Role of neutrophil lymphocyte ratio and platelet lymphocyte ratio as a predictive factor for severity of acute appendicitis

Original Article

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ABSTRACT

Background: Acute appendicitis (AA) is a prevalent disease worldwide. Delay in diagnosis or management could result in complications up to mortality. Timely management is the key to optimal outcomes. The neutrophil lymphocyte ratio (NLR) provides information regarding immune and inflammatory pathways, which makes it a potential marker to predict appendicitis and its severity. Also, changes in platelet lymphocyte ratio (PLR) may be a useful indicator of acute infection, including acute appendicitis.

Objective: To determine whether NLR and PLR can predict the severity of acute appendicitis.

Patients and Methods: This study is a diagnostic test evaluation study carried out in the department of general surgery in two tertiary hospitals from November 2020 to July 2023. The study has two groups of patients, complicated appendicitis, and uncomplicated appendicitis, who underwent appendectomy and included 115 patients.

Results: A normal appendix is diagnosed when NLR less than 3.5 and PLR less than 125, uncomplicated catarrhal appendicitis is diagnosed when NLR ranges from 3.5 to 5.8 and PLR ranges from 125 to 175, complicated phlegmonous appendicitis is diagnosed when NLR ranged from greater than 5.8 to 8.2 and PLR ranged from greater than 175 to 220, complicated gangrenous appendicitis is diagnosed when NLR greater than 8.2 and PLR greater than 220, with acceptable sensitivity and specificity *P value* (*P <0.005*).

Conclusion: NLR and PLR are considered promising markers that can predict both diagnosis and severity of acute appendicitis with acceptable sensitivity and specificity.

Key Words: Acute appendicitis, catarrhal appendicitis, neutrophil lymphocyte ratio, phlegmonous appendicitis, platelet lymphocyte ratio.

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INTRODUCTION

Acute appendicitis (AA) is a frequent etiology of acute abdominal pain. The prevalence of this condition is estimated to be around 7%, with rates of perforation ranging from 17 to 20%. The mortality rate is below 1%, however, it can increase to 50% among the elderly population[1]. Delaying the diagnosis and treatment for AA can result in complications such as perforation, gangrene, and the formation of abscesses within the abdomen[2]. First, in cases of catarrhal appendicitis, inflammation is limited to the lumen with neutrophils present in the mucosa and submucosa. Suppurative appendicitis is characterized by the infiltration of neutrophils that extends to the muscle layers. Transmural inflammation leads to the development of micro-abscesses and thromboses, resulting in necrosis and gangrene of the appendix. Subsequent to ulceration, there is a possibility of perforation occurring, which can result in either localized or widespread inflammation of the peritoneum[3].

The most effective treatment relies on promptly identifying the condition and taking rapid actions[2]. The neutrophil lymphocyte ratio (NLR) can provide valuable information about two distinct immunological and inflammatory pathways, making it a possible indicator for predicting the presence and severity of appendicitis[4]. Platelets are cellular components that aid in regulating different inflammatory diseases. The alteration in the platelet lymphocyte ratio (PLR) can serve as a valuable predictor of acute infection, such as AA[5]. Higher levels of PLR are linked to reactive thrombocytosis and/or lymphopenia. Reactive thrombocytosis may occur during infections due to elevated cytokine levels. Lymphopenia is linked to enhanced neutrophil production and reduced lymphocyte synthesis in the bone marrow. Reactive thrombocytosis is the underlying cause for the rise in PLR[6]. The NLR and PLR are noninvasive and cost-effective indicators of inflammation that can be easily derived from the blood count in emergency settings[7].

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The objective of this study was to evaluate the efficacy of NLR and PLR in distinguishing between uncomplicated and complicated appendicitis.

PATIENTS AND METHODS:

A prospective hospital-based diagnostic test evaluation research that includes patients undergoing surgical intervention for AA in the emergency department of two tertiary hospitals. The study included individuals receiving an appendectomy (both open and laparoscopic) due to clinically confirmed AA with ages ranging from 12 to 60 years. We excluded individuals exhibiting leukopenia, idiopathic thrombocytopenic purpura, essential thrombocythemia, leukemia, lymphoma, patients on immunosuppressive medication, and patients receiving medication that causes abnormalities in the structure and function of thrombocytes.

Ethical consideration: Written informed consent was obtained from the study participants after being adequately briefed about the study goals. The patient was free to withdraw from the study at any moment. The study was conducted in compliance with the principles outlined in the Declaration of Helsinki and was authorized by the Research Ethics Committee.

The study investigates the NLP in cases of acute appendicitis. Examining the PLR in cases of acute appendicitis.

Patients were subjected to a comprehensive medical history, extensive clinical examination, and relevant investigations, including preoperative complete blood count, urine R/E, and ultrasound of the abdomen and pelvis. These tests were necessary to eliminate other potential causes such as mesenteric adenitis and ovarian torsion, which can present similar symptoms to appendicitis. The preoperative complete blood count will analyze the leukocyte count, neutrophil percentage, thrombocyte count, NLR, and PLR to determine the diagnosis and severity of acute appendicitis.

Referring to the Japanese categorization system, AA is divided into two categories: uncomplicated, group A, (catarrhal) and complicated, group B, (phlegmonous or gangrenous) AA[8]. The intraoperative findings for suspecting AA were as follows:[9,10]

Catarrhal appendicitis is characterized by the presence of hyperemia and edema in the appendix. Minimal or absent pericolic fluid with fibrin deposition.

Phlegmonous appendicitis is characterized by an enlarged appendix with a dull outer layer, as well as dilated and congested blood vessels on the surface. Additionally, there is a presence of a thick, purulent fluid on the outer layer of the appendix.

Gangrenous appendicitis is characterized by a friable appendiceal wall that appears purple, green, or black. Necrosis, abscess formation, or perforation.

Patients were discharged from the hospital on the first day after their surgery. Samples were dispatched for histopathological examination. The postoperative outcomes, the occurrence of pelvic abscess, were evaluated over 30 days after the surgery.

Analysis of data using statistical methods

The data were analyzed using statistical measures such as the mean ± standard deviation (± SD), median, range, frequencies (number of cases), and percentages, where applicable. The normality assumption of the numerical data was assessed using the Kolmogorov–Smirnov test (Shapiro–Wilk test). The numerical variables in the study groups were compared using the Student t test for independent samples if the data were normally distributed. If the data were not normally distributed, the comparison was done using the Mann–Whitney U test for independent samples. The paired ttest was used for within-group comparison when comparing normally distributed data. However, if the data is not normally distributed, the Wilcoxon signed-rank test was used for paired (matched) samples. A χ^2 test was conducted to compare categorical data. When the expected frequency is less than 5, an exact test was employed instead. The correlation between different variables was assessed using the Pearson moment correlation equation for linear relationships in normally distributed data, and the Spearman rank correlation equation for non-normal variables. The results were visually represented using a linear regression graph. Accuracy was quantified using the metrics of sensitivity, specificity, positive predictive value, negative predictive value, and overall accuracy. Receiver operating characteristic (ROC) analysis was employed to establish the optimal threshold value for the diagnostic markers under investigation. A probability value (*P value*) below 0.05 was deemed to be statistically significant. Statistical analysis was done using IBM SPSS statistics for windows, Version 22.0. Armonk, NY: IBM Corp.

RESULTS:

There were 115 individuals who had to have an emergency appendectomy, with 60 (52%) of them being females and 55 (48%) being males. The average age of the group was 27.1 years, with the youngest participant being 12 years old and the oldest being 46 years old. There was a total of 15 individuals who had a normal appendix during surgery, with a female-to-male ratio of 1.5 : 1. Our study involved 100 patients with an inflamed appendix. These patients were diagnosed during surgery as having uncomplicated catarrhal appendicitis 34 (34%) patients, complicated phlegmonous appendicitis 51 (51%) patients, or complicated gangrenous appendicitis 15 (15%) patients showing that complicated phlegmonous appendicitis is

the most prevalent type. The incidence of gangrenous appendicitis is twice as high in males compared with females, as indicated in (Table 1).

The NLR was considerably higher in cases with complicated appendicitis compared with uncomplicated appendicitis. The ROC curves were utilized to determine an optimal threshold for the blood test. (Table 2) displays the NLR and the intraoperative finding and classification of appendicitis. The NLR is used to diagnose different types of appendicitis. A normal appendix is diagnosed when the NLR is less than 3.5. Uncomplicated catarrhal appendicitis is diagnosed when the NLR ranges from 3.5 to 5.8. Complicated phlegmonous appendicitis is diagnosed when the NLR ranges from greater than 5.8 to 8.2. Complicated gangrenous appendicitis is diagnosed when the NLR is greater than 8.2.

The PLR was markedly elevated in cases of severe appendicitis compared with uncomplicated appendicitis. The PLR and the intraoperative finding and categorization of appendicitis are displayed in (Table 3). The PLR is used to diagnose different types of appendicitis. A normal appendix is diagnosed when the PLR is less than 125. Uncomplicated catarrhal appendicitis is diagnosed when the PLR is between 125 and 175. Complicated phlegmonous appendicitis is diagnosed when the PLR is between 175 and 220. Complicated gangrenous appendicitis is diagnosed when the PLR is greater than 220.

The occurrence rate of postoperative pelvic abscess was 3% where three patients developed a pelvic abscess and were treated accordingly.

Table 1: Intraoperative subtypes of acute appendicitis

Subtypes of acute appendicitis	Female	Male	Ratio (F : M)	Total (%)
Group (A) uncomplicated catarrhal appendicitis	20	14	1.43:1	34
Group (B) Complicate Appendicitis				
Phlegmonous appendicitis	26	25	1.04:1	51
Gangrenous appendicitis	5	10	0.5:1	15
Total	51	49		100

Table 2: Neutrophil lymphocyte ratio in acute appendicitis

Appendicitis intraoperative findings	NLR Cut off point	Sensitivity %	Specificity %	*P* value
Normal appendix	<3.5	85	81	**< 0.05**
Uncomplicated catarrhal	3.5–5.8	82	78	**< 0.05**
Complicated phlegmonous	>5.8–8.2	79	84	**< 0.05**
Complicated gangrenous	>8.2	83	86	**< 0.05**

Table 3: Platelet lymphocyte ratio in acute appendicitis

Appendicitis intraoperative findings	PLR Cut off point	Sensitivity %	Specificity %	*P* value
Normal appendix	<125	81	85	**≤0.05**
Uncomplicated catarrhal	125–175	83	80	**≤0.05**
Complicated phlegmonous	>175–220	79	76	**≤0.05**
Complicated gangrenous	>220	80	87	**≤0.05**

DISCUSSION

The current study is a diagnostic test evaluation study to evaluate the efficacy of NLR and PLR in detecting uncomplicated and complicated cases of appendicitis. It was carried out on patients who underwent appendectomy and included 115 cases. The study revealed that the rising threshold of NLR is very accurate in predicting the escalating severity of acute appendicitis, with a sensitivity ranging from 79 to 85% and a specificity ranging from 78 to 86%. Similarly, PLR proved to be an effective predictive biomarker for determining the severity of appendicitis, exhibiting a high level of sensitivity and specificity (sensitivity: 79–83%; specificity: 76–87%). According to previous research, alterations in the NLR might serve as an early indication of bacterial and viral infection. Similarly, changes in the PLR may be a valuable indicator of acute infection, such as AA[5].

Multiple researchers are presenting varying cut off values for the diagnostic efficacy of NLR in identifying complicated appendicitis. A study conducted by Muhammad and Mukul showed that AA

was successfully excluded using two specific values of NLR, resulting in a sensitivity of 94% and a specificity of 100%. An NLR of 3.5 was a reliable indicator for the presence of acute appendicitis. Phlegmonous appendicitis had a sensitivity of 78% and specificity of 82% when the cut-off value was set at 6.0. On the other hand, a NLR greater than 8.0 was identified as the cut-off point for gangrenous or perforated appendicitis, with a sensitivity of 80% and specificity of 87%[11]. In a separate study conducted by Mervan and colleagues it was shown that the NLR was considerably greater in instances with complicated appendicitis compared with noncomplicated cases (7.2 vs. 8.4). The study also reported a sensitivity of 62.5% and a specificity of 61.8%[6]. In our study a cut-off value of NLR less than 3.5 was used to diagnose a normal appendix. We diagnosed uncomplicated catarrhal appendicitis when the NLR ranged from 3.5 to 5.8, complicated phlegmonous appendicitis when the NLR ranged from greater than 5.8 to 8.2, and complicated gangrenous appendicitis when the NLR was greater than 8.2. These diagnostic criteria showed acceptable sensitivity and specificity (*P value <0.05*). Therefore, these findings indicate that NLR has a high level of accuracy in identifying AA and is useful in distinguishing between severe appendicitis and simple appendicitis. NLR could have consequences for patients who do not regularly have computed tomography scans, such as pregnant or pediatric patients, as well as in nations or circumstances where access to quick computed tomography scans is restricted. Additionally, it aids in the process of making decisions regarding the prioritization of cases involving patients with clinically or radiologically diagnosed uncomplicated appendicitis who are undergoing conservative treatment[12].

Several studies have examined the use of PLR in the context of acute appendicitis. The study conducted by Fatih *et al*. determined that the cut-off values for diagnosing AA using ROC analysis were a PLR greater than 121.78, which achieved a sensitivity of 100% and a specificity of 42.9%[5]. In a study conducted by Kara *et al*. the average values of PLR were found to be 126.09±56.13 in cases of catarrhal appendicitis, 151.94±84.14 in cases of phlegmon appendicitis (*P value <0.004*), and significantly higher values of 220.69±133.13 were observed in cases of perforated appendicitis (*P value <0.001)*[13]. In a separate study conducted by Mervan *et al*., the researchers compared cases of uncomplicated and complicated appendicitis. They found that the positive likelihood ratio (PLR) was 174 for noncomplicated appendicitis and 217 for complicated appendicitis. The sensitivity was 62.5% and the specificity was 61.8%[6]. In the present study, a normal appendix was identified when the PLR was less than 125. Uncomplicated catarrhal appendicitis was identified when the PLR was between 125 and 175. Complicated phlegmonous appendicitis was identified when the PLR was between 175 and 220. Complicated gangrenous appendicitis was identified when the PLR was greater than 220. These diagnoses were made with high sensitivity and specificity, with a *P value* of less than 0.05. These studies indicate that the PLR could be valuable in distinguishing between AA and a healthy appendix, as well as in predicting the severity of acute appendicitis.

The ability of NLR and PLR to accurately determine the presence of a normal appendix with a satisfactory level of sensitivity and specificity can help minimize the number of cases of negative appendicitis[12]. Elevated levels of NLR and PLR can aid in the early identification of complicated appendicitis cases. Prompt therapeutic intervention can then be administered to mitigate the chances of postoperative complications, such as intra-abdominal abscess or life-threatening peritonitis, which are more prevalent in cases of perforated appendix. Furthermore, these characteristics are cost-effective to assess, readily accessible, and their quick analysis renders them valuable in the emergency department[2].

Intra-abdominal abscess, also known as pelvic abscess, is an often observed and highly dreaded complication that can occur following an appendectomy[14]. In a study conducted by Surabhi *et al*. the occurrence rate of pelvic abscess was found to be 6.9%[15]. Similarly, the current research has found that the occurrence of postoperative pelvic abscesses was minimal (3%).

Our investigation confirms the validity of previously published data that assess the usefulness of NLR and PLR in predicting the severity of appendicitis. As there is currently no clinical scoring system available to predict complicated appendicitis, future research can utilize the results of this study to create a clinical score that incorporates serum biomarkers (NLR and PLR) as parameters. This score would help promote early surgical management of patients with complicated appendicitis, potentially leading to better postoperative outcomes.

CONCLUSION

The NLR and PLR can accurately diagnose a normal appendix and accurately predict the severity of acute appendicitis. This reduces the occurrence of unnecessary appendectomies and prevents complications associated with complicated appendicitis, all without delaying surgical intervention. The NLR and PLR parameters possess characteristics of simplicity, accessibility, cost-effectiveness, patient acceptability, rapid analysis, and availability within the emergency department.

Limitations

One weakness of this study is the tiny sample size. The absence of a correlation between NLR and PLR undermines the reliability of detecting both complicated and uncomplicated appendicitis. The study only examined postoperative pelvic abscesses as potential sequelae.

CONFLICT OF INTEREST

There are no conflicts of interest.

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