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ORIGINAL ARTICLE

Role of neutrophil to lymphocyte ratio in predicting severity of acute appendicitis

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Abstract

Introduction: Acute Appendicitis is a common and urgent surgical illness with protean manifestations, generous overlap with other clinical syndromes and significant morbidity which increases with diagnostic delay. Scoring tools have been criticized for lack of sensitivity and specificity and they don't predict the severity of illness. Our aim was to assess the association between neutrophil-to-lymphocyte ratio and its effectiveness as a tool for predicting the severity of acute appendicitis.

Method: A prospective observational study was conducted at a tertiary care center in adults presenting to the emergency department diagnosed as acute appendicitis from December 15, 2022 to December 16, 2023. The study involved the calculation of Neutrophil to lymphocyte ratio for the enrolled patients using statistical analyses The calculated value can serve as a marker of severity of acute appendicitis.

Result: Among 100 patients included in the study, males predominated- 54 (54%). Majority 58 (58%) had simple appendicitis. The sensitivity, specificity, positive predictive value and negative predictive value were 90.5%, 91.4%, 44.19% and 99.2% respectively. Similarly the area under the ROC curve and cutoff point of neutrophil to lymphocyte ratio for differentiating complicated and uncomplicated appendicitis were 0.945, and 7.54 respectively. A significant association was seen between neutrophil to lymphocyte ratio and the occurrence of complications (p-value < 0.001).

Conclusion: The Neutrophil-to-Lymphocyte Ratio (NLR) can serve as a predictor for severity of acute appendicitis. This has significant implications for prioritizing surgical cases and monitoring patients who are treated conservatively.

Keywords: Appendicitis, Lymphocyte, Neutrophil

INTRODUCTION

Appendicitis is defined as an inflammation of the inner lining of the vermiform appendix that spreads to its other parts. This condition is a common and urgent surgical illness with protean manifestations, generous overlap with other clinical syndromes and significant morbidity which increases with diagnostic delay.[1] Appendicitis is a common presentation with lifetime estimated risk of 7% approximately.[2] Globally, in 2019, there were 17.70 million new cases of appendicitis with an age-standardized incidence rate of 229.86 per 100,000 populations. The mortality risk of this condition is less than 1% in general population but is high in elderly (50%).[3,4]

Currently, there is still no accurate diagnostic method for establishing the diagnosis of acute appendicitis, especially in the early stage.[5] Several scoring systems have been created to facilitate the diagnosis of acute appendicitis, including the Alvarado score[6] and the Raja Isteri Pengiran Anak Saleha Appendicitis Score (RIPASA) score.[7] Nevertheless, the scoring systems now in use exhibit limited sensitivity and specificity, rendering them incapable of providing prognostic value in distinguishing between cases of simple and complex appendicitis.[8] Numerous studies have explored the role of biomarkers in the early diagnosis of acute appendicitis, focusing on indicators such as white blood cell counts (WBC), neutrophil counts, and the neutrophil-lymphocyte ratio (NLR). The diagnostic precision of WBC and neutrophil levels for acute appendicitis has shown variability across different research efforts. Additionally, NLR has demonstrated considerable accuracy in diagnosing acute appendicitis.[9]

Our study aimed to investigate the association of the Neutrophil-to-Lymphocyte Ratio (NLR) in individuals exhibiting symptoms of acute appendicitis with its severity. Our focus was on unraveling the predictive value of NLR – a cost effective parameter, as a biomarker in the clinical presentation of acute appendicitis, shedding light on its potential to serve as an indicator for disease severity.

METHOD

A retrospective study was conducted after obtaining ethical approval from the Institutional Review Committee of Institute of Medicine, Maharajgunj Medical Campus [Reference number: [266 (6-11) E2 079/80]. Data collected from 15 December 2022 to 16 December 2023. The study population included all adult patients (≥18 years of age) who presented to the Emergency Department of Institute of Medicine, TUTH and have been diagnosed to be a case of acute appendicitis either clinically or radiologically. Informed consent (written and/or verbal) was diligently obtained from all participating individuals. Informed consent was obtained from family members of the patients who were mentally unfit to provide consent. Record books were used as the data source. The patients who were pregnant, trauma patients, immunocompromised patients were excluded from the study. Non probability sampling method was used. The sample size was calculated by using following formula:

Sample size (N) = $[\{(Z\ (1-\alpha)\}^2 \times p\ (1-p)\}]/\ d^2$
Where,
Z (1-α) = standard normal variate {at 5% type I error ($p<0.05$, it is 1.96)}
P = expected proportion of sepsis based on previous studies 0.07[10]
d = precision of estimate or absolute error, taken as 5%.
Applying the above values to the formula, sample size is 100.

Operational Definition

Acute appendicitis was categorized into simple and complicated based on clinical finding, radiological finding, per-operative finding and histopathological findings.[11] Based on these findings:

- Simple appendicitis included terms like 'acutely inflamed', 'phlegmonous', 'acute suppurative', 'mildly inflamed with or without peritonitis'.[12]
- Complicated appendicitis included 'gangrenous appendicitis', 'perforated appendicitis', 'local pus collection at operation', 'general peritonitis' and 'intra-abdominal abscess'.[12]

The data obtained were organized in MS Excel 2018, followed by the use of IBM® SPSS® version 22 (IBM Corp., Armonk, USA) for analysis and visualization. Diagnostic accuracy measures-sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and diagnostic efficiency for Neutrophil, Lymphocyte and Neutrophil to lymphocyte ratio were calculated. The performance of Neutrophil to lymphocyte ratio in predicting severity of acute appendicitis was analyzed by calculating the area under the receiver operating characteristics (AUROC) curves. Based on the ROC curve, the best cut off points were chosen.

RESULT

There were 54 (54%) males and 46 (46%) females with age range of 18 to 76 years with mean and median age of 30.34 and 28 years respectively. The standard deviation was 11.07 years.

The mean neutrophil was 80.49 with a standard deviation of 6.05. Similarly, the mean lymphocyte was 10.2 with a standard deviation of 4.75. The mean NLR was 12.02 with SD 10.87. Regarding the histopathological findings, 58% of cases were simple appendicitis and remaining were of complicated appendicitis (Table 1).

Table 1. Biomarkers of the study participants (n= 100)

Characteristics	Range	Mean±SD
Neutrophil (%)	64-96	80.49±6.05
Lymphocyte (%)	2-20	10.2±4.75
Neutrophil/ Lymphocyte Ratio	3.55-48	12.02±10.87
Histopathological Finding	***f* (%)**	
Simple appendicitis	58(58%)	
Complicated appendicitis	42(42%)	

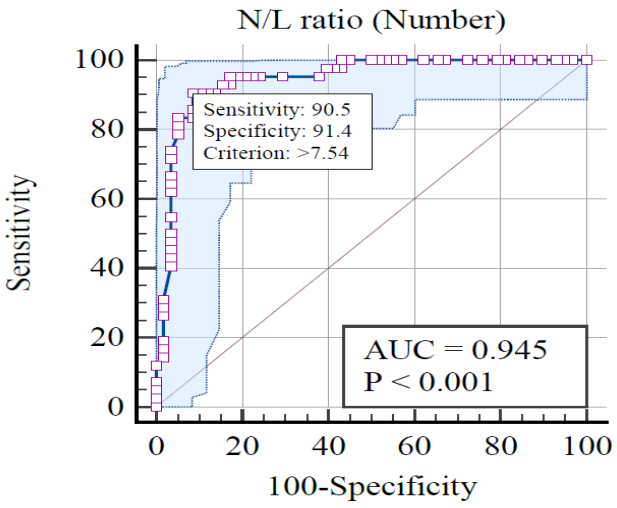

Figure 1. ROC Curve of neutrophil / lymphocyte ratio

The AUC of Neutrophil / Lymphocyte Ratio was 0.945, with sensitivity of 90.5, specificity of 91.4, diagnostic accuracy of 91.34 with a significant p value of <0.001. In our study we found that a cut off of ≥7.54 predicts complicated appendicitis with a 95% confidence interval of 0.881-0.981with a significant P value while other clinically and radiologically confirmed cases along with laboratory findings consistent with acute appendicitis below the cut-off range was found to be simple appendicitis (Table 2).

Table 2. Performance characteristics of NLR

Parameters	AUC	P value	Sensitivity (%)	Specificity (%)	Positive Predictive Value (%)	Negative Predictive Value (%)	Diagnostic Accuracy (%)	Cut off	95% Confidence Interval
Neutrophil / Lymphocyte Ratio	0.945	<0.001	90.5	91.4	44.19	99.22	91.34	≥7.54	0.881- 0.981

in complicated appendicitis compared to simple cases. The diagnostic accuracy of NLR for acute appendicitis was 83.5% sensitivity, 57.7% specificity, with a cutoff of 2.87. For differentiating complicated and simple appendicitis, NLR had 84.6% sensitivity, 56.5% specificity, with a cutoff of 6.59[15]. In our study, a cutoff of ≥7.54 predicted complicated appendicitis, with a 95% confidence interval of 0.881-0.981 and a significant P value.

The main limitation of our study was that it was done in a single center, hence results may not be generalized.

DISCUSSION

In our study, 58% patients had simple appendicitis and 42% had complicated appendicitis. The mean neutrophil to lymphocyte ratio was 12.02. The AUC of Neutrophil/ Lymphocyte Ratio was 0.945, with sensitivity of 90.5, specificity of 91.4, diagnostic accuracy of 91.34 with a significant p value of <0.001.

In a comprehensive meta-analysis by Hajibandeh, et al., involving 8914 patients from seventeen studies, a Neutrophil-to-Lymphocyte ratio (NLR) cutoff of 8.8 was established as indicative of complicated appendicitis, boasting 76.92% sensitivity and 100% specificity, resulting in an AUC of 0.91. An NLR exceeding 4.7 emerged as a significant indicator of acute appendicitis (OR: 128, p < 0.0001), while an NLR surpassing 8.8 strongly predicted complicated appendicitis (OR: 43, p < 0.0001).[13]

In our study, we identified a cutoff of ≥7.54 as a predictor of complicated appendicitis, with a 95% confidence interval of 0.881-0.981 and a significant P value.

In a study led by Fahad S Al Amri, et al. involving 103 individuals, males (50.5%) outnumbered females (49.5%), all diagnosed with acute appendicitis. Neutrophils, lymphocytes, and NLR means were 68.970%, 22.067%, and 5.020, respectively. Complications were present in 31% of cases, showing a significant association between NLR and complications (p = 0.00001).[14] Our study similarly observed a male predominance, with 42% having complicated appendicitis.

Dedi Prasetya, et al.'s study on 121 patients revealed significantly higher Neutrophil and NLR levels in acute appendicitis than in the control group, and greater values

CONCLUSION

In our study, the use of the NLR demonstrated a notable level of accuracy in differentiating between complicated and uncomplicated cases. The performance of neutrophil to lymphocyte ratio in correlating the severity of acute appendicitis revealed outcomes consistent with international studies on diverse populations. Future prospective studies on larger number of patients are needed to confirm and support our findings.

DECLARATIONS

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Conflict of Interest
None

Funding
None

Ethical Clearance
It was obtained from IRC of IOM, TUTH.

Consent of the Study
Written and verbal consent was taken from all the participants. It was taken from available family members if the participant is mentally unfit for consent.

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