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Diagnostic and predictive value of N: L ratio for severity of acute appendicitis

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ABSTRACT

Background: The most frequent surgical emergency in clinical practice is acute appendicitis (AA), which has a lifetime incidence of about 7% per person. In the past, appendectomy was the gold standard for treating AA; however, in recent years, this conventional paradigm of therapy has faced significant challenges. **Aims and Objectives:** To analyze the neutrophil-to-lymphocyte ratio's (NLR) diagnostic and predictive utility in measuring the severity of AA, as well as its potential as a biomarker for distinguishing between individuals with severe and simple appendicitis. **Materials and Methods:** This retrospective study was conducted over a period of 1 year and included a total of 280 patients. **Results:** According to the criteria in methods, a total of 280 cases of AA patients enrolled in the study period. 154 were male and 126 were female. The ages range from 18 to 70 years old with the mean age of 38.56 ± 15.34 years old. The duration of the disease was 2–46 h with the mean duration of 26.89 ± 19.45 h 54 cases were identified as perforated patients, and 226 cases were non-perforated patients. **Conclusion:** According to our findings, the NLR has the potential to be an easy-to-use and reasonably priced biomarker for determining the severity of AA. More severe types, such as perforation or abscess development, are linked to elevated NLR levels.

Key words: N: L ratio; Acute appendicitis; Diagnostic biomarkers and predictive value

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INTRODUCTION

The most frequent surgical emergency in clinical practice is acute appendicitis (AA), which has a lifetime incidence of about 7% per person. In the past, appendectomy was the most effective therapy for AA.[1] However, there has been a significant challenge to this conventional therapy paradigm in recent years. An increasing number of studies attest to the effectiveness of cautious antibiotic-based therapy, which can also prevent problems during anesthesia and surgery.[2] Surgery is still the preferred therapy for complex AA, particularly perforated AA, even though conservative measures have been suggested. The majority of individuals with complex AA who get conservative treatment still require an appendectomy soon after.[3] An improperly treated ruptured appendix can worsen quickly, resulting in multiple organ dysfunction syndrome, septic shock, and even death. As a result, it is imperative to promptly and precisely predict appendiceal perforation. A newly developed measure of inflammation level for assessing severity and forecasting prognosis in inflammatory disorders such infections, sepsis, and malignancies is the neutrophil-to-lymphocyte ratio (NLR). NLR is quite simple to use and may be computed from the outcomes of a standard complete blood count (CBC) test. It does not raise the financial strain on the health care system or inflict further harm on patients. As a result, it has drawn increasing clinical attention.[4] A few recent studies explored its clinical use in AA patients with promising results.[5] This study aims to improve clinical decision-making by assessing the effectiveness of the NLR as an early predictor of perforated AA.

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One of the most frequent surgical emergencies in the world is AA, which can quickly develop into more complex forms such as perforation, abscess development, or widespread peritonitis. To reduce the morbidity and mortality linked to this illness, prompt and precise diagnosis is essential, as is suitable care. AA can have a mild and non-specific clinical appearance that makes it difficult to differentiate from other abdominal illnesses. As a result, diagnostic procedures, including laboratory testing and imaging (computed tomography [CT], ultrasound), are often used.

To analyze the NLR diagnostic and predictive utility in measuring the severity of AA, as well as its potential as a biomarker for distinguishing between individuals with severe and simple appendicitis.

Aims and objectives

To analyze the neutrophil-to-lymphocyte ratio's (NLR) diagnostic and predictive utility in measuring the severity of AA, as well as its potential as a biomarker for distinguishing between individuals with severe and simple appendicitis.

MATERIALS AND METHODS

This retrospective study was conducted over a period of 1 year at DMGMC and H and included a total of 280 patients diagnosed with AA. Patients were selected based on specific inclusion and exclusion criteria.

Inclusion criteria

The inclusion criteria encompassed patients with clinical symptoms and signs consistent with AA, confirmed through clinical examination and imaging modalities such as ultrasound or CT scan. All age groups were considered, provided that CBC reports, including neutrophil and lymphocyte counts, were available for calculating the neutrophil-to-lymphocyte ratio. Only patients who underwent appendectomy with histopathological confirmation of appendicitis were included. Written informed consent was obtained from all patients or their legal guardians in the case of minors. The severity of appendicitis was classified based on intraoperative findings and histopathological examination into uncomplicated and complicated cases, including perforation and abscess formation.

Exclusion criteria

Patients were excluded if they had other inflammatory or infectious conditions that could affect neutrophil or lymphocyte counts, such as inflammatory bowel disease or systemic infections. Those with immunosuppressive conditions, including human immunodeficiency virus/Acquired immunodeficiency syndrome, patients undergoing chemotherapy, or those on immunosuppressive medications, were also excluded. In addition, individuals with pre-existing hematological disorders or malignancies that could alter blood counts, patients with incomplete medical records or missing preoperative CBC reports, and those with a history of prior abdominal surgeries were not included in the study. Pregnant patients were excluded due to physiological variations in immune response and blood parameters.

Statistical analysis

Data were first entered into Microsoft Excel and subsequently analyzed using SPSS (version 27.0; SPSS Inc., Chicago, IL, USA) and GraphPad Prism (version 5) for statistical analysis. Numerical variables were expressed as means and standard deviations, while categorical variables were presented as counts and percentages. Group differences were assessed using two-sample t-tests, which compare the means of independent or unpaired samples. Paired t-tests, accounting for the correlation between paired observations, provided greater statistical power. Chi-square tests (χ^2 tests) were utilized to evaluate hypotheses involving the sampling distribution of the test statistic, which follows a Chi-squared distribution under the null hypothesis; Pearson's Chi-squared test was commonly applied. Depending on the context, either the Chi-square test or Fisher's exact test was used to compare unpaired proportions. T-tests were conducted using standard test statistic formulas, which follow or approximate a t-distribution under the null hypothesis, with specific degrees of freedom applied for each test. P-values were derived from Student's t-distribution tables, with a $P \leq 0.05$ considered statistically significant, indicating rejection of the null hypothesis in favor of the alternative hypothesis.

RESULTS

A total of 280 patients diagnosed with AA were included in the study, comprising 154 males and 126 females. The patients' ages ranged from 18 to 70 years, with an average age of 38.56±15.34 years. The mean duration of symptoms before presentation was 26.89±19.45 h. Based on intraoperative and histopathological findings, 226 patients were categorized as having unperforated appendicitis, while 54 patients had perforated appendicitis.

Comparison of clinical and laboratory findings

Table 1 compares the general clinical and laboratory parameters between the unperforated and perforated appendicitis groups. The mean age of patients with perforated appendicitis (41.59±17.26 years) was significantly higher than that of the unperforated group (34.54±13.17 years) (P=0.001). The total white blood cell (WBC) count was also significantly higher in the perforated

group (13.92±4.79×10^9/L) compared to the unperforated group (11.95±3.69×10^9/L) (P=0.001).

The neutrophil percentage (NEU%) was markedly elevated in the perforated group (90.26±3.12) compared to the unperforated group (78.07±9.93) (P<0.001), whereas the lymphocyte percentage (LYM%) was significantly lower in the perforated group (5.46±1.73) compared to the unperforated group (15.38±8.35) (P<0.001). Consequently, the NLR was significantly higher in perforated appendicitis cases (18.72±7.81) than in unperforated cases (6.98±4.41) (P<0.001).

Other inflammatory markers, such as C-reactive protein (CRP) and procalcitonin (PCT), were also significantly elevated in the perforated group. The mean CRP level was 54.73±52.31 mg/L in perforated cases, compared to 22.95±35.32 mg/L in unperforated cases (P<0.001). Similarly, PCT levels were significantly higher in perforated appendicitis (2.13±4.05 ng/mL) than in the unperforated group (0.65±1.45 ng/mL) (P<0.001).

In contrast, parameters such as hemoglobin levels and hematocrit did not show statistically significant differences between the two groups (P=0.079 and P=0.104, respectively). Platelet count (PLT) was significantly lower in perforated appendicitis cases (190.29±79.56×10^9/L) compared to unperforated cases (226.60±58.42×10^9/L) (P<0.001).

Hospitalization duration was significantly longer in the perforated appendicitis group, with a mean hospital stay of 6.07±4.74 days, compared to 3.02±1.67 days in the unperforated group (P<0.001).

Risk factors for appendiceal perforation

Table 2 presents the analysis of risk factors associated with appendiceal perforation. A higher NEU% (odds ratio [OR]=1.285, P=0.001), increased NLR (OR=1.385, P<0.001), and elevated CRP levels (OR=1.058, P=0.023) were significantly associated with an increased risk of perforation. Similarly, PCT levels showed a significant association with perforation risk (OR=1.031, P=0.035).

While the total WBC count showed a statistically significant association (P=0.041), age did not reach statistical significance as an independent predictor (P=0.134). PLT did not show a significant association with perforation risk (P=0.279).

These findings indicate that elevated NLR, increased NEU%, higher CRP, and PCT levels are strong predictive markers for appendiceal perforation, highlighting their potential role in risk stratification and early surgical intervention.

Table 1: Comparison of general clinical data between the two groups

Parameter	Unperforated group (n=226)	Perforated group (n=54)	P-value
Age (years)	34.54±13.17	41.59±17.26	0.001
Sex (male/female)	126/100	28/26	0.604
WBC (×10^9/L)	11.95±3.69	13.92±4.79	0.001
NEU%	78.07±9.93	90.26±3.12	<0.001
LYM%	15.38±8.35	5.46±1.73	<0.001
NLR	6.98±4.41	18.72±7.81	<0.001
PLT (×10^9/L)	226.60±58.42	190.29±79.56	<0.001
Hb (g/L)	138.27±20.33	132.81±20.90	0.079
HCT	0.41±0.05	0.39±0.06	0.104
CRP	22.95±35.32	54.73±52.31	<0.001
PCT	0.65±1.45	2.13±4.05	<0.001
Duration of disease (hours)	25.53±20.55	28.03±18.48	0.413
Duration of hospitalization (days)	3.02±1.67	6.07±4.74	<0.001

WBC: White blood cell, NEU%: Neutrophil percentage, NLR: Neutrophil-to-lymphocyte ratio, LYM%: Lymphocyte percentage, Hb: Haemoglobin, HCT: Haematocrit, CRP: C-reactive protein, PCT: Procalcitonin

Table 2: Analysis of risk factors for appendiceal perforation

Parameter	OR (95% CI)	P-value
Age (years)	1.035 (1.000–1.072)	0.134
WBC	0.814 (0.674–0.982)	0.041
NEU%	1.285 (1.128–1.464)	0.001
LYM%	1.181 (0.927–1.505)	0.001
NLR	1.385 (1.148–1.672)	<0.001
PLT	1.024 (1.011–1.038)	0.279
CRP	1.058 (0.883–1.268)	0.023
PCT	1.031 (1.103–1.049)	0.035

WBC: White blood cell, NEU%: Neutrophil percentage, NLR: Neutrophil-to-lymphocyte ratio, LYM%: Lymphocyte percentage, CRP: C-reactive protein, PCT: Procalcitonin, OR: Odds ratio

Comparison of clinical characteristics between groups

The perforated group exhibited significantly higher values for age, WBC count, NEU%, NLR, CRP, PCT, and length of hospital stay compared to the non-perforated group. Conversely, the LYM% and PLT were significantly lower in the perforated group.

Multivariate logistic regression analysis revealed that higher levels of WBC count, NEU%, NLR, CRP, and PCT, along with lower LYM%, were significant independent risk factors for early appendiceal perforation in AA patients (all P<0.05).

DISCUSSION

A considerable rise in the percentage of peripheral blood neutrophils and the release of numerous active substances to boost their pathogen clearance capacity occur when bone marrow releases a large number of neutrophils during

inflammation, delays their regeneration, and then engages in phagocytosis.[6] The inflammatory response's cytokines directly accelerate lymphocyte death, resulting in a dramatic decline in the percentage of peripheral blood lymphocytes and, ultimately, a marked rise in the patient's NLR value. A vicious cycle is created when the amount of inflammation is made worse by a further rise in the NLR.[7]

NLR is a straightforward, low-cost indicator of inflammation. The differential WBC counts make it simple to compute. NLR has shown considerable therapeutic potential in various inflammatory conditions. According to studies, it has a significant prediction value for the harmful side effects of radiation therapy in tumor patients, in addition to acting as an independent risk factor for the prognosis of tumor patients.[8] Another indicator of subclinical inflammation is NLR. It is frequently used as an inflammatory index to grade the severity of infectious illnesses and make clinical diagnoses.

The most frequent cause of acute abdomen is alcoholism. Traditional appendectomy has long been the primary therapy for AA since the appendix was once thought to be a deteriorating and worthless organ. Nonetheless, the importance of the appendix in intestinal immunity has been shown by contemporary medicine. The conventional surgical paradigm has been questioned and challenged in recent years due to the ongoing debate and research on conservative treatment of AA.[9] Surgery is necessary for individuals with perforated AA, though, as the condition progresses quickly and can quickly result in septic shock or even death.[10] Thus, it is essential to learn how to identify a perforated appendix early on and how to forecast perforation in AA patients.

With encouraging outcomes, a few recent studies have investigated the therapeutic use of NLR in AA patients. Using NLR by itself or in conjunction with other biomarkers in pediatric AA[11] has been demonstrated to help with AA diagnosis and its implications. The function of NLR in identifying and forecasting complex AA in adults has also been studied. On the other hand, there is disagreement on the cut-off value, sensitivity, and specificity.

This study aimed to assess the predictive and diagnostic value of the NLR for early appendiceal perforation in patients with AA. Initially, univariate and multivariate regression analyses were conducted to identify whether elevated WBC count, NEU%, NLR, CRP, and PCT, along with decreased LYM%, were independent risk factors for early perforation in AA patients. Following this, receiver operating characteristic curve analysis revealed that NLR provided the most significant predictive value for appendiceal perforation. With a diagnostic cutoff of 10.83, the sensitivity and specificity were 0.963 and 0.850, respectively.

In a study by Kelly et al., which reviewed 663 patients over 4 years, an NLR >6.35 or CRP >55.6 mg/L was identified as a diagnostic threshold for assessing the severity of the disease in AA patients, with longer hospital stays observed in those with higher NLR values.[12] Mori et al., identified elevated NLR as an independent risk factor for a higher incidence of complications after appendectomy.[13] Yardimci et al., found that the mean NLR values for simple AA, AA with restrictive peritonitis, and complicated AA were 8.36±5.6, 9.1±6.2, and 10.6±6.4, respectively, indicating that NLR could serve as an effective parameter for assessing the severity of disease in AA patients.[14]

Our study's findings, when paired with findings from other research, indicate that NLR, an emerging inflammatory indicator, may be able to predict early on the level of neutrophil activation and lymphocyte demobilization in the inflammatory state. It can be useful for determining the disease's severity and is comparable to or superior to more conventional biomarkers like PCT and CRP.

NLR is an accurate and affordable marker in some populations and situations, despite the fact that imaging such as ultrasonography, CT, and magnetic resonance imaging are nearly invariably employed in wealthy nations to diagnose AA. For instance, NLR can be applied to pregnant patients when a CT scan is not recommended or in underprivileged areas where there is restricted access to imaging studies right away. The image is still the gold standard for preoperatively diagnosing appendiceal perforation. However, no picture can foretell a future perforation. In instances of simple appendicitis that have been clinically or radiologically proven, this study showed that NLR has the ability to predict perforation. Patients with a higher NLR may undergo surgery sooner, while those with a lower NLR may begin conservative treatment. It may also be used to triage patients and help make decisions about surgical versus conservative management. For patients receiving conservative care, NLR can also be utilized to track therapy response.

The current study does have many drawbacks, though. It is a single-center, retrospective observational research with a limited sample size and stringent selection standards. Patients with chronic appendicitis, antibiotic usage, and prolonged disease duration will be included in our upcoming study. To utilize NLR as one of the criteria to direct the management strategy, we also want to carry out prospective research. We plan to do a bigger prospective, multicentre investigation in the future.

Limitations of the study

This study is limited by its retrospective design, single-center setting, and relatively small sample size of perforated

cases (n=54). Variability in disease duration and prior antibiotic use may also affect NLR values, warranting further investigation.

CONCLUSION

According to our findings, the NLR has the potential as an easy-to-use and reasonably priced biomarker for determining the severity of AA. More severe types, such as perforation or abscess development, are linked to elevated NLR levels. Although NLR can guide therapeutic decisions and aid in early risk stratification, further research is needed to confirm its diagnostic and prognostic utility. For a precise evaluation, it should be combined with further clinical, laboratory, and imaging results. Future research is needed to establish NLR's involvement in ordinary clinical practice and its potential to enhance patient outcomes and minimize healthcare expenditures.

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