



SIGNIFICANCE OF NEUTROPHIL TO LYMPHOCYTE RATIO IN TREATMENT OF COMPLICATED AND NON- COMPLICATED APPENDICITIS IN A TERTIARY CARE CENTER

Surgery

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ABSTRACT

Background: Appendicitis is one of the common surgical causes of acute abdomen. In atypical clinical progression and non-availability of radiological backup in primary health set ups or rural areas, surgeons find difficulty in deciding the future plan of management, which can be either conservative or surgical management or to refer the patient to higher centers. Delay in diagnosis or management may lead to perforation or peritonitis and increased morbidity and mortality. Any investigation which can predict acute appendicitis and its complications at an early stage shall be of great help. Neutrophil to Lymphocyte ratio (NLR) can be a good predictor of severity of a case of acute appendicitis. **Objective:** The present study aims to differentiate non-complicated, acute appendicitis from complicated appendicitis on the basis of Neutrophil to Lymphocyte ratio (NLR). **Methods:** A retrospective study was carried out in the department of Surgery, FAAMCH in a span of one academic year from July 2020 to June 2021. **Results:** Total cases in this study were 124. Male to female ratio was 1.2:1. Most of the patients belong to the age group of 20-30 years. Out of 124 patients, 41 cases were of complicated appendicectomies and 83 cases were uncomplicated ones. The cut-off value of NLR was obtained as 5.550 with sensitivity 85.4%, specificity 68.7%, positive predictive value (PPV) 57.4%, negative predictive value (NPV) 90.5% and accuracy 84.9%. **Conclusions:** Calculation of NLR pre-operatively can be used for differentiating complicated appendicitis from uncomplicated ones which will help the surgeons in periphery and rural areas to decide the future plan of management. From our study, we can state that NLR value of 5.550 can be used for this purpose.

KEYWORDS

Appendicitis, gangrene, neutrophil, lymphocyte, NLR

BACKGROUND

The neutrophil to lymphocyte ratio (NLR) is a readily available parameter which can be calculated from a complete blood count report of an individual. NLR is being used in clinical practice as a marker of inflammation since a long time. It has also been used as a prognostic marker for mortality in patients in sepsis and also used in cancer patients to determine prognosis. NLR can also be used as a biomarker with high index of accuracy when acute appendicitis is suspected in a patient and depending upon the value of NLR it is possible to differentiate an uncomplicated appendicitis from complicated appendicitis which help surgeon for timely interventions to reduce morbidity and mortality in complicated appendicitis.

Appendicitis is one of the commonly diagnosed surgical causes of acute abdomen. But in the setting of atypical clinical progression and non-availability of radiological backup in primary health set ups or rural areas, surgeons often find difficult to decide on the future plan of management, whether to go for conservative management or surgical intervention or to refer the patient to higher facility. This delay in diagnosis and management may lead to perforation or peritonitis, causing high morbidity and mortality. In a lifetime of an individual, the possibility of occurrence of this disease is approximately 7% and with perforation, it is around 17- 20%. The risk of mortality in general population is less than 1% but it can go up to 50% in elderly patients. (1)

Emergency appendectomy is considered to be the gold standard treatment which may be achieved either by open or laparoscopic approach, yet recent studies have shown that cases of acute abdomen can be managed conservatively. However, in cases of acute abdomen with perforation, conservative treatment has negligible role. Hence, any single investigation that can predict complications associated with acute appendicitis at an early stage shall be of tremendous aid. There comes the role of Neutrophil to Lymphocyte ratio (NLR), which has been found to be a good predictor of severity of a case of acute appendicitis. (1)

Diagnosis of acute appendicitis is done on the basis of clinical manifestations, laboratory findings, imaging and/ or scoring systems such as Alvarado scoring system. Among the imaging modalities, ultrasonography and computed tomography have been widely and successfully used in the diagnosis of acute appendicitis and its complications. Computed tomography (CT), has a high accuracy rate in diagnosing an acute case but it has certain drawbacks i.e. it is relatively expensive, has limited availability and not to mention the

associated risk of getting exposed to high doses of radiation. (2)

Currently, in rural set ups and primary health sectors, not a single method is accurate in establishing the stage of the disease proper. In general, total leukocyte count (TLC) as well as neutrophil count are used as diagnostic tools in appendicitis, however, an elevated TLC has no predictive value in differentiating simple from complicated appendicitis. (2) Many laboratory parameters have been used to determine the severity of infectious or inflammatory diseases, yet the availability, accuracy, intelligibility, time-effectiveness, and cost-effectiveness differs from one another. When the relatively high incidence of acute appendicitis is considered, these drawbacks take on great importance. In the last decade, simple parameters included in a standard complete blood count and routine preoperative tests, including neutrophil count, neutrophil ratio, neutrophil-to-lymphocyte ratio (NLR), platelet count (PLT), mean platelet volume (MPV) and serum bilirubin level, have been studied for potential value in diagnosis of complicated appendicitis. (3)

NLR has been shown to have a high accuracy in diagnosing acute appendicitis; however, most of the studies have showed different cut-off values of NLR. Recently, Goodman et al. advocated the use of neutrophil/lymphocyte (N/L) ratio as a diagnostic tool in adults, and a ratio above 3.5 was stated as optimally diagnostic for appendicitis. The neutrophil count highlights active and continuing inflammation, whereas the lymphocyte count highlights the regulatory pathway. (4) Therefore, our primary objective was to investigate whether NLR can distinguish between uncomplicated and complicated appendicitis. Our second objective was to determine cut-off values of NLR for uncomplicated and complicated appendicitis.

METHODS

A retrospective study of the patients who had undergone appendicectomies was conducted in the department of Surgery, Fakhruddin Ali Ahmed Medical College and Hospital, Barpeta (Assam), during the one year period (July 2020 to June 2021). Patients of all age group and both genders operated for suspected acute appendicitis were included in the study. The present study excluded patients with acute abdomen other than appendicitis, patients having significant comorbidities and malignancies. Perforated or gangrenous appendices and appendicular abscesses were referred to as complicated appendicitis.

A total of 124 patients were included in the study after considering

above mentioned criteria. Age, sex, clinical presentation and CBC including total leucocyte count, neutrophil count and lymphocyte count of patients were recorded. NLR was calculated in all patients. The diagnosis of acute appendicitis in our hospital was done according to clinical manifestation, physical examination, laboratory findings and abdominal ultrasound. The final diagnosis was determined by post-operative histopathological findings.

Statistical Analysis

SPSS software was used for statistical analysis. Data obtained from the patient was expressed as mean, standard deviation and percentages where appropriate. A p-value of ≤ 0.05 was considered as statistically significant and results were evaluated within 95% confidence interval. The study also measured sensitivity, specificity, the optimal cut-off point for NLR, area under the curve (AUC) by using Receiver Operating Characteristic (ROC) analysis. The neutrophil count, lymphocyte count and NLR were evaluated for sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy. The cutoff value of NLR for distinguishing complicated appendicitis from the non-complicated ones was determined by receiver operating characteristics (ROC) curves.

RESULTS

The data of total 124 patients who underwent open appendicectomies for acute appendicitis were analysed in the above mentioned study.

Table 1: Age wise distribution of patients presenting with AA

AGE GROUP (years)	No. of PATIENTS (n)	PERCENTAGE (%)
<10	11	8.8%
11-20	29	23.4%
21-30	39	31.4%
31-40	21	17.0%
41-50	15	12.0%
>51	9	7.4%

Table showing the percentage of patients coming with acute appendicitis in various age groups.

Age ranged from 8 years to 60 years and most of the patients were in 21-30 years of age group with mean age of 29 years.

Table 2: Sex distribution of patients presenting with AA

SEX of PATIENTS	No. of PATIENTS (n)	PERCENTAGE (%)
MALE	65	52.4%
FEMALE	59	47.6%

Table showing the sex distribution of all the patients presenting with acute appendicitis.

Among 124 patients in the study, 65 (52.4%) were male and 59 (47.6%) were female. M:F ratio was 1.2:1.

Table 3: Appendix histopathology of patients presenting with AA

HPE status	No. of PATIENTS (n)	PERCENTAGE (%)
Complicated appendicitis	41	33 %
Uncomplicated appendicitis	83	67 %

Table stating the post-operative histopathological findings of all the cases of acute appendicitis.

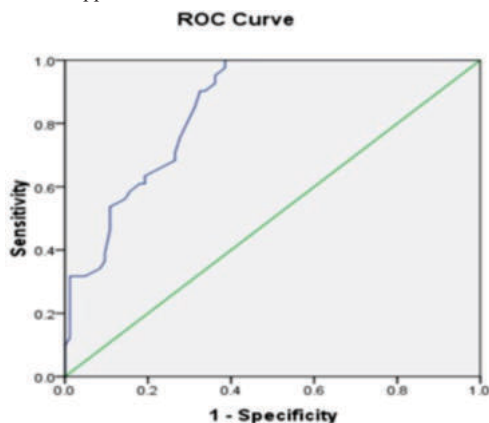


Fig 1: ROC curve for finding the cut-off value of NLR

Out of 124 appendectomy specimens studied, 41 cases showed complicated (perforated/gangrenous) appendicitis. The recommended cut-off value of NLR for complicated appendicitis was determined by using ROC curve analysis. This value was based on most prominent point on the ROC curve by considering the sensitivity (85.4%) and specificity (68.7%). The cut-off value of NLR was obtained as 5.55. The Area under the Curve (AUC) obtained was 0.849. AUC with 95% confidence interval showed Lower Bound 0.785 and Upper Bound 0.914. p value is <0.0001 .

Table 4: Distribution of patients according to the NLR cut-off value

Cut off value of NLR	Complicated AA No. of patients (%)	Non-Complicated AA No. of patients (%)	P value < 0.0001
< 5.55	06	57	
> 5.55	35	26	
	41	83	

Table presenting the number of patients suffering from complicated and non-complicated appendicitis.

p value was calculated by chi square test.

Among 41 patients with complicated appendicitis, 35 patients had high NLR level above the cut-off point.

Among 83 patients with non-complicated appendicitis, 26 patients had high NLR level.

Taking 5.55 as the cut-off value for NLR, following are the statistical parameters:

Sensitivity	:85.4%
Specificity	: 68.7%
Positive predictive value (PPV)	:57.4%
Negative predictive value (NPV)	:90.5%
Accuracy	:84.9%

Fig 2: Statistical parameters of the study

Table 5: Mean NLR values of patients

Patients	Mean NLR	SD (+/-)	Cut off value	P value
Complicated AA	6.27	0.873	5.55	<0.0001*
Non-Complicated AA	4.54	1.29		

Table depicting the mean NLR values in complicated and non-complicated cases of acute appendicitis.

p value calculated by t Test

*Significant ($p < 0.05$)

Preoperative mean NLR levels in complicated AA are significantly raised.

DISCUSSION

Appendicitis is the inflammation of the vermiform appendix. Abdominal pain is the principle symptom of acute appendicitis. Classically, it starts around the umbilicus as dull pain and then migrates to the right iliac fossa, within 4 to 6 hours. This pain in the right iliac fossa is the most reliable diagnostic sign of appendicitis. Rebound tenderness in the right iliac fossa is one of the cardinal signs to diagnosis acute appendicitis. The complicated/perforated appendicitis may also present with fever and rectal fullness. (1) (5)

Confirmatory and early diagnosis of acute appendicitis is not always an easy task. It is further challenging to distinguish clinically between acute, non-complicated appendicitis from a complicated one. Early surgical intervention may lead to removal of normal appendix posing small risk of morbidity. In contrast, a delayed diagnosis and surgical intervention of patients with appendicitis results in increased risk of complications such as perforation, gangrene, abscess and peritonitis.

Based on the study done by Gomes et al. in 2012, we have categorized acute appendicitis into complicated and non-complicated appendicitis. They have classified appendicitis, based on the description of the appendix and the peritoneum, into 5 grades. Grades 1 and 2 correspond to uncomplicated appendicitis and grades 3 to 5 correspond to complicated appendicitis. (6)

Fig 3: Gomes Classification Of Acute Appendicitis

Grades	Findings
0	Normal looking appendix
1	Hyperemia and edema
2	Fibrinous exudate
3A	Segmental necrosis
3B	Base necrosis
4A	Abscess
4B	Regional peritonitis
5	Diffuse peritonitis

Multiple imaging modalities are there to diagnose acute appendicitis. Ultrasound, with an accuracy rate of 71-97%, is less expensive as compared to other methods. Computed tomography has high sensitivity, specificity and accuracy in diagnosing suspected appendicitis. Magnetic resonance imaging has precise diagnostic accuracy in the assessment of acute appendicitis in pregnancy and pediatric patients. However, these radiological investigations are unavailable and cost effective in rural areas, small centers and in regions with poor resource settings.

For this purpose, several biomarkers are being investigated to diagnose acute appendicitis. Many studies stated that NLR is having better diagnostic accuracy for acute appendicitis than C-reactive protein, leucocyte or neutrophil count alone. NLR is also important in prediction and detection of inflammatory and infectious diseases, and their postoperative complications. Recently, it has been stated that NLR can provide diagnostic and prognostic clue in differentiating complicated appendicitis from non-complicated appendicitis. (7) (8) Different authors have stated different cut-off values of NLR. Kahraman S et al suggested the cut-off value of 5.74, with sensitivity of 70.8% and specificity of 48.5%. (7) Ishizuka M et al in their study stated that NLR value of >8 show a significant correlation with gangrenous appendicitis in patients undergoing an appendectomy. (8) In the study by Makki A et al stated NLR cut-off value of 5.74 with a sensitivity of 85.70% and specificity of 61.60%. (9) Sevinc M M et al found NLR value to be 4.8 with sensitivity of 78.4% and specificity of 41.7%.⁽³⁾ Patil S M et al stated that in their study NLR was 5.52 with sensitivity of 71.4% and specificity of 74.7%. (1) Bialas et al found NLR as 3.5 with sensitivity of 77.5% and specificity of 73.3%. The common age group, sex ratio and mean NLR levels of our study were comparable with other studies. (10)

In our study cut-off values of NLR is 5.55 for differentiating complicated acute appendicitis from uncomplicated ones with a better sensitivity and specificity of 85.4% and 68.7% respectively.

CONCLUSIONS

To conclude, calculation of NLR from complete blood count is simple, cost effective and easily accessible parameter which can be employed for differentiating complicated/perforated appendicitis from uncomplicated appendicitis in combination with clinical findings, especially in rural health set ups where advanced facilities for diagnosis are not available. From our study, we can say that NLR value of 5.550 can help us differentiating a case of uncomplicated appendicitis from a complicated one pre-operatively. However, normal value of NLR does not exclude the diagnosis. To find the optimal NLR and to test its accuracy, further prospective multi-centered studies are needed.

Declarations

Ethical Committee Approval: Ethical clearance was taken from ethical committee of the college, Institutional Ethical Committee, Fakhruddin Ali Ahmed Medical College and Hospital, Barpeta, Assam (Reference No. FAAMC&H/P.Est./I.E.C./26/2021/16394).

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