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Original Research Article

TO ASSESS THE SIGNIFICANCE OF TLC, ANC, NLR, AND ABDOMINAL ULTRASONOGRAPHY IN PATIENTS DIAGNOSED WITH ACUTE APPENDICITIS

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ABSTRACT

Background: The diagnosis of acute appendicitis is mostly based on clinical assessment, and prompt action is crucial. Early detection may lead to unnecessary removal of the appendix, while delayed diagnosis can result in complications. Several criteria were periodically examined, but none of them could definitively be considered 100% accurate. Aim: To evaluate the role of total leucocyte count (TLC), absolute neutrophil count (ANC), neutrophil lymphocyte ratio (NLR) and ultrasound abdomen in patients with clinical diagnosis of acute appendicitis.

Materials and Methods: The study was conducted on 100 patients. Patients with clinical features of acute appendicitis aged between 15 and 65 years were included in this study. he neutrophil Lymphocyte ratio would be obtained by dividing the percentage of neutrophils to the percentage of lymphocytes from the data available from differential leukocyte count. All patients was subjected to ultrasound examination of abdomen. Based on evidence in medical literature diagnostic categories for ultrasound abdomen are as follows.

Results: 86 cases (86%) had histopathologically proven features of acute appendicitis. There were 4 cases (4%) of gangrenous appendix. Congestion of appendix (normal appendix) was seen in 14 cases (14%). 90 Patients (90%) was diagnosed to have acute appendicitis by ultrasonography. Ultrasound could diagnose appendiceal perforation in 6 cases (6%). Probable appendicitis was given in 11 cases (11%) and normal appendix in 7 (7%) of cases. Appendix could not be visualised in 3 cases (3%). Out of the total 90 cases diagnosed as acute appendicitis by ultrasound only 78 cases were histopathologically proven appendicitis. Neutrophil lymphocyte ratio (NLR) categorised as number of cases with NLR between 0 -2.5, 2.5 to 5, 5 – 7.5 and 7.5 and above. There were 17 (17%) ,63 (63%), 12 (12%), 8(8%) cases in each of these cases respectively. Out of the 86 cases of acute appendicitis 16 patients had NLR between 0-2.5 and remaining 70 patients had NLR > 2.5. 49 patients had NLR between 2.5 to 5, 9 patients with NLR between 5 to 7.5 and 8 patients with NLR > 7.5. TLC was elevated in 8 out of the 14 cases of negative appendicectomy. ANC was elevated in 11 out of 14 cases of negative appendicectomy. NLR was elevated in 13 out of 14 cases of negative appendicectomy. There was one case in which all the parameters were normal in the study and histopathology was positive for appendicitis.

Conclusion: We concluded that total leucocyte count is a not specific marker for predicting acute appenditicitis, though absolute neutrophil count and neutrophil lymphocyte ratio are better markers for predicting acute appendicitis. Ultrasound of abdomen has 90% accuracy rate in predicting acute appendicitis.

Keywords: Total leucocyte count, Absolute neutrophil count, Neutrophil lymphocyte ratio, Ultrasound abdomen, Acute appendicitis.

INTRODUCTION

Abdominal pain is one of the commonest complaints encountered by a surgeon in the emergency. Acute appendicitis is the most common surgical cause of abdominal pain.[1] It is estimated that as much as 6-7% of the general population will develop appendicitis during their lifetime, with incidence peaking in the second decade of life.[2] The classical picture of appendicitis like fever, vomiting and right iliac fossa pain, tenderness and rebound tenderness may not be present in all cases. Despite many diagnostic tools and scoring methods used to aid the clinical diagnosis of Acute Appendicitis such as Alvarado score and RIPASA score, negative appendicectomy is somewhat acceptable traditionally even to the tune of 20-30 percent in literature.[3]

However, with the availability of modern gadgets for investigation this rate of negative appendectomy doesn't seem plausible, though the lack of availability of this equipment in rural areas may limit their use. Although early appendicectomy has markedly reduced the complications, but at the same time led to an increase in error during diagnosis thereby resulting in more negative appendicectomies.[4]

Leukocytosis has a sensitivity of 87.3% and specificity of 64.3 %, C-RP has sensitivity of 70.4% and specificity of 64.3%, IL-6 has a sensitivity of 78% and specificity of 50 %, IL -10 has a sensitivity of 40.8% and specificity of 92.9 % 5. USG alone has a sensitivity and specificity of 81% and 88 % respectively, CT combined with USG has 96 % sensitivity and 89% specificity6. None of the lab investigations or radiological investigations have been found to be 100% sensitive and specific for the diagnosis of acute appendicitis. A combination of various laboratory investigations such as elevated WBC count and positive CRP, IL-6 IL-10 has been used to diagnose appendicitis with 100 % sensitivity but with only 42.9 % specificity.[5]

The total leukocyte count, absolute neutrophil count, neutrophil lymphocyte ratio are simple, quick, inexpensive, easy to interpret without causing any additional financial burden to the patient.

The present study on the "evaluation of total leukocyte count, absolute neutrophil count, neutrophil lymphocyte ratio and ultrasound abdomen" has been designed specifically with an aim to diagnose acute appendicitis so as to reduce negative appendicectomies by including all parameters in diagnosis and avoid delayed diagnosis to decrease the morbidity and mortality associated with complicated appendicitis. Ethical consideration definitely come to exist as far as negative appendicectomy is concerned, at the same time the future of negative appendicectomy in relation to medicolegal consideration is not clear.

MATERIAL AND METHODS

The study was conducted at Department of General Surgery at Bhagat Phool Singh Government Medical College for Women, Khanpur Kalan, Sonipat, Haryana with written and informed consent of the participants. The study was done over a period of 18 months after ethical committee approval. The study is a cross sectional observational study. The study was conducted on 100 patients. Patients with clinical features of acute appendicitis aged between 15 and 65 years were included in this study. Patients with Age < 15 years and > 65 years Diabetes, hypertension or other immunocompromised patients and Pregnant female were excluded from the study.

Methodology

Detailed history taking and clinical examination of abdomen of all patients of clinical diagnosis of acute appendicitis aged between 15 and 65. Venous blood sample was collected from each patient in purple vacutainer at the time of admission under aseptic precautions. Samples was send to central hematology lab and run on hematological analyser before hand for complete blood count and differential leukocyte count. Slide preparation of Peripheral blood smear with leishmann staining will be done and complete blood count, differential leukocyte count was obtained. In case of disputes, blood counts obtained from Peripheral blood count will be considered final. Absolute Neutrophil count will be obtained from evaluation of peripheral blood smear. The percentage of neutrophils divided by 100 multiplied to the total leukocyte count gives the Absolute Neutrophil count. The neutrophil Lymphocyte ratio would be obtained by dividing the percentage of neutrophils to the percentage of lymphocytes from the data available from differential leukocyte count. All patients was subjected to ultrasound examination of abdomen. Based on evidence in medical literature diagnostic categories for ultrasound abdomen are as follows.

Statistical Analysis

The collected data will be entered into microsoft excell spread sheet. Mean +-SD was calculated for quantitative data using student 't' test / Kruskal wallis test. Percentage and proportion was calculated for qualitative data. Chi Square will be used to find out the association for categorical data.

RESULTS

In this cross-sectional observational study 100 patients were enrolled after fulfilling the inclusion criteria. No patient was excluded from the study after enrolment as the investigation reports were collected from the respective departments. No patient suffered any harm due to the study. Table shows the age wise distribution of the patients underwent appendicectomy procedure. Age group between 21-30 years had the maximum number of

cases 36 (36%) where as age group age less than 20 years had the minimum number of participants 17(17%). The minimum age of the participants was 15 years and the maximum age was 64 years. The mean age of the study population was 32.65 years with a standard deviation of 13.48. Of the total 100 participants 32(32%) patients were of female gender and the remaining 68 (68%) cases were of male gender.

86 cases (86%) had histopathologically proven features of acute appendicitis. There were 4 cases (4%) of gangrenous appendix. Congestion of appendix (normal appendix) was seen in 14 cases (14%). 90 Patients (90%) was diagnosed to have acute appendicitis by ultrasonography. Ultrasound could diagnose appendiceal perforation in 6 cases (6%). Probable appendicitis was given in 11 cases (11%) and normal appendix in 7 (7%) of cases. Appendix could not be visualised in 3 cases (3%). Out of the total 90 cases diagnosed as acute appendicitis by ultrasound only 78 cases were histopathologically proven appendicitis. [Table 1]

Between the range of 4000 -11000 cells/mm3 there 54 cases (54%) and number of cases with total leucocyte count more than 11000cells /mm3 was 46 (46%). 48 patients out of the 86 histopathologically proven cases had leucocyte count within a normal range of 4000-11000cells /mm3. 38 cases out of the 86 cases had a elevated leucocyte count. 6 out of the 14 cases of congestion of appendix had leucocyte in normal range. [Table 2]

Absolute neutrophil count (ANC) was divided into categories. There was 22 cases (22%) with ANC in normal range (between 2000-6000cells /mm3), and 78cases (78%) with ANC more than 6000 cells/mm3. Elevated ANC (>6000cells/mm3) was seen in 63 cases of acute appendicitis and remaining 19 patients had normal ANC.All 4 patients with gangrenous appendix had elevated ANC. 11 out of 14 patients with congestion of appendix had elevated ANC. [Table 4]

Neutrophil lymphocyte ratio (NLR) categorised as number of cases with NLR between 0 -2.5, 2.5 to 5, 5 – 7.5 and 7.5 and above. There were 17 (17%) ,63 (63%), 12 (12%), 8(8%) cases in each of these cases respectively.

Out of the 86 cases of acute appendicitis 16 patients had NLR between 0-2.5 and remaining 70 patients had NLR > 2.5. 49 patients had NLR between 2.5 to 5, 9 patients with NLR between 5 to 7.5 and 8 patients with NLR > 7.5. [Table 6]

The minimum value of TLC in this study was 4500cells/mm3 and maximum TLC was 18,000cells/mm3 with a mean of 10,650 cells /mm3 and standard deviation of 2823.22. The minimum value of ANC was 2679 and maximum value was 15,120 cells /mm3 with a mean of 8033cells /mm3 and standard deviation of 2624. The minimum value of NLR was found to be 1.25 and maximum value was 12.71 with a mean of 4.04 and standard deviation of 1.94. Out of the 100 cases 86 cases were histopathologically proven to be acute appendicitis, remaining 14 cases showed congestion of Appendix suggesting negative appendicectomy. [Table 8]

TLC was elevated in 8 out of the 14 cases of negative appendicectomy. ANC was elevated in 11 out of 14 cases of negative appendicectomy. NLR was elevated in 13 out of 14 cases of negative appendicectomy. There was one case in which all the parameters were normal in the study and histopathology was positive for appendicitis. [Table 10]

Table 1: Basic profile of the participants

AGE	No. of cases	Percentage
< 20	17	17.0%
21-30	36	36.0%
31-40	24	24.0%
> 40	23	23.0%
Gender		
FEMALE	32	32%
MALE	68	68%
Histopathology report		
Acute appendicitis	86	86%
Congestion of appendix	14	14%
USG ABDOMEN		
Acute appendicitis	90	90%
Appendix not visualised	3	3%
Normal appendix	7	7%

Table 2: Ultrasound abdomen and histopathology report

	HISTOPATHOLOGY REPORT		**Total**
USG ABDOMEN	acute appendicitis	congestion of appendix	
acute appendicitis	78	12	90
No appendicitis	8	2	10
Total	86	14	100

Table 3: Total leucocyte count and histopathology report

		HISTOPATHOLOGY REPORT		**Total**
		acute appendicitis	**congestion of appendix**	

TLC GROUP	11000 & above	38	8	46
	4000-11000	48	6	54
Total		86	14	100

Table 4: Sensitivity and Specificity of Total leucocyte count and histopathology report

STATISTIC	VALUE	95% CI
Sensitivity	44.19%	33.48 % to 55.3%
Specificity	42.86%	17.66 % to 71.14%
Positive likelihood Ratio	0.77	0.46 to 1.29
Negative Likelihood Ratio	1.3	0.69to 2.45
Positive Predictive Value	82.61%	74% to 88.00%
Negative Predictive Value	11.11%	6.22% to 19.06%
Accuracy	44.00%	34.08% to 54.28%

The chi-square statistic is 0.8137. The p-value is .367025

Table 5: Absolute neutrophil count and histopathology report

	Value (in cells/mm3)	HISTOPATHOLOGY REPORT		Total
		acute appendiciti s	congestion of appendix	
ANC GROUP	>6000	67	11	78
	2000-6000	19	3	22
Total		86	14	100

Table 6: Sensitivity and Specificity Absolute neutrophil count and histopathology report

STATISTIC	VALUE	95% CI
Sensistivity	77.91%	67.67 % to 86.14%
Specificity	76.60%	61.97% to 87.7%
Positive likelihood Ratio	3.33	1.96 to 5.65
Negative Likelihood Ratio	0.29	0.19 to 0.44
Positive Predictive Value	85.90%	78.20 to 91.18%
Negative Predictive Value	65.45%	55.28% to 74.39%
Accuracy	77.44%	69.39% to 84.23%

The chi-square statistic is 0.0031. The p-value is .955615

Table 7: Neutrophil lymphocyte ratio and histopathology report

		HISTOPATHOLOGY REPORT		Total
		acute appendicitis	congestion of appendix	
NLR GROUP	>2.5	70	13	83
	0-2.5	16	1	17
Total		86	14	100

Table 8: Neutrophil lymphocyte ratio and histopathology report

STATISTIC	VALUE	95% CI
Sensistivity	81.40%	71.55 % to 88.98%
Specificity	7.14%	0.18 % to 33.87%
Positive likelihood Ratio	0.88	0.73 to 1.05
Negative Likelihood Ratio	02.6	0.37 to 18.12
Positive Predictive Value	84.34%	81.86% to 86.54%
Negative Predictive Value	5.88%	0.89 % to 30.30%
Accuracy	71.00%	61.07 % to 79.64%

The chi-square statistic is 1.121. The p-value is .289704

Table 9: histopathologically proven appendicitis and investigations and histopathologically negative appendix and investigations

Parameter	Acute Appendicitis (HPE)
USG	78
TLC	38
ANC	67
NLR	70
histopathologically negative appendix and investigations	
Parameter	Congestion of appendix
USG	12
TLC	8
ANC	11
NLR	13

Ultrasound diagnosed acute appendicitis in 12 cases in which histopathology showed congestion of appendix.

Table 10: Comparison of different parameter

Parameter	Elevated (Number of cases)	Normal (Number of cases)
Comparison of USG with other		

parameters		
TLC	7	5
ANC	9	3
NLR	11	1
TLC and other parameters		
USG	7	1
ANC	8	0
NLR	8	0
ANC and other parametres		
USG	9	2
TLC	8	3
NLR	11	0
NLR and other parameters		
USG	11	2
TLC	8	5
ANC	11	2

DISCUSSION

Appendicectomy is one of the most common emergency surgeries performed by young Surgeons. Acute Appendicitis is the most common surgical cause of abdominal pain1. Even with the availability of modern techniques Acute Appendicitis is essentialy a clinical diagnosis, which can result in negative appendicectomies. The negative Appendicectomy rate is around 20-30% in literature3. The incidence of negative appendicectomy is higher in females than males and highest in women belonging to the child bearing age. The incidence of negative appendicectomy was 2.5 times higher in females aged 15 to 24 years than that of males of the same age group.[2] The principal concept of “primum nil nocere” (first do no harm should be kept in the minds of surgeons in any surgical procedure. The prevention of progression from uncomplicated appendicitis to complicated appendicitis through a timely intervention must be the focus of management.[29] However preventing complications can lead to negative appendicectomy thereby inviting the post-operative issues associated. Thus there is a absolute need for accurate pre-operative diagnosis in cases of suspected acute appendicitis.

The current study is a cross sectional observational study to evaluate the role of total leucocyte count, absolute neutrophil count, neutrophil lymphocyte ratio and ultrasound abdomen in patients with clinical diagnosis of acute appendicitis. Evaluating the above parameters in acute appendicitis is economically feasible, easily available in the emergency settings. In a developing nation like India where rural healthcare is of utmost importance, we conducted this study in our institute located in a rural area of state Haryana to evaluate the role in diagnosis of acute appendicitis.

This study was conducted in 100 patients belonging to the age group between 15- 65 years who underwent appendicectomy. The total leucocyte count, absolute neutrophil count, neutrophil lymphocyte ratio was evaluated and ultrasound abdomen was done preoperatively. The histopathological report was followed up. No patients details was lost during the study.

In this study there was 32 females (32%) and 68 males (68%). The minimum and maximum age was 15, 65 years respectively with a mean of 32.65 and a standard deviation of 13.48. The minimum total leucocyte count was 4500cells/mm3 and maximum value was 18,000cells/mm3 with a mean of 10,650 cells/mm3 and a standard deviation of 2823. The absolute neutrophil count varied from 2679cells/mm3 to 15,120 cells/mm3 with a mean of 8033 and standard deviation of 2624. The neutrophil lymphocyte ratio varied from 1.25 to 12.71 with a mean of 4.04 and a standard deviation of 1.94. Ultrasound abdomen showed acute appendicitis in 90 cases (90%).

In a study by Hajibanded, a systematic review and metaanalysis of neutrophil lymphocyte ratio to predict acute appendicitis and its severity, the NLR at 4.7 had sensitivity and specificity of 88.8 % and 90.9 % respectively.[6] Another retrsospective study by Sahin et al on 106,[7] patients showed that a NLR of 4.68 was associated with acute appendicitis, with a sensitivity and specificity of 65.3% and 54.7% respectively. A NLR of 5.74 was associated with complicated appendicitis.[7] In a study by Salman Ahmed and et al in 2019, the sensitivity and specificity neutrophil lymphocyte ratio in diagnosing acute appendicitis was done as retrospective analysis. 372 patients were included in the study. The median age was 27 years and the cut off values for diagnosing acute appendicitis was 4.2. The sensitivity and specificity was 79.5 and 67% respectively.[8]

A retrospective cross sectional study of neutrophil to lymphocyte ratio in diagnosing acute appendicitis was done by Ahmad et al The NLR for acute Appendicitis was 3.11 and perforated appendix was 6.17. The sensitivity was 75.23%, 76.32 % for NLR in acute appendicitis and perforated appendix respectively and specificity was 68.70%, 58.72 % respectively. The study results were concluded that NLR can be used as reliable adjunct in diagnosing acute appendicitis.[4]

The current study also shows a sensitivity and specificity of 81% and specificity 07% at a cut off value of 2.5. The results obtained are similar to that available in literature. NLR alone cannot be used in the accurate diagnosis of acute appendicitis, by

along with other parametres like total leucocyte count, absolute neutrophil count and ultrasound abdomen, it can be useful adjunct in diagnosing acute appendicitis and thereby preventing negative appendicectomy.

In a prospective study by Shehzadi Rimsha Fatima, A combined diagnostic accuracy of total leucocyte count, neutrophil percentage and ultrasound abdomen was done im 2019-20.TLC > 11,000cells/mm3 and neutrophil >75% were considered positive for appendicitis and in ultrasound non-compressible, blind-ending, non-peristaltic bowel loop originating from the cecum (appendix), loculated para-cecal collection, and/or the finding of an appendicolith was considered positive. The diagnostic accuracy of TLC > 11,000/mm3 was 82.94%, with sensitivity 83.10% and specificity 82.14%. The accuracy of the neutrophil test was 88.82%, with sensitivity 88.03% and specificity 92.86%. The accuracy of ultrasound was 88.24% with sensitivity 89.44%and specificity 82.14%. cases having TLC > 11,000/mm3, neutrophil count > 75%, and ultrasonographic features showing non-compressible, blindending loop, and diameter of the appendix > 7 mm were combined into one group. The combined accuracy was 94.71 % with sensitivity and specificity was 94.71%, 97.18%, 82.14% respectively.[9] The results of ultrasound were similar in term of Sensitivity and diagnostic accuracy with our current study. The results with respective to neutrophil count were comparable but the results of total leucocyte count were not similar.

A cross sectional observational study of total leucoyte count on predicting the degree of acute appendicitis was done by Bilal M and et al in 2019. The study included 238 patients. 198 patients (82.3 %) had normal TLC range.[10] The study concluded that contrary to the impression that a normal TLC rules out acute appendicitis. The results of the study was similar to the results of the current study. The age groups included in the study were comparable. Males were more in both the age groups. The median age was 27 years and in current study was 32 years. 54% of patients had normal TLC range who were histopathologically diagnosed as acute appendicitis.

The predictive value of leucocytosis in diagnosing acute appendicitis was done by Saleem et al in 2017. A total of 180 patients were included in the study. This study was similar to current study in gender distribution only. The total count was elevated in 129 patients (71.6%), which was higher than a current study which had elevated total counts only in 46 cases (46%). The difference in results could be due the inclusion of cases as leucocytosis as total count >10000cells/mm3 when compared to the current study in which >11000cells/mm3 is considerd as leucocytosis. The study also included patients aged >10years also in inclusion criteria.[11]

A systematic review and meta-analysis on the role of ultrasound in appendicitis was done by Vanja Giljaca and et al,[12] studies were combined which included 2871 participants from a time duration from 1994 to 2014 by two authors independently. The Sensitivity and Specificity of ultrasound was 69 % and 81 % respectively corresponding to 95% confidence intervals.[13] In the Current Study ultrasound had high sensitivity of 90 % but a lower Specificity of 14%. The value of Ultrasound for diagnosis of acute appendicitis was done as a descriptive prospective study by Benedetto et al from April 2015 to April 2016. The sensitivity and specificity were 90% and specificity was 100 %.[14] The Sensitivity of Ultrasound was similar to that of our current study.

CONCLUSION

All these results helped us to conclude that total leucocyte count is a not specific marker for predicting acute appenditicitis, though absolute neutrophil count and neutrophil lymphocyte ratio are better markers for predicting acute appendicitis. Ultrasound of abdomen has 90% accuracy rate in predicting acute appendicitis. None of the investigations could single handedly predict the presence of early appendicitis, a combination of all parametres together can reduce negative appendicectomy rate.

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