

## HISTOPATHOLOGICAL STUDY OF ACUTE APPENDICITIS, THE ROLE OF NEUTROPHIL TO LYMPHOCYTE RATIO IN ITS DIAGNOSIS

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### Abstract

Acute appendicitis is one of the commonest surgical emergencies. The diagnosis is still doubtful in a number of cases. Neutrophil/Lymphocyte ratio (N/L R) is a simple, applicable hematological test which carried out to find if there is any relationship between this ratio and acute appendicitis and to see could the ratio be used as a diagnostic tool rather than white blood cell count (WBC) alone.

This study was carried out on 70 patients aged (9-45) years who was admitted to hospital with suspicion of acute appendicitis, latter on, they underwent appendectomy. Preoperative blood sample was collected from each patient for WBC and differentials leukocyte count. Postoperatively appendectomy specimens were taken to histopathological examination, which shows 52 cases of inflamed appendix and 18 normal appendices.

When the (N/L R) and (WBC) were correlated with results of histopathology, it was found that there is a relationship between acute appendicitis and (N/L R), especially if we use the ratio at cut off point which was  $>2.6$  (p value  $<0.05=0.0001$ ), The sensitivity was 80.76% while the specificity was 72.22% and accuracy was 78.57%, while the results showed that the (WBC) alone had a limited role in diagnosis of acute appendicitis (p value  $>0.05=0.219$ ).

In *conclusion*, there is a strong relationship between (N/L R) and acute appendicitis.

### Introduction

The appendix is a wormlike extension of the cecum and for this reason, it has been called the vermiform appendix. Its average length is 5-10 cm. Appendicitis is an inflammation of the inner lining of the vermiform appendix that spreads to other parts. Appendicitis may occur for several reasons, such as an infection of the appendix, but the most important step is the obstruction of the appendiceal lumen (Santacrose, 2005). Despite the diagnostic and therapeutic advancement in medicine, still acute appendicitis remain a clinical emergency and its diagnosis is clinically augmented by few laboratory investigations and imaging techniques (Khan *et al*; 2004). The Neutrophil/Lymphocyte ratio (N/L R) is defined as the absolute Neutrophil count divided by

the absolute lymphocyte count. The ratio is a good parameter to assess the stress and severity of inflammation. The ratio consist of 2 components (or could be calculated as):  $n/l = \text{neutrophil\%} / \text{lymphocyte\%}$  (that counted from differential leukocyte count). The ratio depends on some factors such as: Absolute neutrophils count, Absolute lymphocyte count. (Zahorec, 2001). Sex, Race and Age of the individual (Khidhir, 2005).

### Patients and methods

This study was carried out at sulaimania emergency hospital between 15 July 2005 – 15 November 2005, on 70 cases, 38 (54.28%) male and 32 (45.72%) female patients who admitted to hospital with suspicion of acute appendicitis.

After history taking and clinical examination blood samples were taken from them as they were clinically diagnosed as acute appendicitis, and send for total white blood cell count and differential leukocyte count. Then underwent appendectomy operation. The appendix (biopsy) prepared for histopathological examination. Before tissue processing the form for each case was prepared that contain all necessary information about the patient age and gender, day of operation, name of surgeon, then each biopsy was labeled and send for tissue processing. Statistical analysis done by using (STATGRAPHICS plus) for Windows

Version 4 (2/15/99), analysis done by descriptive statistic and finding sensitivity, specificity, positive and negative predictive values with accuracy by the following equations;  
 Sensitivity = TP/TP + FN  
 Specificity = TN/TN+FP  
 Predictive Value (PV) of positive test = TP/TP+FP  
 Predictive Value (PV) of negative test = TN/TN+FN  
 Accuracy =TP+TN/TOTAL TP (true positive), FN (false negative), TN (true negative) and FP (false positive)  
 Chi-squares used for testing significance level, which was less than 0.05.

**Results**

**Table I: Distribution of age groups**

Age groups(G)	Age(years)	Male	Female	Frequency & %
1	1-10	2	3	5 (7.12%)
2	11-20	13	15	28 (40%)
3	21-30	19	9	28 (40%)
4	31-40	4	4	8 (11.46%)
5	41-ON	0	1	1 (1.42%)
		38	32	70 (100%)

**Table II: Correlation between age groups and histological result**

Age groups(G)	Inflamed	Normal
1	4	1
2	18	10
3	24	4
4	6	2
5	0	1
	52 (71.29%)	18 (25.71%)

**Table III: Correlation between gender and histological result**

Gender	Inflamed	Normal
Male	33	5
Female	19	13
Total	52	18

Chi-square =10.90, Degree of freedom=3 , p<0.05 hence the distribution is significance (0.0123)

**Table IV: Mean and SD of age, N/L R, and WBC for Male and Female**

Gender	Age		WBC		N/L R		Frequency
	Mean	SD	Mean	SD	Mean	SD	
Male	22.36	6.79	9439.4	3277.32	3.68	1.38	38
Female	20.75	9.38	9628.1	3451.34	3.49	2.11	32
Total							70

**Table V: Mean and SD age, N/L R, and WBC for normal and Inflamed group**

Histology	Age		WBC		N/L R	
	Mean	SD	Mean	SD	Mean	SD
Inflamed	21.57	7.09	9865.3	3156	4.0	1.73
Normal	21.77	10.60	8290.8	3725	2.32	1.15

**Table VI: The specificity, sensitivity, with accuracy and the Predictive values of N/LR in the diagnosis of acute appendicitis**

N/LR	Inflamed	Normal	Total
$\geq 2.6$	42(TP)	5(FP)	47
$\leq 2.6$	10(FN)	13(TN)	23
TOTAL	52	18	70

Sensitivity =  $TP/TP + FN = 42/42+10 = 80.76\%$ , Specificity =  $TN/TN+FP = 13/13+5 = 72.22\%$   
 Predictive Value of positive test =  $TP/TP+FP = 42/42+5 = 89.36\%$ , Predictive Value of negative test =  $TN/TN+FN = 13/13+10 = 56.52\%$ , Accuracy =  $78.57\%$ , Chi-square =  $14.70$ , Degree of freedom =  $1$   
 $p < 0.05$  hence the distribution is significance ( $=0.0001$ )

**Table VII: The specificity, sensitivity, with accuracy and the Predictive values of WBC in the diagnosis of acute appendicitis**

WBC	Inflamed	Normal	Total
$\geq 10000$	28(TP)	6(FP)	34
$\leq 10000$	24(FN)	12(TN)	36
Total	52	18	70

Sensitivity =  $TP/TP + FN = 28/28+24 = 53.84\%$ , Specificity =  $TN/TN+FP = 12/12+6 = 66.66\%$   
 Predictive Value (PV) of positive test =  $TP/TP+FP = 28/28+6 = 82.35\%$ , Predictive Value (PV) of negative test =  $TN/TN+FN = 12/12+24 = 33.33\%$ , Accuracy =  $57.14$ , Chi-square =  $1.5$ , Degree of freedom =  $1$ ,  $p > 0.05$  hence the distribution is not significance ( $0.219$ )

## Discussion

In present study the results shows that male to female ratio was (1.73:1) and the mean age for all inflamed groups (52) patients was 21.57.

Fortunately our results will go or near to the most of the international reference and value till now and in addition to these international reference.

Our study agrees with the following results;

Study that done by Asfar *et al.* (2000) on 78 patients he found that the mean age was (25±10.8).

Choi (2000) in his study on 557 patient found that the disease is more prevalent in 2<sup>nd</sup>-3<sup>rd</sup> decade of life.

Regarding male to female ratio our results are similar to the study done by

Wu *et al* (2003) on 260 patients male to female ratio was 1.6: 1.

Also our results are also similar to the results of Choi (2000) who found in his study that male to female ratio is 1.13: 1. While there is marked differences between our results and that obtained by Asfar (2000) who found that male to female ratio is 2.2:1.

Concerning histological results the findings of this study are in agreement with that of Choi (2000), who classified the patients according to the results of histology in to two major groups (normal and inflamed). Also the results of this study are in agreement with that of Lee and Sung (2004).

The rate of negative appendicectomy in

our study was 25.72%. Which is lie within the normal range that accepted by most international reference, which is 15%-30%.

Similar results were reported, Lee and Sung (2004) found that the rate was 22%. While some authors reported higher percentage which was 36.17% by Wysochi and Bebyn (2000) and other lowest percentage of 19.2% and 18.7 by Asfar et al (2000) And Choi (2000) respectively.

In present study results show that there is a relationship between the severity of inflammation of appendix and the (N/LR) as the ratio increase with the severity of the inflammation. These results are similar to results of present study table VI in that there is increase in the N/L ratio from normal to inflamed group.

Wysochi and Bebyn (2000) found that there is increase in the ratio of N/L in the patients who have appendicitis, but in their study they classify the patients (67) to 2 groups: Group (1) inflamed: the mean ratio was 11.4. and Group (2) normal: the mean ratio was 3.4.

From the results of our study it was clear that, the values of N/L ratio for both (normal group and inflamed group) was slightly lower than the values that used by others.

The explanation for this point may be related to the following fact:

1-Factors including (genetics, race, age, dietary pattern, sex, altitude, environmental factors) affect both total and differential leukocyte counts, tables (IV&V).

2-In our study, which was carried out on 70 patients from sulaimania, the normal hematological values for both (Neutrophil and lymphocyte) for this society were used and depended on. So N/L ratio of 1.88 considered as normal for adult male and ratio of 1.92 normal for adult female because the absolute count for them is such; Neutrophil count is, 65.47 (adult male), 65.62 (adult

female). Lymphocyte count is 34.27 (adult male), 34.16 (adult female). (Khahir, 2005) but the results of this study show that the mean N/LR in normal group (18 patients) was 2.32 and not (1.8 or 1.9) this differences is due to the following factors;

A. The normal group (18) cases in this study are histological normal (they have normal appendix).we don't mean that they are completely physiologically normal they may have some other pathology that bringing them to emergency room rather than appendicitis (may be one of differential diagnosis of it).

B. This group (normal group) were under stress both (psychological and physical) because of the (environment of the hospital, and decision of operation, and pain), and we should not forget that the ratio may be a good parameter for assessment of stress.

3- One of most important factors is time: the maximum response for the ratio (N/LR) may be seen after 5-8 hours (median 6 hours) after insult, while in present study most of the cases were came to the hospital either too late or earlier than this period a little number of them were came to hospital at the correct time (i.e. between 5-8 hrs), so the blood collected either too late or earlier, The results of our study showed that the (WBC) could not be use as a parameter for diagnosis of acute appendicitis because during this study it has became clear that from our results we founded that, there is no cut off point that we can depend on it for accurate diagnosis. Starting from 4000/mm<sup>3</sup> till 12000/mm<sup>3</sup>. Even at cut off point 10000/mm<sup>3</sup>, which is, consider as a cut point for diagnosis of acute appendicitis.

This study is in complete agreement with the results reported by; Stefanutti *et al* (2002), who found that the count on admission has no proven additional value in diagnosis of acute appendicitis?, Choi (2000), who found that, the total

white blood cell count is an unreliable predictor of appendicitis. And Anderson *et al* (2000), who demonstrated that the WBC count has low specificity for appendicitis and a number of bacterial and viral diseases, may also lead to leukocytosis. While on the other hand the results of this study are completely difference from other studies which are hold by the following researchers; Khan *et al* (2004), a total 259 patient included, he found that the count increase in 185 patients at cut point ( $11000/\text{mm}^3$ ), sensitivity was 83%, and specificity was 62%. While in our study 23 patients out of 70 had WBC equal or more than  $11000/\text{mm}^3$  sensitivity was 53.84%, and specificity was 66.66%.

Lee and Sung (2004) found in their study on 69 patients, the count at cut off ( $10000/\text{mm}^3$ ) can be used in diagnosis and in his study he found sensitivity was 68.5, specificity was 86.0 while in this study the sensitivity was 53.84%, specificity was 66.66% at cut off point ( $10000/\text{mm}^3$ ).

Graffeo and Counselman (1996), Kumar and Michael. (1994). Found that in

appendicitis cases, the average WBC count is 12,000 and 90% of patients had counts over 10,000. However in 10% of appendicitis cases the WBC count is normal.

## Conclusions

In this study the results shows that;

1. The rate of negative appendicectomy in our society was (25.7%) which lie with in the range that's accepted internationally (15%-30%).
2. From the histological results and in correlation with Neutrophil /lymphocyte ratio it was found that there is a strong relationship between this ratio and acute appendicitis. So this new simple and available test (N/L) ratio could help us to reach the more accurate diagnosis.
3. WBC could be omitted in diagnosis of acute appendicitis because no definite cut point could be used and depended on for the purpose of diagnosis

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