ROLE OF NEUTROPHIL/LYMPHOCYTE RATIO IN DIAGNOSIS OF ACUTE APPENDICITIS

Faruk Hassan Faraj *, Sherko Abdullah Molah Karim *
and Fattah Hama Rahim Fattah ***

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ABSTRACT

Background

Acute appendicitis is one of the most common causes of acute abdomen. Its accurate diagnosis and immediate surgery are important, because the disease itself and its operation carry a potential risk of morbidity and mortality. The aim of this study is to detect the role of Neutrophil/Lymphocyte Ratio in diagnosis of acute appendicitis and detection of the severity of the inflammation.

Objectives

The relation between the values of NLR and positive appendectomy and normal appendectomy. The relation between Neutrophil Lymphocyte Ratio and the degree of severity of inflammation in acute appendicitis.

Methods

This prospective study was performed in Emergency Hospital of Slemani from February, 25th, 2012 to November, 29th, 2012 on 200 patients who were admitted with clinical suspicion of acute appendicitis. Data were collected regarding demographical aspects of patients, presentations, pre operative care, investigations including complete blood counts, histopathological examination of the all specimens after surgery.

Results

There were 78(39%) males and 122 females (61%). Male: female ratio was 1:1.25. The age ranges from 5 to 67 years. The mean age of acute appendicitis was 25.94±12.4. Histopathological examination revealed normal appendix in 74 patients. The normal appendectomy rate was (36.7%). The rate of normal appendectomy in females was (43.3%), while among males it was (26.9%). In (85%) of patients with acute appendicitis there were elevated Neutrophil Lymphocyte Ratio (NLR) ≥ 3.5 with specificity of (72%), and accuracy of (80%), and Neutrophil Lymphocyte Ratio was increased with increasing the degree of inflammation.

Conclusion

The Neutrophil Lymphocyte Ratio is an easy and applicable investigation which can be helpful in diagnosis of acute appendicitis, and detecting the severity of the inflammation.

Keywords: *Acute Appendicitis, Neutrophil/Lymphocyte Ratio.*

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* Department of Surgery, School of Medicine, Faculty of Medical Sciences, University of Sulaimani.
Correspondence: faruk.kurda@gmail.com.
** Ranya General Hospital.
*** Department of Community Medicine, School of Medicine, Faculty of Medical Sciences, University of Sulaimani

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INTRODUCTION

Acute appendicitis is one of the most common causes of acute abdomen [1]. It is an acute inflammation of the vermiform appendix, which thought to be initiated by progressive increases in intraluminal pressure that compromises venous outflow [2]. The mucous secretion in the closed appendix, distal to the obstructed point, will result in a rise in intraluminal pressure. Perfusion to the inner layers of the appendiceal wall is compromised, and tissue ischemia, progressing to necrosis, begins [3]. Ischemic injury and stasis of intraluminal contents, which favor bacterial proliferation, trigger inflammatory responses. These responses are including tissue oedema and neutrophilic infiltration of the lumen, muscular wall, and periappendiceal soft tissues [2].

The diagnosis of acute appendicitis is essentially clinical; however, a number of investigations and imaging study have been assisted the diagnosis [4]. Neutrophil / Lymphocyte Ratio is defined as the percentage of neutrophil divided by the percentage of lymphocyte. (N/L R= Neutrophil % / Lymphocyte %). Inflammation is induced by chemical mediators that are produced by host cells in response to injurious stimuli [2]. When a microbe enters a tissue, the presence of infection is sensed by resident cells, mainly macrophages, but also dendritic cells, mast cells, and other cell types [2]. These cells secrete molecules (cytokines and other mediators) that induce and regulate the subsequent inflammatory response. Some of these mediators promote the efflux of plasma and recruitment of circulating leukocytes to the site where the offending agent is located [5].

The recruited leukocytes are activated and they try to remove the offending agent by phagocytosis. The principal leukocytes in acute inflammation are neutrophils (polymorphonuclear leukocytes) [6]. Leukocytes may be divided into two broad groups: the phagocytes and the immunocytes. Granulocytes, which include three types of cell, neutrophils (polymorphs), eosinophiles, and basophiles, together with monocytes comprise the phagocytes. The lymphocytes and plasma cells are the immunocytes [5]. Mild leukocytosis, ranging from 10,000 to 18,000 cells/mm^3 is usually present in patients with acute, uncomplicated appendicitis which is more common in child and young adult with appendicitis [7]. In older adult, the leukocyte count and differential are normal more frequently than in young adults. White blood cell counts above 18 000 cells/mm^3 raise the possibility of a perforated appendix with or without an abscess [7]. Pregnant women normally have physiologic leukocytosis that can reach (15 000 – 20 000) as their pregnancy progresses [8]. In a stable or normal state, the bone marrow storage compartment contains 10-15 times the number of granulocytes found in the peripheral blood. After 6-10 hours, the neutrophils can perform their phagocytic function in the tissues and they spend on average 4-5 days in the tissues before they are destroyed [6]. An increase in circulating neutrophils to levels greater than 75% is one of the most frequently observed blood count changes [5]. In acute appendicitis, the leukocytosis is often accompanied by a moderate polymorphonuclear predominance (more than 75%) [7].

Lymphocytes are the immunologically competent cells that assist the phagocytes in defense of the body against infection and other foreign invasion. The immune response depends on two types of lymphocytes, B and T cells [5]. Lymphocytosis often occurs in infants and young children in response to infections that produce a neutrophil reaction in adults [6]. Lymphopenia may occur in a variety of immunodeficiency syndromes, major surgery, sepsis, and extensive tissue injury which may be accompanied by neutrophilia. Neutrophil/ Lymphocyte Ratio will increase and may reflect the severity of infection or stressful condition [6].

MATERIALS AND METHODS

This is a prospective study, on 200 patients, who were admitted to accident and emergency hospital of Sulaimanyah from February, 25th, 2012 to November, 29th, 2012 with suspicion of acute appendicitis, and then they underwent appendicectomy. Data were collected regarding history, physical examination, demography (name, age, sex) of the patients, presentations, and investigations including complete blood counts. Data also were collected regarding the histopathological examination of the appendix of each patient to confirm or rule out the acute appendicitis and detection the severity of the inflammation. This is a prospective cross sectional descriptive study, and the statistical analysis was performed by using (SPSS) statistical program. Qualitative data was expressed as numbers and percentage while quantitative data was expressed as mean ±standard deviation (SD). Probability value < 0.05 was regarded as a statistical significant value.

RESULTS

In the 200 patients with suspected acute appendicitis who were admitted in Emergency Hospital of Slemani,

There were 78 (39%) males and 122 (61%) females, with male:female ratio of 1:1.25. They had been suspected acute appendicitis and underwent appendectomy. One hundred twenty six patients had inflamed appendix, the age rang was 5-67 years and the mean age was 25.94±12.4. There were 56 (44.4%) males, and 70 (55.6%) females as shown in table (1). Age and sex distribution shown in table (1).

In this study, 74 patients had normal appendix. The normal appendectomy rate was (36.7%) and 126 patients had inflamed appendix (63.3%), Figure (1)

Acute appendicitis can be classified histopathologically in to 3 subtypes, which are simple acute appendicitis, acute suppurative, and acute gangrenous [7, 9].

Twenty one patients who had normal appendix, were male; the rate of negative appendectomy among males was (26.9%). Fifty three patients who had normal appendix, were female; the rate of negative appendectomy among females was (43.3%), as shown in table (2).

Out of 126 patients with inflamed appendix;

Acute appendicitis: includes 42 (33.3%) patients.

Acute suppurative: includes 64 (50.8%) patients.

Acute gangrenous: includes 20 (15.9%) patients.

As shown in figure (2).

Table 1. The age and sex distribution with duration of illness in this study in inflamed group only.

Appendicitis	Frequency	Percent
Gender		
Male	56	44.4
Female	70	55.6
Total	126	100.0
Age		
10 or less	3	2.4
11-20	49	38.9
21-30	41	32.5
31-40	16	12.7
41-50	9	7.1
51-60	7	5.6
More than 60	1	.8
Total	126	100.0
< 24 hours	74	58.7
24-48 hours	36	28.6
> 48 hours	16	12.7
Total	126	100.0

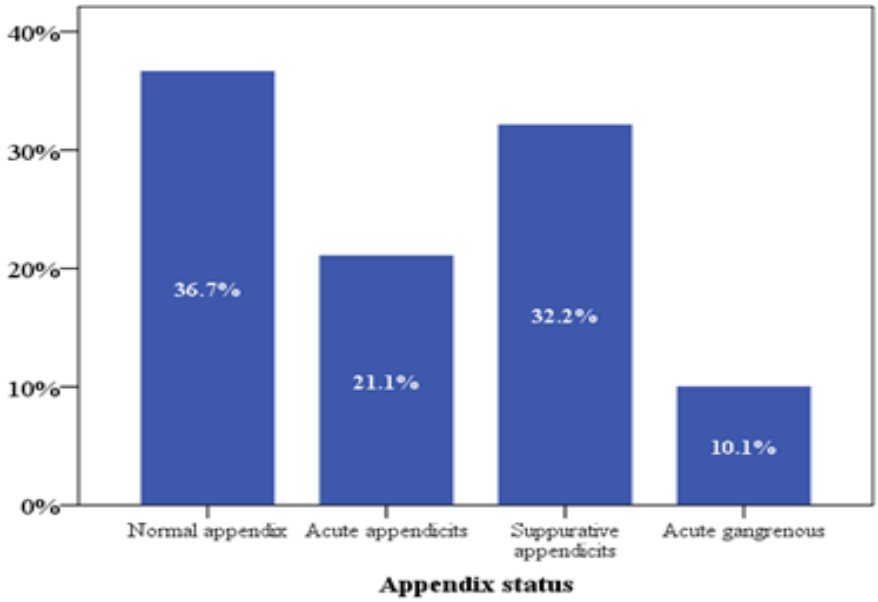

Figure 1. Bar chart shows the percentage of normal and subtypes of acute appendicitis.

Table 2. The number and percentage of negative appendicectomy in both genders.

Gender	No. and percentage	No. and percentage of –ve appendicectomy	No. and percentage of +ve appendicectomy
Male	78 (39%)	22 (26.9%)	56 (73.1%)
Female	122 (61%)	52 (43.3%)	70 (56.7%)
Total	200	74	126

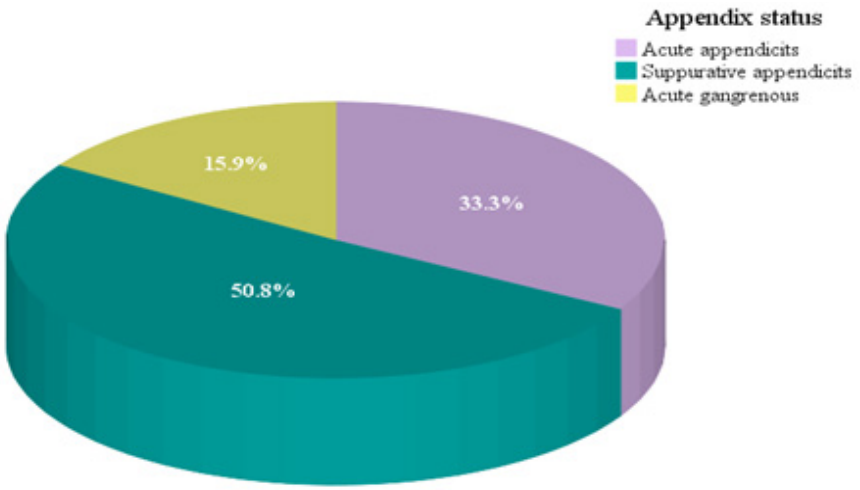

Figure 2. Pie chart is showing the percentage of subtypes of acute appendicitis among the inflamed group (the severity of appendicitis).

In this study, we found that the neutrophil was increased with increasing the degree of inflammation, while the lymphocyte was decreased; hence, the NLR was increased as shown in table (3) and table (4).

Acute appendicitis

The mean of neutrophil percentage was 73.93%, and the SD of 9.2, The mean lymphocyte percentage was 21.56%, and the SD of 7.9, The mean NLR was 4.10, and the SD of 2.1.

Acute suppurative

The mean of neutrophil percentage was 81.11%, and the SD of 6.6, The mean of lymphocyte percentage was 14.58%, and the SD of 6.2, The mean of NLR was 6.53, and the SD of 2.9.

Acute gangrenous

The mean of neutrophil percentage was 83.68%, and the SD of 5.2, The mean of lymphocyte percentage was 11.86%, and the SD of 3.7, The mean of NLR was 7.9, and the SD of 2.8, as shown in table (4)

In this study, we used the cutoff point of ≥ 3.5 for detecting sensitivity, specificity, and accuracy [9, 14, 18, 19, 20]. The results were as follow;

Sensitivity: 85%, Specificity: 72%, Positive predictive value: 84%

Negative predictive value: 74%, Accuracy: 80%, as shown in table (5)

The mean NLR was 6 in acute appendicitis regardless of the degree of the inflammation, as shown in figure (3).

In this study, we found the low mean of NLR in the age group below 10 years and the peak was at 31-40 years age group and it increased in age group above 60 years, as shown in figure (4). Less than 10 years the mean of NLR was 2.7, 11-20 years the mean of NLR was 6.1, 21-30 years the mean of NLR was 5.6, 31-40 years the mean of NLR was 6.6, 41-50 years the mean of NLR was 6.1, 51-60 years the mean of NLR was 5.7, and above 60 years the mean of NLR was 8.3, as shown in figure (4) (p=0.407)

In this study, we found that the mean of NLR is directly proportional with duration of the abdominal pain, as shown in figure (5)

P value = 0.478 (not significant)

Table 3 Mean WBC and NLR in normal appendix and acute appendicitis, P. Value = 0.001 (significant)

Parameters	Normal appendix Mean ±Std. Deviation	Appendicitis Mean±Std. Deviation	P values
Neutrophil (%)	66.5 ± 10.5	79.1± 8.3	0.001
Lymphocyte (%)	27.6± 9.7	16.4± 7.5	0.001
WBC	10551.2± 4076.9	12732.8± 3745.10	0.001

Table 4. The mean of WBC, Neutrophil, Lymphocyte, and NLR with the subtypes of acute appendicitis. P. Value = 0.001 (significant).

	Mean	Std. Deviation	P values
WBC			
Acute appendicitis	10931.9	2838.4	0.001
Suppurative appendicitis	13891.7	3598.0	
Acute gangrenous	12863.0	4574.1	
Neutrophil (%)			
Acute appendicitis	73.93	9.2	0.001
Suppurative appendicitis	81.11	6.6	
Acute gangrenous	83.68	5.2	
Lymphocyte (%)			
Acute appendicitis	21.56	7.9	0.001
Suppurative appendicitis	14.58	6.2	
Acute gangrenous	11.86	3.7	
NLRatio			
Acute appendicitis	4.10	2.1	0.001
Suppurative appendicitis	6.53	2.9	
Acute gangrenous	7.90	2.8	

Table 5. Sensitivity, specificity, and accuracy of NLR and WBC in diagnosis of acute appendicitis.

Tests	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
NL ratio	85	72	84	74	80
WBC	63	67	78	55	67

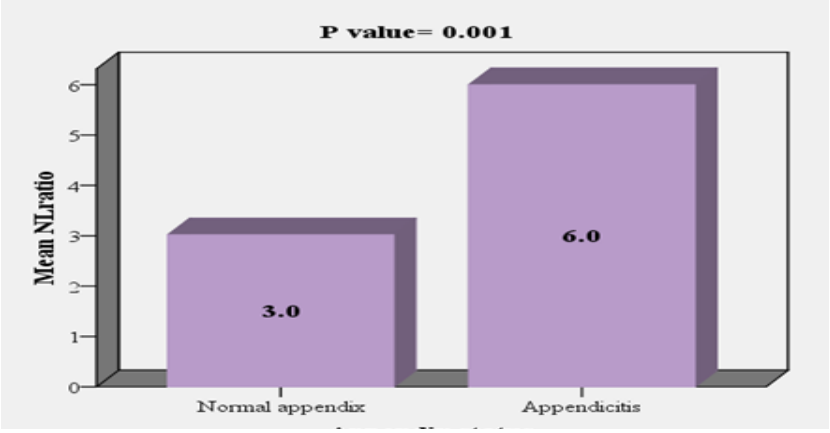

Figure 3. Bar chart shows the mean NLR in normal appendix and acute appendicitis.

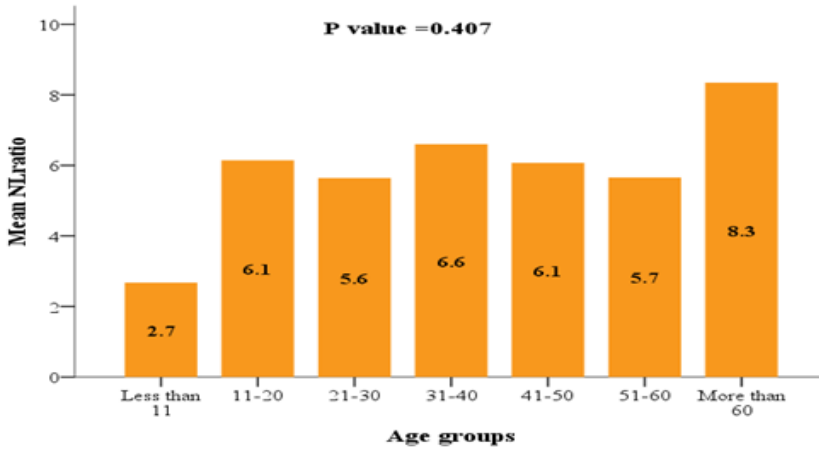

Figure 4. Bar chart shows the mean NLR in different age groups.

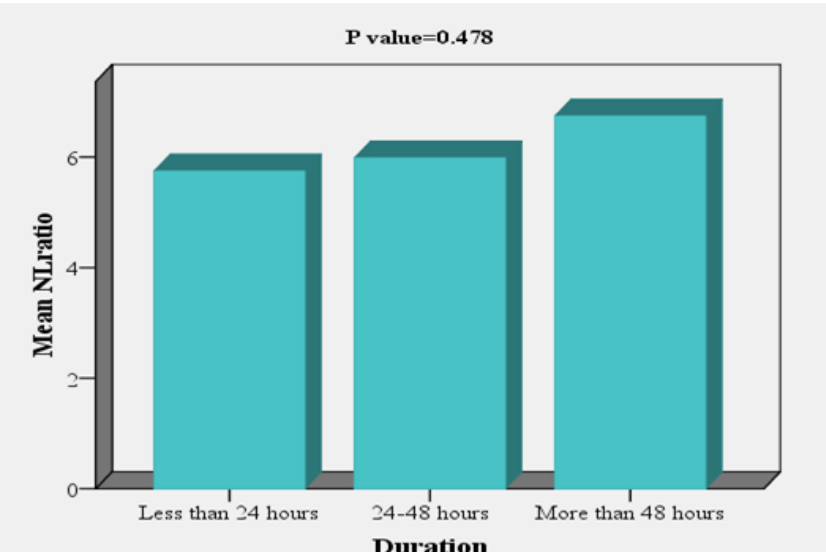

Figure 5. Bar chart shows the mean NLR and duration of the illness.

DISCUSSION

The symptoms of acute appendicitis may be very non-specific, mimicking other abdominal conditions. Acute appendicitis is sometimes difficult to decide the operative management, because it carries the morbidity and mortality [9]. In our study, the age range was 5-67 years and the mean age for patients with acute appendicitis was 25.94 ± 12.4. [10] Male: female ratio was 1:1.25. Acute appendicitis is more common in the 2nd and the 3rd decade of life which was shown in table (1), and this is compatible with other studies [1, 10] . Our result of the mean age of patients with acute appendicitis is near the results of some international studies [10-13]. In our study, females more affected by acute appendicitis than male and regarding the male:female ratio, our result is compatible with some studies [11, 14, 15], and differ from other studies [12, 13, 16, 17].

The rate of normal appendectomy in our study is (36.7%). Among the males is (26.9%), while among females is (43.3%). About 1/3 of our cases underwent negative appendectomy. Females constituted the larger group because of various other conditions that may mimic acute appendicitis. This rate is more than the international studies [7, 9, 13, 14, 15, 17] . Our results were similar to a study was done in 2011, they reported a negative appendectomy rate of 33.1% (26.8% for male and 38.3% for females), which was done on 127 patients [11, 15]. While other studies have showed a lower rate. A study in 2010 reported a negative appendectomy rate of (24%) [7], and a study in 2007 reported 23% [17].

Some studies reported a rate of less than 20% [9, 12, 13, 15]. Our explanations are, it may be due to absence of CT scan for diagnosis of difficult cases, overcrowding the Emergency Hospital with underestimation of the cases and may be due to high false positive Sonographic reports. In our study, (58.7%) of patients were visited the hospital and admitted in the 1st 24 hours from the onset of the pain. This may indicate an improvement in health education level of people. Good assessment of patients in the reception unit of surgical department may play a role. It may also be due to preciese decision of early admission as shown in table 1.

In our study, the most common histopathological type of acute appendicitis is acute suppurative and the least common type is acute gangrenous, figure 4. Our result is differ from a study was done in 2011 on 127 patients and the result was that the simple acute appendicitis is the most common type and acute gangrenous is the least common type [11].

In our study, we found that the NLR was increased with increasing the degree of inflammation of the appendix with statistically significant P value (p = 0.001) which is similar to the results of other study that showed the mean of NLR was increasing gradually corresponding to increase in the degree of inflammation [7]. In our study, we used NLR of ≥ 3.5 as a cut off point like the most of the international studies [9, 14, 18, 19]. In our study, the sensitivity of NLR in diagnosis of acute appendicitis is (85%) and this is similar to a study was done on this subject and the result was that (88%) of patients with acute appendicitis had a NLR ≥ 3.5 [9]. In our study, the sensitivity of NLR in diagnosis of acute appendicitis is more than Total Leukocyte Count (TLC) and NLR is more accurate than TLC, the same result was found by other studies [14, 9, 18, 19].

Some studies found that, if an elevated NLR is observed, the possibility of acute appendicitis is increased in patients with clinically suspected acute appendicitis [12, 16, 20]. In this study, the mean of NLR is directly proportional with the duration of the abdominal pain (figure 5), P value = 0.478 (not significant).

Our explanations are; there was different time of admission from the onset of pain and taking the blood samples with the time of surgery, and this may affect the results, because the ideal time of neutrophil response to inflammation is about 5-8 hours. Receiving antibiotics before admission or before surgery may affect the neutrophil response to inflammation. Threshold of pain is differ from patient to patient which may affect the body response to inflammation. We neglected some factors which may affect the body response to inflammation like genetics, dietary pattern, environmental factors, some diseases such as diabetes mellitus, and especially psychological stress because NLR may change in any stressful conditions. NLR will increase with increasing the degree of inflammation, and the degree of inflammation in acute appendicitis is greatly affected by the causative agent (obstructive or not) rather than the duration of pain.

In conclusion, in this study, we found that patients with acute appendicitis may have central abdominal pain then will shift to the right iliac fossa, and this pattern of pain is present in half of the patients (50.8%). The rate of negative appendectomy in Emergency Hospital of Slemani is about (36.7%), which is more than the international standard which is about (15-20%). There is strong relation between; NLR and acute appendicitis, NLR and the degree of severity of inflammation. NLR

appears to be of greater diagnostic accuracy than WBC in diagnosis of acute appendicitis with an adjunct to clinical examination. NLR is a simple, easy applicable, cost-effective, acceptable by the patient, and available test that can help the surgeon in diagnosis of acute appendicitis and detection its severity.

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