Neutrophil-to-lymphocyte ratio as a predictor of peritonitis in acute appendicitis

Atmanand Verma, Ismail A. Shafik, Abd R. Mashour, Ahmad Y.A. Dayem

Department of General Surgery, Faculty of Medicine, Cairo University, Cairo, Egypt

Correspondence to Ahmad Y.A. Dayem, MD, Department of General and laparoscopic Surgery, Kasr Al Ainy Faculty of Medicine, Cairo University, Cairo 11787, Egypt. Tel: 01111786150; e-mail: dr_ahmadyahia@yahoo.com

Background
Acute appendicitis (AA) is one of the most common causes of acute abdomen. Several imaging, laboratory and inflammatory markers, and scoring systems were developed to diagnose AA, but early and accurate diagnosis is still a matter of debate, despite great advances in diagnosis. Failure to diagnose AA at early stages can lead to severe complications. Neutrophil-to-lymphocyte ratio (NLR) is a potential marker to predict appendicitis and its severity. The neutrophil count highlights active and continuing inflammation, whereas the lymphocyte count highlights the regulatory pathway. This study was conducted to evaluate the validity and diagnostic accuracy of NLR to distinguish noncomplicated and complicated appendicitis with or without peritonitis.

Patients and methods
A total of 94 patients diagnosed as AA who underwent appendectomy were included in our study. NLR was generated from absolute count of total leukocyte count. Perioperative and histopathological findings were compared with NLR as an outcome predictor. Receiver operating characteristic curve analysis was performed to determine the cutoff value of NLR for AA and its severity.

Results
NLR mean correlated ($P<0.001$) in noncomplicated and complicated AA with or without peritonitis. The receiver operating characteristic curve identified that patients with NLR greater than eight had sensitivity 100%, specificity 89.1%, and a 96% area under curve (AUC) in complicated AA with peritonitis. Similarly, NLR 5.3–8.0 had sensitivity 94.7% and specificity 58.7 and 63% AUC in complicated AA without peritonitis and NLR less than equal to 5.3 had sensitivity 88.9%, specificity 85.3% with AUC of 91% noncomplicated appendicitis.

Conclusion
NLR predicts both diagnosis and severity of AA. This may have implications for prioritizing cases for surgery, for monitoring conservatively treated patients, and for patients (pregnant and pediatric) who do not routinely undergo computed tomography scan.

Keywords:
acute appendicitis, lymphocyte, neutrophil, peritonitis

Introduction

Acute appendicitis (AA) is one of the most common causes of acute abdomen with lifetime prevalence of 7% and perforated appendicitis at the rate of 18–34% [1,2]. Although a majority of patients have classical presentation in the emergency department of this disease, early and accurate diagnosis is still a matter of debate. Also, imaging modalities have improved in diagnosis of this disease, but widespread availability and affordability is a matter of concern for developing countries. Failure to diagnose AA at early stages can lead to severe complications like perforated appendicitis, peritonitis, and sepsis, which increases hospital costs, unnecessary costly imagings, and laparotomy. There have been numerous screening and scoring systems for diagnosis of AA like Alvarado, Antigen Induced Release (AIR) score and Raja Isteri Pengiran Anak Saleha Appendicitis (RIPASA) score, but none of the scoring systems have shown diagnostic accuracy in complicated appendicitis.

Several laboratory and inflammatory markers are introduced for diagnosis of AA. Total leukocyte count (TLC) is mostly elevated in AA, however, elevated TLC has no predictive value in differentiating noncomplicated and complicated appendicitis. Elevated serum bilirubin and C-reactive protein have shown good predictability in distinguishing noncomplicated

and complicated appendicitis, but cost and avaibility of tests should be considered [3].

Neutrophil-to-lymphocyte ratio (NLR) is a simple, inexpensive, easily available blood test that can be drawn from routine absolute blood count. NLR provides information regarding two different immune and inflammatory pathways, which may make it a potential marker to predict appendicitis and its severity. The neutrophil count highlights active and continuing inflammation, whereas the lymphocyte count highlights the regulatory pathway.

We aimed to perform a prospective observational study to determine the predictive value of NLR in patients with clinical suspicion of AA. Our main objective was to investigate whether NLR can predict AA and whether it can distinguish between noncomplicated and complicated appendicitis with or without peritonitis by determining cutoff values of NLR.

Patients and methods
We conducted a prospective observational study of 94 patients who underwent appendectomy for AA between December 2021 and May 2022. This research was performed at the Department of General Surgery, Cairo University Hospitals. Ethical Committee approval and written, informed consent were obtained from all participants.

For each patient, we gathered demographic information, laboratory test results, and imaging studies. Exclusion criteria were immunocompromised patients, previous abdominal surgery, and patients with chronic medical debilitating disease.

All patients aged 18–60 years, both sexes, including pregnant patients, were diagnosed with AA based on classical presentation, including those with features of peritonitis, blood count, and abdominal ultrasound by senior consultant surgeon. Intraoperative findings of appendicitis varieties with fluid collection and postoperative histopathological results were also collected.

NLR was generated from routine absolute TLC. This NLR was compared with the intraoperative findings and postoperative appendectomy specimens.

Statistical analysis
All collected data were revised and checked for completeness and accuracy. Analysis of data was performed using software MedCalc (Acacialaan 22, Ostend, Belgium), version 20.110.

Description of variables was presented as follows:

(1) Description of quantitative variables was in the form of mean, SD, and minimum and maximum.
(2) Description of qualitative variables was in the form of numbers and percent.
(3) Data were explored for normality using Kolmogorov–Smirnov test of normality. The results of Kolmogorov–Smirnov test indicated that most of data were normally distributed (parametric data), so parametric tests were used for most of the comparisons.

Comparison between quantitative variables was carried out by one-way analysis of variance, which was used to test the difference between the means of several subgroups of a variable.

The diagnostic performance of a test or the accuracy of a test to discriminate diseased cases from normal cases was evaluated using receiver operating characteristic curve analysis. The cutoff point was estimated to discriminate between the two populations, with sensitivity and specificity.

The significance of the results was assessed in the form of P value that was differentiated into:

(1) Nonsignificant when P value greater than 0.05.
(2) Significant when P value less than equal to 0.05.
(3) Highly significant when P value less than equal to 0.01.

Results
Our study included 94 appendectomy patients of which 43 (45.7%) patients were male and 51 (54.3%) patients were female in the age range of 18–60 years with mean age of 29.3 years (Table 1). Clinical examination, ultrasound abdomen, and intraoperative findings of appendicitis showed three categories of presentation: those are noncomplicated appendicitis, complicated appendicitis without peritonitis, and complicated appendicitis with peritonitis.

NLR values were compared with the complicated appendicitis with or without peritonitis and

Table 1 Sex distribution

Demographic data	Case (appendicitis) (N=94)
Males [n (%)]	43 (45.7)
Females [n (%)]	51 (54.3)
Age (years)	
Mean±SD	29.3±11.04
Range	

noncomplicated AA (Table 2). NLR had significant predictive value for complicated appendicitis with peritonitis at cutoff level greater than 8, with sensitivity 100%, specificity 89.1%, positive predictive value (PPV) 86.7%, and negative predictive value (NPV) 100% with area under curve (AUC) of 0.968. Similarly, NLR had significant predictive value for complicated appendicitis without peritonitis at the cutoff level less than equal to 8, with sensitivity 94.7% and specificity 58.7%, PPV 36.7% and NPV 97.8% with AUC of 0.639, whereas NLR also had significant predictive value for noncomplicated appendicitis at the cutoff level less than equal to 5.3, with sensitivity 88.9%, specificity 85.3%, PPV 76.3%, and NPV 92.9% with AUC of 0.915.

The results of receiver operating characteristic curve analyses for the following comparisons:
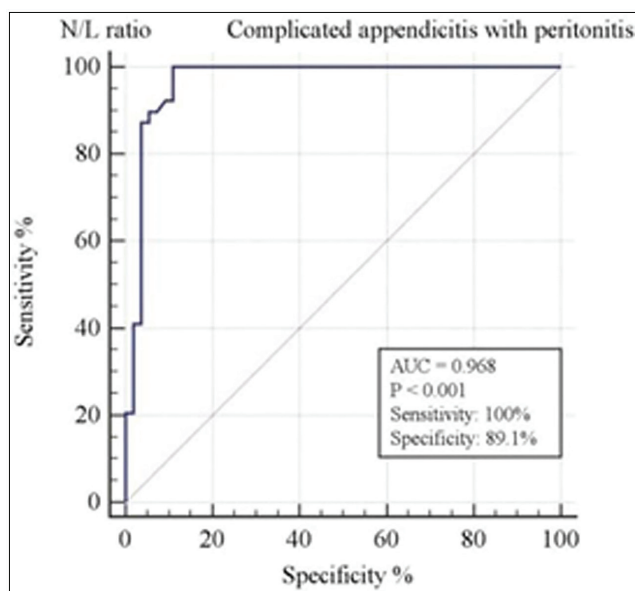
(1) Complicated appendicitis with peritonitis (Fig. 1).
(2) Complicated appendicitis without peritonitis (Fig. 2).
(3) Noncomplicated appendicitis (Fig. 3).

Table 2 Neutrophil-to-lymphocyte ratio relation with appendicitis classification

Appendicitis	NLR		P value
	Mean	SD	
Complicated with peritonitis	12.77	5.42	<0.0001*
Complicated without peritonitis	5.39	1.59	
Noncomplicated	3.52	3.08	1–2, 3
			2–3

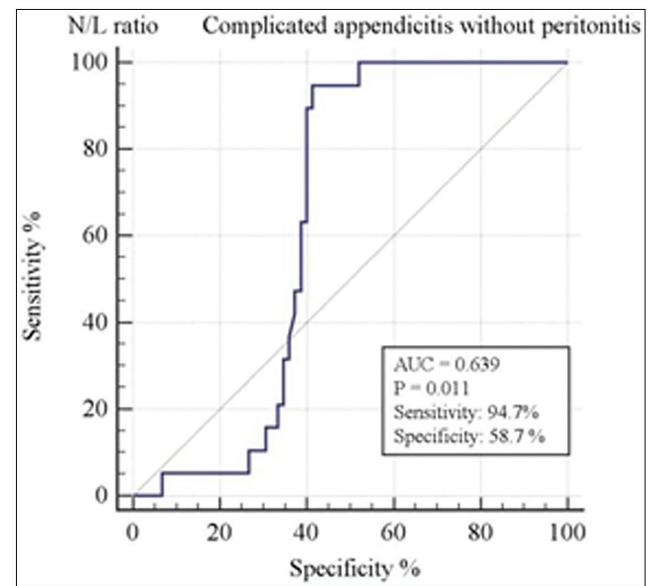NLR, Neutrophil-to-lymphocyte ratio.

Fig. 1

ROC curve predicting the relation of NLR with complicated appendicitis with peritonitis. NLR, neutrophil-to-lymphocyte ratio; ROC, receiver operating characteristic.

Discussion

The diagnosis of AA has significantly improved, however, it is still difficult to make an early and precise diagnosis. A typical presentation and delayed diagnosis create a number of diagnostic risks that may result in misdiagnosis and/or unnecessary surgery. Patients typically arrive with the normal symptoms of AA, but atypical presentations, such as those that are already

Fig. 2

ROC curve predicting the relation of NLR with complicated appendicitis without peritonitis. NLR, neutrophil-to-lymphocyte ratio; ROC, receiver operating characteristic.

Fig. 3
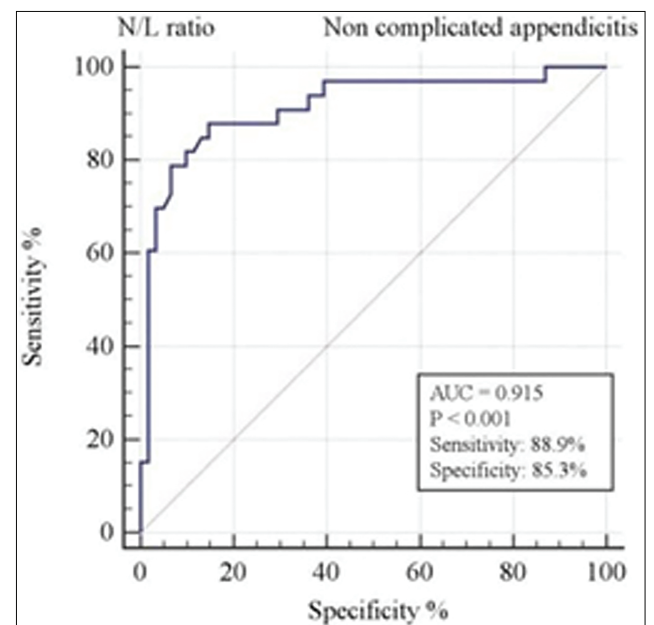
ROC curve predicting the relation of NLR with noncomplicated appendicitis. NLR, neutrophil-to-lymphocyte ratio; ROC, receiver operating characteristic.

perforated or show evidence of peritonitis after an attack of appendicular pain, are also not unusual. In order to avoid complications like perforation leading to peritonitis, sepsis, the necessity for a laparotomy, and a lengthy hospital stay, it is vital to identify and differentiate AA as early as possible.

Our research intends to identify NLR as a new, quick, affordable, and easily accessible predictor of disease severity in terms of AA. In the preoperative diagnosis of AA, some authors contend that NLR is a valid predictor of inflammation [4].

In our study, patients' ages ranged from 18 to 58 years old, with a mean age of 29.3 years and an SD of 11.04 years. Our study included 94 patients of AA. The sex distribution was 45.7% males and 51.3% females showing female predominance of AA although male predominance remains higher in other studies [1,5].

According to reports, the incidence of appendicular perforation ranges from 18 to 34%, and it increases in the elderly [2]. AA with perforation and severe peritonitis has a 5% fatality rate [5]. In our study, two-thirds of the patients had a complicated form of AA, of which 42.5% had complicated AA with peritonitis and 21.3% had complicated AA without peritonitis, with the remaining one-third having a noncomplicated form of AA. In our trial, there was no patient death.

Due to its simplicity of extraction from either the absolute or differential white blood cell count, NLR has become a novel inflammatory marker that can predict both simple and complex appendicitis. To help in the decision-making process when deciding between an operational and nonoperative course, we created cutoff points of NLR for each patient who reported to our emergency room with symptoms of abdominal pain that suggested appendicitis and its severity in the current study.

In the present study, NLR was significantly higher in cases with complicated AA with peritonitis, in comparison with cases with complicated without peritonitis and noncomplicated cases ($P \leq 0.05$). NLR shows significant predictive value for complicated appendicitis with peritonitis at the cutoff level greater than 8, with sensitivity 100%, specificity 89.1%, PPV 86.7%, and NPV 100%, respectively, with AUC of 0.968.

NLR has significant predictive value for complicated appendicitis without peritonitis at the cutoff level less than equal to 8, with sensitivity 94.7%, specificity 58.7%, PPV 36.7%, and NPV 97.8%, respectively, with AUC of 0.639. NLR has significant predictive value

for noncomplicated appendicitis at the cutoff level less than equal to 5.3, with sensitivity 88.9%, specificity 85.3%, PPV 76.3%, and NPV 92.9%, respectively, with AUC of 0.915.

In the present study, based on intraoperative findings, NLR was significantly lower in cases with catarrhal appendicitis in P less than equal to 0.05. Also, cases of suppurative appendicitis had significant lower NLR than gangrenous and perforated cases ($P \leq 0.05$). Our study showed good results in comparison with other studies performed earlier for appendicitis severity [3,6,7].

Although nowadays computed tomography scan is commonly used for diagnosis of AA to balance the risk of a negative appendectomy with the risk of delayed surgery, the advantages of NLR are routinely done in blood tests, affordable, widespread available, noninvasive, repeatable, and it can be considered as an accurate marker that has a great potential to facilitate decision-making in selected populations and settings. In this study, we found that NLR, in addition to predicting appendicitis, can distinguish between complicated and noncomplicated appendicitis. This property of NLR may have implications in terms of prioritizing the cases with clinically or radiologically confirmed uncomplicated appendicitis waiting for emergency appendectomy in busy general surgical settings: patients with higher baseline NLR who are at higher risk of perforation could be operated earlier either by open or laparoscopic procedure.

Furthermore, considering the growing interest in conservative management of noncomplicated AA in recent years, the aforementioned property of NLR may potentially have a role in patients with radiologically confirmed noncomplicated appendicitis who are treated conservatively in terms of monitoring the response to conservative management, predicting the risk of complications, and recognizing the failure of conservative management. NLR may also play an important role in diagnosing appendicitis in selected population (pregnant and pediatrics), countries, and settings where 'twenty-four seven' access to immediate computed tomography for every single patient is limited.

The result of our study suggests that NLR is a promising inflammatory marker that can predict AA in patients with clinical suspicion of appendicitis and also can potentially distinguish noncomplicated and complicated appendicitis. According to our research, chances of developing severe complications like perforation and peritonitis following attack of AA increase exponentially as NLR value increases.

Conclusion

This study shows that the NLR can be a cheap and quick tool to apply in emergency departments to differentiate noncomplicated and complicated appendicitis with peritonitis with acceptable sensitivity and specificity. The chances of developing complication following appendicitis increase exponentially as NLR value increases. NLR also has potential to facilitate early decision-making for patients in need of operative management and follow-up of conservative management of appendicitis.

Conflicts of interest
There are no conflicts of interest.

Reference

1 Shimizu T, Ishizuka M, Kubota K. A lower neutrophil to lymphocyte ratio is closely associated with catarrhal appendicitis versus severe appendicitis. Surg Today 2016; 46:84–89.

2 Sirikurnpiboon S, Amornpornchareon S. Factors associated with perforated appendicitis in elderly patients in a tertiary care hospital. Surg Res Pract 2015; 2015:847681.

3 Hajibandeh S, Hajibandeh S, Hobbs N, Mansour M. Neutrophil-to-lymphocyte ratio predicts acute appendicitis and distinguishes between complicated and uncomplicated appendicitis: a systematic review and meta-analysis. Am J Surg 2020; 219:154–163.

4 Kahramanca Ş, Özgehan G, Şeker D, Gökce Eİ, Şeker G, Tunç G, et al. Neutrophil-to-lymphocyte ratio as a predictor of acute appendicitis. Turk J Trauma Emerg Surg 2014; 20:19–22.

5 Sartelli M, Baiocchi GL, Di Saverio S, Ferrara F, Labricciosa FM, Ansaloni L, et al. Prospective observational study on acute appendicitis worldwide (POSAW). World J Emerg Surg 2018; 13:1–0.

6 Beecher SM, Hogan J, O'Leary DP, McLaughlin R. An appraisal of inflammatory markers in distinguishing acute uncomplicated and complicated appendicitis. Dig Surg 2016; 33:177–181.

7 Delgado-Miguel C, Muñoz-Serrano AJ, Estefanía K, Velayos M, Serradilla J. Neutrophil-to- lymphocyte ratio as a predictor of peritonitis in acute appendicitis in children. Cir Pediatr 2019; 32:185–189.