

Role of Neutrophil to Lymphocyte Ratio to Predict Acute Appendicitis and to Distinguish between Complicated and Uncomplicated Appendicitis: A Cross-Sectional Study

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Abstract

Introduction: Acute appendicitis (AA) is the most common surgical presentation requiring emergency operative treatment. The symptoms in many of the patients with acute appendicitis may be very non-specific, mimicking other acute abdominal conditions. Accurate and prompt diagnosis of acute appendicitis reduces the risk of perforation and negative appendectomy rate.

Objectives: To assess the diagnostic value of neutrophil-to-lymphocyte ratio (NLR) in predicting acute appendicitis and to determine a cut off value of neutrophil-to-lymphocyte ratio to distinguish between complicated and uncomplicated acute appendicitis.

Methods: A cross sectional study was conducted from April, 2019 to July, 2021 in the Department of Surgery, Regional Institute of Medical Sciences (RIMS) Hospital, Imphal, Manipur. Patient with acute abdomen who underwent appendectomy during the study period were included in the study. Age, gender, occupation, religion and family history were the independent variable. Neutrophil to lymphocyte ratio and TLC were the dependent variable. Data collected were analyzed using SPSS-version-21. Chi-square test and Fisher's exact test were used for proportions. ANOVA and independent t test were used for comparing means. A p-value of <0.05 was taken as significant.

Results: 100 patients were recruited for the study and 66% were males. Histopathological Examination (HPE) reported 84 cases of uncomplicated acute appendicitis, 13 cases of complicated acute appendicitis (abscess and perforation) and 3 cases with normal appendix. NLR >3.5 had a sensitivity of 92.7% and specificity of 66.7% for diagnosing acute appendicitis. Sensitivity and specificity of NLR taking 8 as the cut-off point to distinguish between complicated and uncomplicated Acute Appendicitis was 92.3% and 100% respectively.

Conclusion: A NLR greater than 3.5 may be considered as a simple and sensitive indicator for the diagnosis of acute appendicitis. A NLR of 8 can be used as a cut-off value to distinguish between complicated and uncomplicated appendicitis.

Keywords: Acute Abdomen, Gangrenous, Perforated, Sensitivity, Specificity.

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Introduction

Acute appendicitis (AA) is the most common surgical presentation requiring emergency operative treatment [1]. The annual incidence of acute appendicitis is estimated to be 100 per 100000 of population, with a lifetime risk of 8.6% for men and 6.7% for women [2-4]. The accurate distinction of acute appendicitis into complicated or uncomplicated can be difficult. Several scoring systems, including Alvorado and RIPASA score have been introduced to diagnose acute appendicitis [5,6]. But they lack sensitivity and specificity and also cannot predict the severity of acute appendicitis.

Complications such as perforation of the appendix and development of intra abdominal abscesses are associated with substantial increase in morbidity and mortality, especially in elderly population [8]. Length of hospital stay is also prolonged by such complications requiring extended treatment, causing additional financial burden on each affected household [9]. Perforation usually occurs after 48 hours from the onset of symptoms, which may result in generalized peritonitis with development of septic shock. It can also be accompanied by complications in the form of multiple intraperitoneal abscesses [10].

White blood cells (WBC) counts are mostly elevated in patient with appendicitis; however, an elevated WBC count has no predictive value in differentiating simple and complicated appendicitis [11-13]. Determining a simple tool or marker which can reliably diagnose appendicitis and differentiate between uncomplicated and

complicated appendicitis is still an area of focus.

MRI and CT scan though can give more accurate information about acute appendicitis and whether complicated or uncomplicated, they are not widely available and needs patient preparation and are costly. More over CT scan involves exposure to ionizing radiation. Neutrophil to lymphocyte ratio (NLR) is a simple inexpensive marker of subclinical inflammation, which is easily calculated from differential WBC count and done routinely in almost all health centres [14]. NLR provides information about both immune and inflammatory pathways thus helping in diagnosing appendicitis and predicting its severity. The neutrophil count is a marker of ongoing inflammation, whereas the lymphocyte count points to the regulatory pathway [15].

The symptoms in many of the patients with acute appendicitis may be very non-specific, mimicking other acute abdominal conditions. The decision, whether to operate or not maybe important but equally difficult, as surgical intervention carries a definite risk of morbidity and mortality. A precise and early diagnosis reduces the risk of complications in acute appendicitis and negative appendectomy rate. Since elevated total leukocyte count (TLC) and neutrophil count have low specificity and is unreliable for diagnosis, a search for another diagnostic parameter is required. The NLR seems to be a more sensitive parameter than TLC [16].

The study therefore is taken up to assess the diagnostic value of neutrophil-to-lymphocyte

ratio in predicting acute appendicitis and also as a parameter in prediction of complicated or uncomplicated acute appendicitis.

Materials and Methods

A cross sectional study was conducted from April, 2019 to July, 2021 in Manipur at the Department of Surgery, RIMS among those patients who attended Department of Surgery, including emergency casualty and OPD and got admitted with clinical signs and symptoms of acute appendicitis and underwent appendectomy during the study period. Those who refused to participate, those with co-morbid conditions viz. severe heart disease, severe psychiatric illness, pregnancy and those with other acute infection were excluded from the study. A sample size of 100 was calculated and convenient sampling was done to recruit them. Variables like age, sex, neutrophil count, lymphocyte count and TLC were analyzed and dependent variables were NLR, complicated acute appendicitis (abscess and perforation) and uncomplicated appendicitis.

Data collection

Particulars of patients were taken from record card followed by detailed history and thorough physical examination. Sample of blood 2ml in EDTA vial for complete haemogram, 2ml in sodium fluoride vial for blood sugar, 3ml for serum urea serum

electrolytes, urine sample for urine analysis was collected. Chest X-Ray taken as routine investigation. Ultrasonography was done to support the clinical diagnosis and whenever needed CT imaging was done. Neutrophil/Lymphocyte ratio (NLR) was calculated by dividing the percentage values of neutrophil and lymphocyte obtained.

$$\text{NLR} = \frac{\% \text{ of neutrophil obtained}}{\% \text{ of lymphocyte obtained}}$$

Under strict aseptic and antiseptic condition, the appendectomy specimen was preserved in formalin and sent to pathology laboratory for histopathological examination. The histopathological findings were used for the confirmation of appendicitis and complications. Sensitivity, specificity, and positive predictive value of the NLR were calculated. The collected data were entered and analyzed in SPSS (IBM) version 21. Summarization of data were carried out by using descriptive statistics such as mean, median, standard deviation and percentages. Either χ^2 test or Fisher's exact test were used for categorical variables, and t-test or ANOVA for continuous variables. P-value < 0.05 was taken as statistically significant. Ethical approval was obtained from the institutional Research Ethics Board before the commencement of the study

Results

Table 1: Distribution of patients (N=100)

Sl.no.	Characteristics	No. of Patient	Percentages
1.	Gender	Male	66
		Female	34
2.	Age	1 – 10 years	5
		11- 20 years	53
		12- 30 years	30
		> 30 years	12
3.	Intraoperative findings	Inflamed appendix	87
		Abscess	5

		Perforated	8	8.0
4.	HPE report	Inflamed	84	84.0
		Gangrenous	13	13.0
		Normal	3	3.0
5.	Appendicitis	Uncomplicated	87	87.0
		Complicated	13	13.0

Table 2: Association between appendicitis and NLR (N=100)

Characteristics		Appendicitis		P value
		Yes	No	
NLR	≥ 3.5	90	1	0.021*
	< 3.5	7	2	

*Fisher exact test

Table 3: Association between type of appendicitis and other variables (N=100)

Variables	Appendicitis (mean ± SD)		Total	P Value
	Uncomplicated	Complicated		
Age in years	21.39±6.18	24.54±22.18	21.8±9.69	0.277
WBC count	12571.84±1717.13	19653.85±1353.77	13492.5±2917.76	<0.001
Neutrophil percentage	71.72±4.16	82.77±3.53	73.16±5.52	<0.001
Lymphocyte percentage	15.38±3.18	9.41±2.42	14.6±3.68	<0.001
NLR value	4.89±1.15	9.14±1.67	5.44±1.89	<0.001

Table 4: Association between NLR > 8 and complicated appendicitis (N=100)

Characteristics		Complicated appendicitis		P value
		Yes	No	
NLR	≥ 8	12	0	0.021*
	< 8	1	87	

*Fisher exact test

During the study period, 100 patients who underwent emergency appendectomy were included in the study, out of which there were 66 male and 34 female patients as shown in table 1. Acute appendicitis was found to be more common in the second decade. During the intra-operative finding, 87 patients had inflamed appendix, 5 patients had abscess and 8 patients had perforated appendicitis. The final diagnosis of acute appendicitis and complicated or uncomplicated acute appendicitis was based on HPE report. In this study, there were 84 cases of uncomplicated acute appendicitis, 13 cases of complicated

acute appendicitis (abscess and perforation) and 3 cases with normal appendix.

As shown in table 2, HPE report of appendicitis was associated with $NLR \geq 3.5$ and it was found to be statistically significant. The sensitivity and specificity of $NLR \geq 3.5$ to determine appendicitis was 92.7% and 66.7% respectively.

With true positive 90 and true negative 2,

Sensitivity = true positive/(true positive + false negative) × 100

$$= 90/(90+2) \times 100 = 97.7\%$$

Specificity = true negative/(true negative + false positive)x100

$$= 2/(2+1) \times 100 = 66.7\%$$

As shown in table 3, the mean value of WBC count, neutrophil percentage and NLR value were significantly higher among the complicated appendicitis than uncomplicated appendicitis. The mean value of lymphocyte percentage was significantly lower among the complicated appendicitis than uncomplicated appendicitis. There was no significant association between age and complicated appendicitis.

As shown in table 4, $NLR \geq 8$ was significantly associated with complicated appendicitis. Sensitivity and specificity of NLR taking 8 as the cut-off point to distinguish between complicated and uncomplicated Acute Appendicitis was 92.3% and 100% respectively.

With true positive 12 and true negative 87,

Sensitivity = true positive/(true positive + false negative)x100

$$= 12/(12+1) \times 100 = 92.3\%$$

Specificity = true negative/(true negative + false positive)x100

$$= 87/(87+0) \times 100 = 100\%$$

Discussion

In this study, out of 100 patients 66 were males and 34 were females. In a similar study by Kelly ME *et al* [17], also reported 57.3% of their study populations to be male. Male to female ratio in this study was 1.94:1 correlating to other studies that found males with AA more than female [18-20]. This study also showed that 8 out of 13 complicated AA cases were male, which may be due to increased cases of AA in male.

The mean age of the patients in this study was 21.8 years. Kelly ME *et al* [17] also reported a mean age of 23.6 years among their study population. In this study maximum cases of

acute appendicitis occurred in 11 to 20 years group (53 cases) followed by 21 to 30 years group (30 cases). It corresponds with various other studies that shows that AA is most common in second decade of life [19-22]. Lohar HP *et al* [23] in his study showed that highest number of cases of acute appendicitis were in 11-20 years group followed by 21-30 years group. Minimum age of the patient in this study group was 8 years and maximum was 66 years old. Both these patients had complicated acute appendicitis (perforation). Such findings have been reported by Bickell NA *et al* [24] where they showed that ruptured appendix being more common in extremes of age.

In this study a cut-off value of 3.5 for NLR was found to have a sensitivity of 92.7% and specificity of 66.7%. Goodman *et al* [25] have done extensive study on NLR as a diagnostic tool for acute appendicitis. They concluded that a NLR higher than 3.5 was a very sensitive indicator for the diagnosis of acute appendicitis.

Adnan N *et al* [26] also studied the diagnostic importance of NLR in childhood appendicitis, they concluded that a cut-off value of 3.5 could predict acute appendicitis. Similar study was done by Yazici M *et al* [27] and they retrospectively studied the neutrophil/lymphocyte ratio in children who underwent emergency appendectomy. They reported 90.2% of acute appendicitis patients had NLR more than 3.5. Studies done by Bialas M *et al* [28] and Choi WJ *et al* [29] also showed $NLR > 3.5$ as a predictor for acute appendicitis.

In this study $NLR \geq 8$ was significantly associated with complicated appendicitis (abscess and gangrene formation). Ishizuka M *et al* [30] with their study on patients undergoing emergency appendectomy found that NLR greater than 8 was significantly associated with gangrenous appendicitis. Hajibandeh S *et al* [15] did extensive research

involving seventeen studies with 8914 patients to determine whether NLR can predict acute appendicitis and if it could distinguish between complicated and non-complicated acute appendicitis. Their result showed that $NLR >4.7$ independently predicts acute appendicitis and $NLR >8.8$ had sensitivity of 76.92% and specificity of 100% in diagnosing complicated appendicitis. Similar study done by Miguel CD *et al* [31] found that a $NLR >8.75$ could differentiate between complicated and non-complicated acute appendicitis. Yardiminci S *et al* [32] also found that neutrophil/lymphocyte ratio greater than 7.95 could distinguish between acute appendicitis with perforation and other acute appendicitis.

Acute appendicitis if left untreated, may progress and could perforate and lead to abscess formation. The leukocyte count is highest during the acute phase of insult, during this stage there is greater increase in the number of neutrophil than lymphocyte. Later on, with the progress of disease there is fall in lymphocyte count, with the largest decrease occurring in gangrenous appendicitis [16]. This phenomenon may explain the rise in NLR with severity of the disease and a higher value in complicated appendicitis. Leukocytosis is a marker of any infection or inflammation. Many studies have been conducted to use it as a diagnostic marker for Acute appendicitis. Sasso RD *et al* [33] in their study found that 99% of their patient with acute appendicitis had leukocyte count more than $10,000/mm^3$. Similar results were also shown by Hossain MM *et al* [18]. The result of this study also showed mean WBC count of $13492.5 /mm^3$ (more than $10,000/mm^3$).

Conclusion

A $NLR \geq 3.5$ may be considered as a simple and sensitive indicator for the diagnosis of acute appendicitis with a sensitivity of 92.7% and specificity of 66.7%. NLR of 8 can be

used as a cut-off value to distinguish between complicated and uncomplicated AA. In this study it has a sensitivity of 92.3% and specificity of 100%.

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