

Prospective Validation of Neutrophil-to-Lymphocyte Ratio as a Diagnostic and Management Adjunct in Acute AppendicitisMeha Ghodawat¹, Kartikey Shukla², Manoj Kela³, Priyal Jain⁴¹Ex Senior Resident, Government Medical College, Ratlam, (M.P.)²Senior Resident, MCh Plastic and Reconstructive Surgery, KGMU Lucknow (U.P.)³Professor & Head, Department of General Surgery, SAMC and PG Institute, Indore (M.P.)⁴Assistant Professor, Department of Forensic Medicine, Government Medical College, Ratlam (M.P.)

Received: 25-09-2023 / Revised: 28-10-2023 / Accepted: 30-11-2023

Corresponding Author: Dr. Priyal Jain

Conflict of interest: Nil

Abstract:

Background: Acute appendicitis (AA) is one of the most common abdominal emergencies worldwide. Patients presenting with appendicitis may vary in severity. We conducted this study aiming to prospectively examine the role of NLR in assessing the severity of appendicitis, length of hospital stay, and rate of postoperative complications. We have 3 objectives namely to study neutrophil and lymphocyte count in appendicitis cases, to study various correlation and association regarding severity of appendicitis and neutrophil to lymphocyte ratio (NLR) & to study the validity of neutrophil to lymphocyte ratio (NLR) in predicting the severity, length of hospital stay and 30 day complication rate. The study was conducted in the department of general surgery at SAMC & PGI Indore (M.P.) from January 2018 to June 2019 on 100 patients which were selected according to inclusion and exclusion criteria Receiver Operating Characteristic (ROC) curve analysis was used for determining optimal cut-off value of NLR for complicated AA. Most of the patients with AA were in the age group of 20-29 years with M:F ratio of 1.56:1. Mean NLR of patients treated surgically was raised (8.5±5.6) compared to conservatively treated patient (4.34). This value has sensitivity of 91% and specificity of 89% with Area Under Curve (AUC) of 0.941 with 95% confidence interval 0.895 to 0.987 and p value of <0.005.

Keywords- Acute appendicitis (AA), Neutrophil to lymphocyte ratio (NLR).

This is an Open Access article that uses a funding model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>) and the Budapest Open Access Initiative (<http://www.budapestopenaccessinitiative.org/read>), which permit unrestricted use, distribution, and reproduction in any medium, provided original work is properly credited.

Introduction

Acute appendicitis is one of the most common abdominal emergencies worldwide. Recognition of acute appendicitis as a clinical entity is attributed to Reginald Fitz, who presented a paper to the first meeting of the Association of American Physicians in 1886 entitled 'Perforating inflammation of the vermiform appendix'. Advances in modern radiographic imaging have improved diagnostic accuracy, however the diagnosis of appendicitis remains essentially clinical, requiring a mixture of observation, clinical acumen and surgical science and as such it remains an enigmatic challenge and a reminder of the art of surgical diagnosis.

Acute appendicitis is relatively rare in infants, and becomes increasingly common in childhood and early adult life, reaching a peak incidence in the teens and early 20s. After middle age, the risk of developing appendicitis is quite small. The incidence of appendicitis is equal among males and females before puberty. In teenagers and young adults, the male-female ratio increases to 3:2 at age 25; thereafter, the greater incidence in male declines [1].

There is no unifying hypothesis regarding the aetiology of acute appendicitis. Decreased dietary fibre and increased consumption of refined carbohydrates may be important. The cause remains poorly understood, with few advances in the past few decades. Traditionally, the diagnosis of appendicitis is based on clinical judgment. However, numerous publications report a range of adjuncts to help formulate decision-making in difficult scenarios [2]. Some surgeons utilize scoring systems like Alvarado and RIPASA to aid in the diagnosis [3-4]. Modelled decision support systems are being developed [5]. Additionally, the role of routine radiological assessment is contentious, and there is debate regarding which modality to use. A Cochrane review in 2011 highlighted that in selected patients, some could be managed conservatively with antibiotics [6]. Recent randomized controlled trials including metaanalyses have supported this management approach [7-10]. However, for this strategy to be successful, it is vital that patients with simple uncomplicated appendicitis are delineated and

commenced on early antibiotic therapy [10-11]. Various authors have already mentioned neutrophil-to-lymphocyte (NLR) ratio as a useful adjunct in predicting the severity of appendicitis, post-operative complications, and length of stay [12-13]. NLR is a useful, simple, and inexpensive marker of subclinical inflammation, which is easily calculated from the differential white cell count (WCC) [13]. It has been shown that it provides information regarding two different immune and inflammatory pathways (acute inflammation and regulatory pathway) [14]. Already, NLR has been demonstrated to correlate with acute activity in other inflammatory conditions like inflammatory bowel disease and acute cholecystitis. There has been growing interest in evaluating the correlation of NLR with the outcome of different cancers like colorectal, gastric, and other solid neoplasms. Authors has reported that their analysis using the correlation of NLR to length of stay was equivocal. However, the majority of data to date on NLR predictive value is retrospective. Our aim was to prospectively examine the role of NLR in assessing the severity of appendicitis, length of stay, and rate of post-operative complications.

Objectives

Study of Acute appendicitis according to two main etiologies under following headings:

- ❖ To study neutrophil and lymphocyte count in appendicitis cases
- ❖ To study various correlation and association regarding severity of appendicitis and neutrophil to lymphocyte ratio (NLR).
- ❖ To study the validity of neutrophil to lymphocyte ratio (NLR) in predicting the severity, length of hospital stay and 30 day complication rate

Material and Methods

The study conducted IN DEPARTMENT OF GENERAL SURGERY AT SAMC & PGI INDORE FROM JANUARY 2018 TO JUNE 2019.

THE WORK STARTED AFTER THE REVIEW AND APPROVAL OF PROTOCOL OF STUDY BY PROFESSIONAL ETHICS AND RESEARCH COMMITTEE. WE INCLUDED 100 PATIENTS ACCORDING TO INCLUSION CRITERIA

- Patients of both the sexes from age 10 years to 60 years will be taken.

Inclusion criteria-

- All patients with age group between 10 to 60 with acute/ sub-acute/ and chronic abdominal pain admitted and suspected to have appendicitis were followed and investigated.
- All patients of suspected appendicitis, documented by various investigations including histopathological examination.
- All patients confirmed by surgical treatment suspected to be having features of appendicitis.

Exclusion Criteria-

- Patients of age group below 10 years and above 60 years are not included in the study.
- Patient not willing for study.
- Other nonspecific pain

Methodology-

Patients coming in surgery opd, emergency as well as referred patients from some other health centres were admitted and following details were recorded.

- A. Particulars like. - name, age, sex, religion, socio-economic status etc.
- B. Various Lab Investigations eg. CBC, CRP (if done)
- C. Imaging: - Usg, X-Ray, CT scan (If done).

We Divided Patients in two groups based on their treatment modality i.e., one group which was treated conservatively and the other which was treated by surgical operation (both open and laparoscopic).

Based on the data collected we calculated Mean and Standard Deviation of various counts and Neutrophil to Lymphocyte Ratio (NLR) for above mentioned two groups.

We validated Neutrophil to Lymphocyte Ratio (NLR) in predicting treatment modality (i.e., Conservative vs operative), length of hospital stay and 30 day complication rate.

We used SPSS software for data analysis, as well as for plotting ROC Curve

Observation and Results

In the present study male to female ratio was 1.56 as shown in table 1.

Table 1: Shows male female ratio in the present study

MALE	FEMALE
61	39

When divided in various age groups maximum No of cases were found in the 10 to 39 years and among them maximum cases were in 20-29 years age group (table 2 and Figure 2).

Table 2: Shows age group wise distribution in the present study.

Age group (in Years)	No. Of Cases	%
10-20	19	19
21-30	40	40
31-40	20	20
41-50	11	11
51-60	10	10
total	100	100

Youngest male was 11 years old whereas youngest female was 10 years old. Eldest person in both genders were 60 years old. Present study shows that majority of appendicitis cases coming to hospital are acute in nature with 84 cases while recurrent cases are 10%. Perforated cases are lowest in number i.e.,6% (table 3).

Table 3: showing No of various type of appendicitis cases

Appendicitis	ACUTE	RECURRENT	perforated
No. Of Cases	84	10	6
%	84	10	6

Patients were treated with mainly two modalities i.e., surgical and conservative. As evident from data that majority of the patients were treated surgically either open surgery or laparoscopically as compared to conservatively (table 4).

Table 4: Showing No of cases treated by various treatment modalities.

Treatment Modality	conservative	Open appendicectomy	Laparoscopic Appendicectomy
No. Of Patients	18	72	10
%	18	72	10

As in our setup appendicitis cases usually comes in emergency so number of open appendicectomy are higher compared to laparoscopic appendicectomy.

All the relevant laboratory investigation were done. We observed various ranges in each parameter and calculated mean for each parameter (table5).

Table 5: Showing ranges and mean of various parameters in the present study

Lab investigation	Minimum	Maximum	Mean
Total WBC count	4800	25700	12016
Neutrophil %	48	95	78.78
Lymphocyte %	3	43	13.74
Haemoglobin (gm/dl)	7.4	16.7	12.3
Platelets (in Lac)	0.78	6.57	2.70

We also calculated WBC count in acute, recurrent and perforated appendicitis with mean and standard deviations (table 6).

Table 6: showing Average White blood cells count in various types of appendicitis

Appendicitis	ACUTE	RECURRENT	Perforated
Average Wbc count	11627	13830	14433
SD	± 4115	± 4525	± 1908
Neutrophils Count	78.50	77.7	84.5
SD	± 8.6	± 6.3	± 8.8
Lymphocyte Count	14.08	13.2	9.8
SD	± 6.7	± 3.01	± 6.21

As we can see average WBC count is highest in perforated appendicitis, lowest in acute appendicitis and in between in recurrent appendicitis.

Neutrophil count is highest in perforated cases whereas lymphocyte count was highest in acute

appendicitis cases. NLR ratio is highest in perforated appendicitis and lowest in recurrent appendicitis cases. It was in between in acute appendicitis cases (table7).

Table 7: showing Average NLR Ratio and standard deviation (SD) in various types of appendicitis

Appendicitis	NLR Ratio / SD
Acute	7.5 \pm 5.7
Recurrent	6.1 \pm 1.9
Perforated	10.9 \pm 4.7

Hospital stay in various cases ranges from 3 days to 32 days with mean duration for acute appendicitis was 7.3 days, for recurrent appendicitis 8.4 days and 7.3 days for recurrent appendicitis.

There was only one case in which hospital stay was more than 30 days and he was the same case in which 30-day complication was present.

We then divided the cases into groups based on the treatment modality i.e., conservatively treated and surgically treated and calculated various parameters including various counts for both the groups (table 8).

Table 8: showing mean and standard deviation of various counts in differently treated patients.

Parameter	Conservative	Surgical
Hb gm/dl	11.32	12.5
SD	1.61	2.0
TLC	10894	12262
SD	3447	4244
Neutrophil %	71.7	80.3
SD	9.0	7.5
Lymphocytes %	21.9	11.9
SD	7.7	4.5
Platelets in Lac	2.98	2.63
SD	1.48	1.0

We found that patients treated surgically were having higher average total leucocytes count and neutrophil % whereas patient treated conservatively were having higher average lymphocyte%.

NLR ratio was higher in patient with surgical treatment as compared to patient treated conservatively. Also, standard deviation was high in surgically treated patient compared to conservatively treated patients (table 9).

Table 9: showing NLR Ratio and Standard Deviation in different Treatment Modality

Treatment Modality	NLR With SD
Conservative	3.6 \pm 1.0
surgical	8.5 \pm 5.6

Cut off value of NLR for conservative treatment is 4.34 with 91 % sensitivity and 89 % specificity. After applying student t test and Man Whitney test, we obtained p value for NLR ratio is < 0.05 which is statistically significant.

ROC Curve obtained using SPSS software which shows area under the curve is 0.941.

Discussion

Study was conducted at Sri Aurobindo Institute of Medical sciences and PG Institute on 100 patients with diagnosis of Appendicitis. The case series was conducted for a limited period on limited number of patients with an objective to study Prospective validation of neutrophil-to-lymphocyte ratio as a diagnostic and management adjunct in acute appendicitis. Study was also directed to compare the role of various scoring systems and outcome of acute pancreatitis in both the groups.

In our study of 100 patients with Appendicitis, 84 patients have acute appendicitis, 10 have recurrent appendicitis and 6 have perforated appendicitis. Patients of age group between 21 to 40 years were most affected accounting 60% (60 patients) of the total patients while patients of age group 50-60 years were least commonly affected (10%). Of all the patients in our study, 61% (61 patients) were males while 39% (39 patients) were females.

In other similar studies done by various authors Kelly ME et al [12], Faraj et al [15], Patil SM et al [16], Rudimen R [17], Ishizuka M [18] maximum number of cases were observed in 21-40 years of age group.

In present study we found NLR ratio to be high which underwent surgical treatment compared to patient who were treated conservatively. Other authors i.e., Kelly ME et al [12], Faraj et al [15], Patil SM et al [16], Rudimen R [17], Ishizuka M

[18] and many more have found similar results in their study.

In the present study we have found cut off value of NLR for conservative treatment is 4.34 with sensitivity of 91 % and specificity of 89 %. Kelly ME et al found cut off NLR value for negative appendectomy in appendicitis cases was 4.7 which is in conformity with present study however sensitivity and specificity was lower than the present study. We observed length of hospital stay in conservatively treated patients was 6 days (median value) whereas it was 7 days (median value) for surgically treated patient, and it was statistically significant. Kelly ME et al [12] found similar difference in hospital stay of one day in patient having simple and severe appendicitis. They too found it statistically significant.

Similarly Kahramanca S et al [19] did similar study in which they studied 1067 patient as compare to present study with 100 patient. In their study males were 66.5 % as compared to 60 % in present study. They found mean NLR values for G1a (positive appendectomy) and G1b (negative appendectomy) were 9.85 ± 8.68 (SD) and 7.77 ± 6.59 (SD) whereas in present study we observed mean NLR Ratio 8.5 ± 5.6 for surgically treated patient. The difference could be due to variation in study population and number of cases. They found cut off value of of NLR 4.68 for acute appendicitis to differentiate normal appendix from inflamed appendix. Our study found cut off value for NLR is 4.34 for conservative treatment in a case of acute appendicitis.

Ptila SM et al [16] also did similar kind of study in which they studied 127 patients and 64 % were males which is comparable to our study where 61% were males. Maximum cases were in the age group of 11 to 40 years which is also the same in our study. Mean NLR ratio was higher in complicated (perforated) cases compare to non-complicated cases which is in conformity to observation made in present study. They recommended cut off value for NLR in complicated appendicitis cases was 5.552 with area under the curve was .84 and 95 % confidence interval between 0.766 and 0.913 whereas in present study we observed cut off value of NLR for conservatively treated cases was 4.34 with area under the curve was 0.941 with 95 % confidence interval 0.895 to 0.987. the difference between cut off value of NLR is because of difference in the criterion.

Rudimen R et al [17] found mean NLR ratio in perforated appendicitis cases was 11.40 ± 5.69 which is slightly higher to observation in the present study of 10.9 ± 4.7 . similarly, Ishizuka

M¹⁸ et al observed cut off value for NLR was 8 in gangrenous appendicitis whereas we determined cut off value of NLR for conservative treatment which was 4.34.

Conclusion

Median duration for hospital stays in conservatively treated patient was 6 days with 25 & 75 percentile were 5 days and 7 days respectively. Median duration for surgically treated patient was 7 days with 25 & 75 percentile were 5 and 9 days respectively. The difference was statistically significant and p value is 0.035 which is <0.05.

When we compare Haemoglobin level, neutrophil count, lymphocyte count & platelet count individually on the basis of treatment (patient treated conservatively and patient treated surgically), we found relation was statistically non-significant.

References

1. The vermiform appendix. In: Norman SW, Christopher JKB, Ronan O'Connell editors. Bailey & Love's Short Practice of Surgery. # 26. Boca raton: CRC press; 2013. p. [1201-3].
2. Waxman BP (2015) Treating uncomplicated appendicitis without surgery: will computer tomography scans and antibiotics triumph over clinical acumen and surgical dogma? ANZ J Surg 85(11):800
3. Chong CF, Adi MI, Thien A, Suyoi A, Mackie AJ, Tin AS et al (2010) Development of the RIPASA score: a new appendicitis scoring system for the diagnosis of acute appendicitis. SingapMed J 51: 22–225
4. Jang SO, Kim BS, Moon DJ (2008) Application of Alvarado score in patients with suspected appendicitis. Korean J Gastroenterol 52: 27–31
5. Bolger JC, Kelly ME, Barry K (2015) Acute appendicitis in the adult population: modelled decision analysis supports a conservative approach. J Gastrointest Surg 19(12):2249–2257
6. Wilms IM, De Hoog DE, De Visser DC, Janzing HM (2011) Appendectomy versus antibiotic treatment for acute appendicitis. Cochrane Database Syst Rev 11:CD008359
7. Di Saverio S, Sibilio A, Giorgini E et al (2014) The NOTA study (non operative treatment for acute appendicitis): prospective study on the efficacy and safety of antibiotics (amoxicillin and clavulanic acid) for treating patients with right lower quadrant abdominal pain and long-term follow-up of conservatively treated suspected appendicitis. Ann Surg 260(1):109–117 Ir J Med Sci
8. Foell D, Bahde R, Senninger N (2015) The non operative treatment for acute appendicitis (NOTA) study: is less surgery better surgery? Ann Surg 265(6):83–84
9. Rocha LL, Rossi FM, Pessoa CM, Campos FN,

- Pires CE, Steinman M (2015) Antibiotics alone versus appendectomy to treat uncomplicated acute appendicitis in adults: what do meta-analyses say? *World J Emerg Surg* 10:51
10. Vons C, Barry C, Maitre S et al (2011) Amoxicillin plus clavulanic acid versus appendectomy for treatment of acute uncomplicated appendicitis: an open-label, non-inferiority, randomised controlled trial. *Lancet* 377(9777): 1573–1579
 11. Ehlers AP, Talan DA, Moran GJ, Flum DR, Davidson GH (2016) Evidence for an antibiotics-first strategy for uncomplicated appendicitis in adults: a systematic review and gap analysis. *J Am Coll Surg* 222(3):309–314
 12. Kelly ME, Khan A, Riaz M et al (2015) The utility of neutrophil-to lymphocyte ratio as a severity predictor of acute appendicitis, length of hospital stay and postoperative complication rates. *Dig Surg* 32(6):459–463
 13. Shimizu T, Ishizuka M, Kubota K (2015) A lower neutrophil to lymphocyte ratio is closely associated with catarrhal appendicitis versus severe appendicitis. *Surg Today*. doi:10.1007/s00595-015-1125-3
 14. Heinrich PC, Castell JV, Andus T (1990) Interleukin-6 and the acute phase response. *Biochem J* 265:621–636
 15. Faraj FH, Karim SAM, Fattah FHR (2015) of neutrophil/lymphocyte ratio in diagnosis of acute appendicitis. *JSMC*, 2015 (Vol 5) No.2: 85-93.
 16. Patil SM, Khaparde SH and Deshmukh SD(2018) retrospective study on Significance of Neutrophil to Lymphocyte Ratio in Patients Undergoing Appendectomy *JMSCR Volume 06 Issue 12 December 2018* 929-933.
 17. Rudimen R, Ruchimat T and Ferdinand Y (2017) Diagnostic value of C-reactive protein and neutrophil-limphocyte ratio in perforated appendicitis. *Int Surg J*. 2017 Oct;4(10):3196-3200.
 18. Ishizuka M, Shimizu T, Kubota K. Neutrophil-to lymphocyte ratio has a close association with gangrenous appendicitis in patients undergoing appendectomy. *Int Surg*. 2012; 97:299-304.
 19. Kahramanca S, Ozgehan G, Seker D, Gökce EI, Seker G, Tunç G, et al. Neutrophil-to-lymphocyte ratio as a predictor of acute appendicitis. *Ulus TravmaAcilCerrahiDerg*. 2014; 20:19-22.