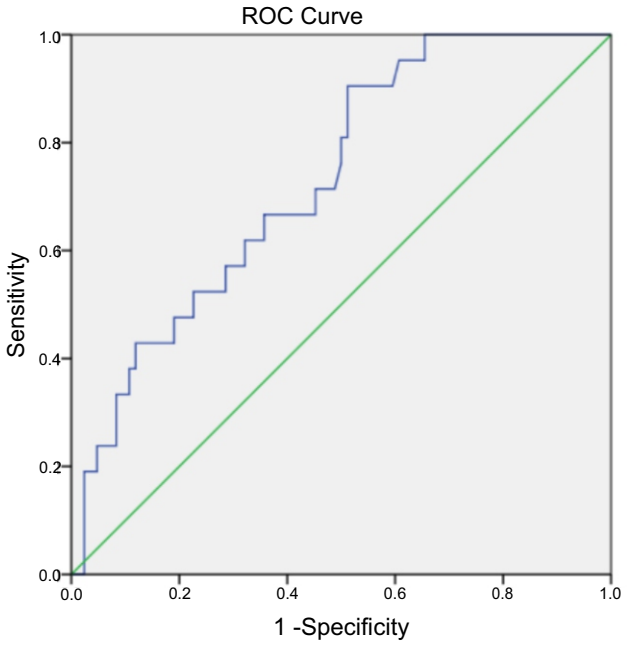


Figure 1: ROC Curve for NLR differentiating perforated and non-perforated appendicitis (N=105)

DISCUSSION

In the current study, the incidence of perforated appendicitis was found to be only 20%, while the remaining 80% had non-perforated appendicitis, in line with study conducted by Zeb *et al.*, in which 19.5% incidence of perforated appendix was observed [12]. However, Al Amri *et al.*, found higher proportion (31%) of patients to have perforated appendicitis [13]. In contrast, Ali *et al.*, found only 9% of patients with perforated appendicitis] [14]. Abdominal pain is universally reported symptom, with delayed presentation associated with higher risk of perforation.This aligns with the findings, where patients with perforated appendix had longer duration of symptoms compared to those with non-perforated appendicitis [15].

NLR has emerged as valuable biomarker in predicting perforated appendicitis, providing cost-effective alternative to imaging techniques, especially where resources are limited [16, 17]. In this study, mean NLR value was significantly higher in perforated appendicitis group (14.7 ± 12.6) compared to non-perforated group (7.36 ± 8.93) (p = 0.010), and greater proportion of patients with perforated appendicitis (66.7%) had NLR values above predicted cut-off (5.71), whereas larger number of patients with non-perforated appendicitis (61.9%) had NLR values below the cut-off (p = 0.010), yielding sensitivity of 66.7% and specificity of 62%.These findings align with existing literature, where studies have reported an association between high NLR and appendiceal perforation. Gunasekaran *et al.*, found that patients with perforated appendicitis had a mean NLR of 8.8 compared to 3.2 in non-perforated cases (p-value <0.001) and also determined that NLR at a cut-off of 3.78 yielded a sensitivity of 65.9% and specificity of 93.1% for differentiating between perforated and non-perforated appendicitis [18].However, in a study by Chen *et al.*, NLR at a cut-off >10.83 demonstrated higher predictive values (sensitivity 96.3% and specificity 85.0%) for early perforation [19]. NLR has been identified as an independent predictor for complicated appendicitis, with cut-off values of >1.7 and >10.1 predicting complicated appendicitis with sensitivities of 74% and 68.57% and specificities of 69% and 56.98% [20].These findings further support the role of NLR as predictive marker for appendiceal perforation. Given that NLR can be derived from routine blood tests, its use as a diagnostic adjunct in suspected appendicitis cases may enhance early detection and improve clinical decision-making, particularly in settings where advanced imaging modalities are not readily available.

This study is limited by its relatively small sample size and single-center design, which may restrict the generalizability of the findings. Additionally, the absence of serial NLR measurements and reliance on a single preoperative value may affect the accuracy of predictive

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assessment. Future studies should include larger, multicenter cohorts and evaluate serial NLR trends to improve predictive accuracy for appendiceal perforation. Combining NLR with other inflammatory markers and clinical scoring systems may further enhance diagnostic precision.

CONCLUSIONS

The study highlighted the potential of NLR as predictive marker for distinguishing between perforated and non-perforated appendicitis. Its clinical utility is supported by identified cut-off value of 5.71, suggesting its role in aiding timely intervention and reducing complications. The findings reinforce the importance of NLR, particularly in identifying patients at higher risk of appendiceal perforation.

Authors' Contribution

Conceptualization: LG, MA
Methodology: MA, LG, QD, MN, KSA, MS
Formal analysis: MA
Writing and editing: MA, QD, MN, KSA
Review and Editing: MA, LG, QD, MN, KSA, MS

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

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