

Diagnostic Value of Neutrophil Lymphocyte Ratio in Detection of Acute Appendicitis

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Abstract

Background: The diagnosis of acute appendicitis (AA) sometimes is illusive and the accompanying clinical and laboratory manifestations cannot be used for definitive diagnosis. **Objective:** This study aimed to evaluate the diagnostic value of neutrophil/lymphocyte ratio (NLR) in detection of AA. **Materials and Methods:** This is a cross-sectional study that included a total of 80 adult patients with AA and 62 age- and gender-matched patients with abdominal pain due to causes other than AA. Three milliliter of peripheral blood were collected from each participant. The NLR was calculated by dividing the absolute neutrophil count by the absolute lymphocyte count. Receiver operating characteristic curve was used to assess the diagnostic value of NLR in detection of AA cases. **Results:** Mean NLR in AA patients was 7.18 ± 2.11 compared with 2.68 ± 1.08 in patients with abdominal pain due to causes other than AA with a highly significant difference. The area under the curve was 0.916 (95% confidence interval = 0.842–0.989), $P < 0.001$. The sensitivity and specificity of the test at $NLR = 4.45$ were 90% and 83%, respectively. **Conclusions:** NLR is an easy, inexpensive test that can be used for AA detection. This test is more sensitive and more specific than either total white blood cell or absolute neutrophil count.

Keywords: Acute appendicitis, diagnosis, neutrophil lymphocyte ratio, receiver operating characteristic

INTRODUCTION

Appendicitis is an inflammation of the vermiform appendix and represents the most common cause of acute abdomen and emergency surgical indication in the world. Acute appendicitis (AA) has a life risk of 8.6% in males and 6.7% in females.^[1] The disease is characterized by a wide range of symptoms that overlap with other gastroenterological, gynecologic, or urologic conditions, such as peptic ulcer disease, Meckel's diverticulum, Crohn's disease, gastroenteritis, irritable bowel disease, ectopic pregnancy, endometriosis, testicular or ovarian torsion, pelvic inflammatory disease, urinary tract infection, and renal stones.^[2]

AA diagnosis depends on clinical features and radiological investigation.^[3] However, early diagnosis is challenging because differential diagnosis of appendicitis is so extensive. Patients may not have any abdominal discomfort early in the disease process. Furthermore, many patients may not present with the classically described history or physical findings.^[2] The effectiveness of ultrasonography as a tool to diagnosis appendicitis is highly operator dependent. Even in very

skilled hands, the appendix may not be visualized. Its overall sensitivity is 0.86, with specificity of 0.8. The sensitivity and specificity of computed tomography (CT) are 0.94 and 0.95, respectively. Thus, CT imaging, given its high negative predictive value, may be helpful if the diagnosis is in doubt, although studies performed early in the course of disease may not have any typical radiographic findings.^[4]

Many screening and scoring tools have been used to aid the diagnosis of AA such as Alvarado score^[5] and the RIPASA score.^[6] However, these scores have low sensitivity and specificity and cannot be used for predicting the severity of AA.^[7]

As an inflammatory disorder, AA involves a certain degree of leukocytosis. Nevertheless, the white blood cell (WBC)

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count is only mildly to moderately elevated in approximately 70% of patients with simple appendicitis (with a leukocytosis of 10,000–18,000 cells/ μ L). A “left shift” toward immature polymorphonuclear leukocytes is present in >95% of cases.^[2]

Thus, finding an alternative marker possessing high sensitivity and specificity which can be used for early detection and differentiate complicated from noncomplicated cases is still a subject of interest.

Neutrophil-lymphocyte ratio (NLR) could be an important measure of systemic inflammation as it is readily available, cost-effective, and could be calculated easily.^[8] During the last few years, NLR has been shown to indicate the degree of body inflammation in a variety of inflammatory illnesses and are associated with the stage and grade of a particular illness.^[9,10] This study aimed to assess the diagnostic value of NLR in the detection of AA.

MATERIALS AND METHODS

The study population

This is a cross-sectional study that was conducted Al-Yarmook Teaching Hospital, Baghdad, Iraq, from November 2018 to January 2019. The study included a total of 80 adult patients with AA. The diagnosis of AA was made with a combination of clinical, laboratory, and imaging findings, and then confirmed with surgical operation. The patients underwent emergency or urgent appendectomy according to their condition. Other age- and sex-matched 62 patients suffering from abdominal pain due to causes other than AA (assigned here as controls) were also recruited to represent control group. Patients with urinary tract infection and those with a known history of autoimmune diseases were excluded from the study.

Ethical consideration

This study was approved by the Review Board of Tropical-Biological Research Unit/College of Science/University of Baghdad. A written consent from each participant was obtained prior to sample collection after explaining the aim of study. Each patient was given the complete unconditioned choice to withdraw anytime. The confidentiality of data throughout the study was guaranteed and the patients were assured that data will be used for research purpose only.

Socio-demographic and clinical data including, age, sex, body mass index (BMI), vomiting, nausea, anorexia, diarrhea, and constipation were collected through direct interview.

Sample collection and laboratory investigations

Three milliliter of peripheral blood were collected from each participant. Hematology auto analyzer (Huroba ABX/India) was used to measure blood parameters. NLR was calculated by dividing the absolute neutrophil count by the absolute lymphocyte.

Statistical analysis

All statistical analyses were performed using SPSS statistical software, version 24 (SPSS, IBM company, Chicago, Illinois, USA). The normal distribution of continuous data

was tested with Shapiro–Wilk test. Normally distributed variables were presented as mean \pm standard deviation categorical variables were expressed as counts and percentages. For comparison between two groups of continuous data, independent *t*-test was used, and for comparison between categorical variables, Chi-square test was performed. Receiver operating characteristic (ROC) curve analyses was used evaluate the diagnostic value of NLR in detection of AA. The correlation between NLR and each of disease duration and number of attacks was explored using Pearson’s correlation. For all tests, a significant level of statistics was considered when $P < 0.05$.

RESULTS

The mean age of the AA patients and controls was 31.11 ± 8.2 years and 36.84 ± 11.52 years, respectively with no significant difference. Likewise, the two groups were comparable in respect to BMI, gender distribution, Hb concentration, frequency of nausea, and absolute lymphocyte count. However, patients with AA showed significantly higher frequency of vomiting, anorexia, and constipation (72.5%, 95%, and 57.5%, respectively) than controls (32.26%, 37.1%, and 12.9%, respectively). In contrast, AA patients had significantly less frequency of diarrhea than controls (8.75% vs. 54.84%).

Absolute neutrophil count than patients with other causes of abdominal pain ($4.61 \pm 1.4 \times 10^3/\text{ml}$ vs. $3.72 \pm 1.22 \times 10^3/\text{ml}$). As *per se*, patients with AA demonstrated significantly higher mean WBC and absolute neutrophil count ($17.94 \pm 4.33 \times 10^3/\text{ml}$ and $13.69 \pm 4.87 \times 10^3/\text{ml}$, respectively) than controls ($9.18 \pm 2.86 \times 10^3/\text{ml}$ and $6.21 \pm 1.61 \times 10^3/\text{ml}$, respectively) as shown in Table 1.

Neutrophil lymphocyte ratio

Mean NLR in AA patients was 7.18 ± 2.11 compared with 2.68 ± 1.08 in controls with a highly significant difference [Figure 1].

Diagnostic value of neutrophil lymphocyte ratio

ROC curve was used to assess the diagnostic value of NLR in detection of AA cases compared with other abdominal

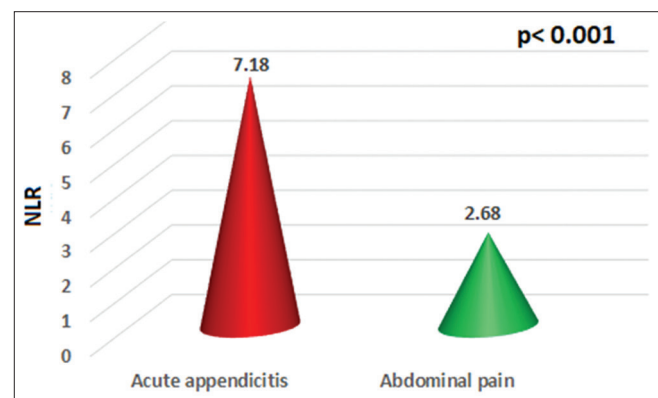


Figure 1: Neutrophil/lymphocyte ratio in patients with acute appendicitis and those with other causes of abdominal pain

pain. The results are depicted in Figure 2. The area under the curve (AUC) was 0.916 (95%confidence interval [CI] = 0.842–0.989), $P < 0.001$. The sensitivity and specificity of the test at NLR = 4.45 were 90% and 83%, respectively.

Table 1: Demographic and clinical characteristics of the patients

Characteristics	Patients (n = 80), n (%)	Controls (n = 62), n (%)	P
Age (years)	31.11 ± 8.2	36.84 ± 11.52	0.127
Range	18–48	20–57	
BMI (kg/m ²)	26.83 ± 3.46	27.88 ± 4.9	0.512
Gender			
Male	49 (61.25)	39 (62.9)	0.840
Female	31 (38.75)	23 (37.1)	
Vomiting			
No	22 (27.5)	42 (67.74)	<0.001
Yes	58 (72.5)	20 (32.26)	
Nausea			
No	19 (23.75)	15 (24.19)	0.951
Yes	61 (76.25)	47 (75.81)	
Diarrhea			
No	73 (91.25)	28 (45.16)	<0.001
Yes	7 (8.75)	34 (54.84)	
Anorexia			
No	4 (5)	39 (62.9)	<0.001
Yes	76 (95)	23 (37.1)	
Constipation			
No	34 (42.5)	54 (87.1)	<0.001
Yes	46 (57.5)	8 (12.9)	
Hb (g/dl)	13.14 ± 3.1	12.92 ± 2.66	0.781
Total WBC (×10 ³ /ml)	17.94 ± 4.33	9.18 ± 2.86	<0.001
Neutrophil (×10 ³ /ml)	13.69 ± 4.87	6.21 ± 1.61	<0.001
Lymphocyte (×10 ³ /ml)	2.06 ± 0.83	2.41 ± 0.68	0.221

BMI: Body mass index, Hb: Hemoglobin, WBC: White blood cell

For total WBC, the AUC was 0.887 (95%CI = 0.807–0.966), $P < 0.001$. The sensitivity and specificity was 80% at cut off value of WBC = 12.9×10^3 /ml. Almost similar results were obtained from absolute neutrophil count where the AUC was 0.795 (95% CI = 0.677–0.913), $P < 0.001$. The sensitivity and specificity were 80% at cut off value of neutrophil = 10.8×10^3 /ml [Figure 3].

DISCUSSION

According to the results of the present study, the NLR has a very good diagnostic value for detection of AA. Furthermore, this diagnostic value exceeds that for both total WBC and absolute neutrophil. In accordance with these result is a large number of studies worldwide. In Turkey, Yilmaz and Ayhan Acar^[11] evaluated the diagnostic and reliability of NLR in detection of pediatric AA. The AUC was 0.694, while the sensitivity and specificity were 84.2% and 56.7%, respectively, at cut off value of NLR = 3.5. Almost very close results were obtained by several international studies.^[12-16] Furthermore, a recent meta-analysis included 17 observational studies with a total of 8914 patients with AA. After adjusting for the possible confounders, NLR of >4.5 was found to be independent predictor for AA, and NLR >8.8 independent predict complicated appendants with acceptable sensitivity and specificity.^[3] However, a higher sensitivity (97.1%) and very specificity (25%) were reported in another study.^[17]

What makes NLR a potential marker for AA is that it provides information for two important pathways in the body which are immune and inflammatory pathways. The typical histological characteristics of AA are mucosal ulceration and transmural infiltration of neutrophils, which implies no involvement of lymphocytes. However, in a more chronic stage of appendicitis, infiltration of lymphocytes is observed.^[18] On the other hand, abdominal pains due to other causes may be attributed to some infectious agent such as intestinal protozoa and enteric

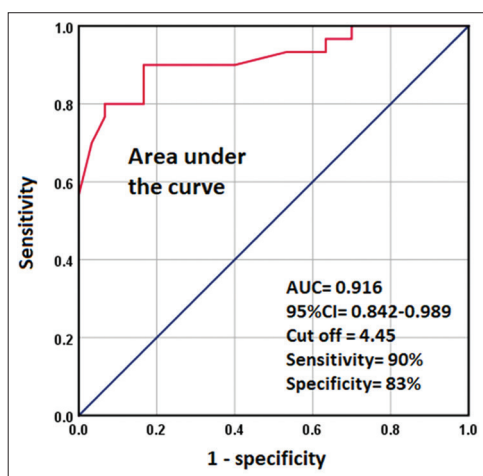


Figure 2: Receiver operating characteristic curve for neutrophil/lymphocyte ratio in the context of discrimination between acute appendicitis and control

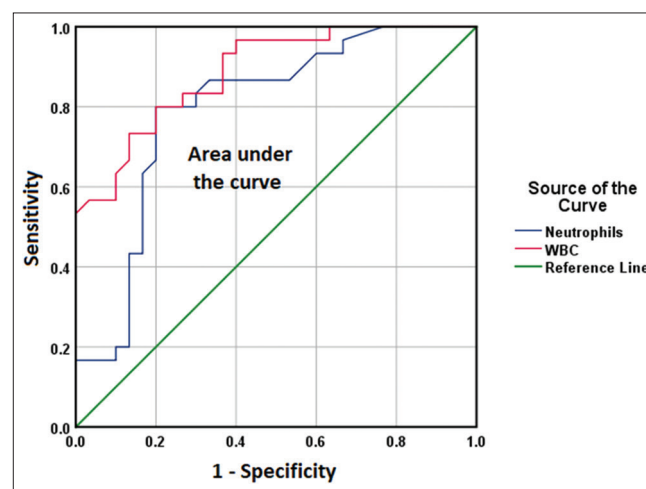


Figure 3: Receiver operating characteristic curve for total white blood cell and absolute neutrophils in the context of discrimination between acute appendicitis and control

bacteria. In these circumstances, the role of neutrophils is less prominent, while there will be a specific immune response characterized by proliferation and infiltration of lymphocyte.^[19]

Of note, NLR cannot be the sole tool for diagnosis of AA. However, such ratio has important clinical implications. For example, it helps in decreasing the negative appendectomy. That is because surgeons generally have low threshold for achieving appendectomy depending on the reasonable clinical suspension to avoid possible complication like perforation.^[20] However, such strategy increases the negative appendectomy to up to 25%.^[21] Thus, NLR has a great potential to facilitate decision-making in these settings. Another clinical application of NLR is in terms of AA management. Recently, there is a growing interest in conservative management of uncomplicated AA. In this regard, NLR can be used for monitoring the response to this type of treatment. Finally, NLR becomes an appropriate diagnostic tool for AA in settings where twenty four/day for seven days access to other diagnostic tools, such CT scan, is limited, or to reduce the exposure to ionizing radiation in certain patients including pregnant women and pediatric patients.

A chief limitation for this study was that the diagnostic value of NLR in the context of differentiation between complicated and uncomplicated AA was not performed because the time limitation and data shortage. Another limitation is the relatively small sample size which undoubtedly reduce the statistical power of the study.

However, the present study provides a further evidence about the role of NLR as an easy, routine leukocyte count and inexpensive test that can be used for AA detection. This test is more sensitive and more specific than either total WBC or absolute neutrophil count.

CONCLUSIONS

NLR is an easy, inexpensive test that can be used for AA detection. This test is more sensitive and more specific than either total white blood cell or absolute neutrophil count.

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Conflicts of interest

There are no conflicts of interest.

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