

Predicting Complicated Appendicitis Based on Neutrophil to Lymphocyte Ratio, A Study in University Hospital of Nepal

Shrestha B,¹ Koju R,¹ Makaju Shrestha S,¹ Shrestha K,² Hada G,¹ Shakya YR,¹ Karmacharya RM,¹ Malla BR¹

¹Department of Surgery

²Research and Development Division

Dhulikhel Hospital, Kathmandu University Hospital,
Kathmandu University School of Medical Sciences,
Dhulikhel, Kavre, Nepal.

Corresponding Author

Bikesh Shrestha

Department of Surgery,

Dhulikhel Hospital, Kathmandu University Hospital,
Kathmandu University School of Medical Sciences,

Dhulikhel, Kavre, Nepal.

E-mail: bikeshsht@gmail.com

Citation

Shrestha B, Koju R, Makaju Shrestha S, Shrestha K, Hada G, Shakya YR, et al. Predicting Complicated Appendicitis Based on Neutrophil to Lymphocyte Ratio, A Study in University Hospital of Nepal. *Kathmandu Univ Med J.* 2023;83(3):270-4.

ABSTRACT

Background

Acute appendicitis is one of the most common causes of acute abdomen requiring surgical treatment. Accurately diagnosing appendicitis and identifying complicated appendicitis can be difficult at times.

Objective

To evaluate the ability of the neutrophil-to-lymphocyte ratio (NLR) to differentiate between uncomplicated and complicated appendicitis.

Method

This was a prospective hospital-based observational study conducted at the Department of Surgery, Dhulikhel Hospital, Kathmandu University Hospital from July 2021 to December 2022. Patients with the clinical diagnosis of acute appendicitis who had undergone emergency appendectomy were included in the study. Informed consent was taken from each patient and data collection was done by filling the proforma.

Result

A total of 218 patients were included in the study. Male: female ratio was 1.18:1. Mean age of patients was 28.58 ± 16.65 (3-78) years. A significant correlation was found between increasing neutrophil count and neutrophil-to-lymphocyte ratio with complicated appendicitis. However, no significant correlation was found between White Blood Cell counts and complicated appendicitis. Neutrophil-to-lymphocyte ratio > 12.6 was found to be associated with complicated appendicitis.

Conclusion

A simple, cost-effective, and yet perfect test is not available for identifying complicated appendicitis. Increased Neutrophil count and neutrophil-to-lymphocyte ratio can indicate complicated appendicitis. Elevated WBC counts alone has no role in differentiating complicated appendicitis. According to the results of our study, an neutrophil-to-lymphocyte ratio of 12.6 can help to differentiate complicated from uncomplicated appendicitis.

KEY WORDS

Appendectomy, Appendicitis, Lymphocyte count, Neutrophils, Receiver operating characteristic curve

INTRODUCTION

Acute appendicitis is one of the most common causes of acute abdomen presenting to the hospital requiring surgical treatment.¹ The lifetime risk of suffering from acute appendicitis is 8.6% in male and 6.7% in female population respectively.² Incidence of appendicular perforation can go up to 17-20%.¹ Classical presentation of acute appendicitis with migratory pain from the abdomen to the right iliac fossa, nausea, vomiting, and low-grade fever in some patients are well-known symptoms of patients with appendicitis. Despite of these well-known clinical symptoms of appendicitis, early diagnosis can sometimes be challenging.³ Although acute appendicitis is mainly diagnosed clinically, there are few laboratory tests and radiological investigations which can be done to support the diagnosis. Failure in diagnosis and treatment of acute appendicitis in an early stage of the disease may lead to complications like perforation, abscess, and peritonitis which can lead to increased morbidity and even mortality.⁴ Many scoring systems have been used to aid the diagnosis of acute appendicitis including the commonly used Alvarado score and the Raja Isteri Pengiran Anak Saleha Appendicitis (RIPASA) score.^{5,6} Elevated WBC count has no predictive value in distinguishing complicated appendicitis from simple appendicitis.⁴ The neutrophil count suggests continuing inflammation while the lymphocyte count highlights the regulatory pathway.⁷ Bacteremia is the main sequelae of acute appendicitis.⁸ Leucocytosis and increased Neutrophil to leukocyte ratio can be taken as indicators of bloodstream infection.⁹ Neutrophil to Lymphocyte ratio, thus can be used as a simple and inexpensive marker of subclinical inflammation which can be calculated from the differential WBC counts.¹⁰

METHODS

This was a prospective hospital-based observational study conducted at the Department of Surgery, Dhulikhel Hospital, Kathmandu University Hospital from July 2021 to December 2022, after approval of the Institutional review committee (KUSMS-IRC). The sample size of 218 was calculated with an estimated prevalence of 17% with a 95% confidence interval. A total of 218 patients admitted to the Surgery Ward of Dhulikhel Hospital, Kathmandu University Hospital with the clinical diagnosis of acute appendicitis who had undergone emergency appendectomy were included in the study. Informed written consent was taken from every patients enrolled in this study. Diagnosis of appendicitis was confirmed by histopathology reports. Complicated appendicitis was defined as gangrenous, perforated, and appendicular abscess formation. Patients undergoing Interval appendectomy and patients with a previous history of chemotherapy or other immunosuppressive status were excluded from the study. SPSS 20.0 (SPSS Inc., Chicago, IL, USA) was used for data analysis. Frequency

analysis was performed for scalar and ordinal variables. For nominal variables, descriptive analysis was performed with the calculation of mean, range, and standard deviation. An Independent sample t-test was performed for the comparison of parametric scalar variables between the two groups. For nonparametric categorical variables, the Chi-square test was performed. The cutoff values of parameters for discrimination of the groups were determined using the Receiver Operating Characteristic (ROC) analysis. A p-value of less than 0.05 was considered significant.

RESULTS

This study comprised of 218 patients with acute appendicitis who underwent emergency appendectomy among whom 118 (54.13%) were male patients and 100 (45.87%) were female patients. The mean age of the patients was 28.58 ± 16.65 years. The age of patients ranged from 3 years to 78 years. Figure 1 shows the distribution of patients according to different age groups. The highest number of patients belonged to the age group of 20-40 years.

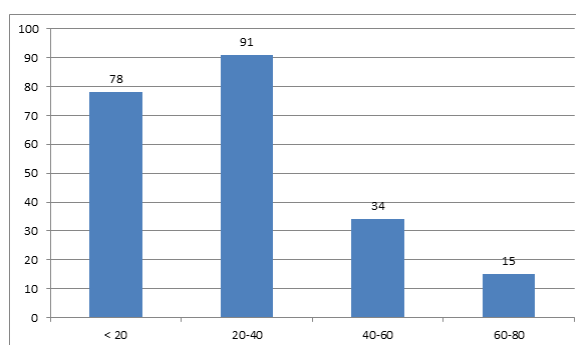


Figure 1. Distribution of Patients according to Age Group

Among 218 patients, 173 patients had uncomplicated appendicitis whereas 45 patients had complicated appendicitis. There was no significant difference in mean age between patients with uncomplicated and complicated appendicitis (28.14 ± 15.25 vs 30.29 ± 21.31 ; $p = 0.42$).

Table 1. Distribution of Patients according to sex in uncomplicated and complicated appendicitis groups.

	Uncomplicated appendicitis	Complicated appendicitis	p-value
Male	95	23	0.648
Female	78	22	

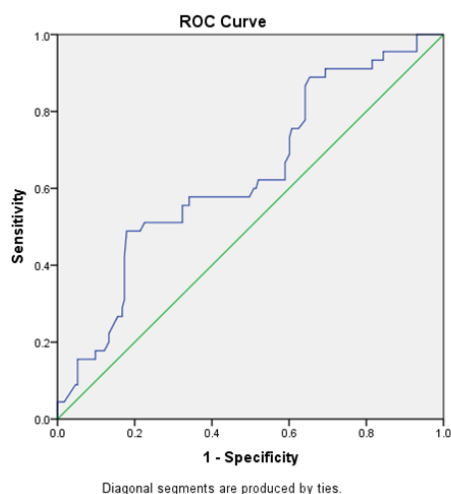
As shown in table 1, there is no significant difference between male and female patients in the uncomplicated and complicated acute appendicitis group ($p=0.648$).

As shown in table 2, the Neutrophil to Lymphocyte ratio (NLR) and Neutrophil count are significantly high in patients with complicated acute appendicitis. However, there is no significant difference between White Blood Cell (WBC) Counts in patients with complicated and uncomplicated acute appendicitis.

Table 2. Relationship between parameters and patients in uncomplicated and complicated appendicitis groups

		Number of patients	Mean	Standard deviation	p-value
Neutrophil to Lymphocyte ratio (NLR)	Uncomplicated appendicitis	173	8.63	5.47	0.003
	Complicated appendicitis	45	11.56	6.62	
White Blood Cell (WBC) Count	Uncomplicated appendicitis	173	14544.51	4488.36	0.269
	Complicated appendicitis	45	13706.67	4624.75	
Neutrophil percentage (N)	Uncomplicated appendicitis	173	80.97	9.22	0.012
	Complicated appendicitis	45	84.67	6.4	

The recommended cutoff value of the NLR was based on the most prominent point on the Receiver Operating Characteristic curve for sensitivity (0.489) and specificity (0.821) as shown in figure 2. These 2 parameters indicated a cutoff value of 12.64, the recommended cutoff value was defined as 12.6. The area under the receiver operating characteristic curve was 0.634.

**Figure 2.** ROC curve of NLR for Uncomplicated and Complicated appendicitis.

DISCUSSION

Acute appendicitis is one of the most common causes of surgical emergencies. Appendicitis is more prevalent in 2nd and 3rd decades of life.¹¹ Increased amount of lymphoid tissue in the submucosa of the appendix could be the cause of increased incidence of appendicitis in patients of younger age group.¹² In our study, 91(41.7%) patients were of the age group 20-40 years. As found in our study, acute appendicitis is more common in male population.^{13,14} However, some studies have found increased incidence

in female.¹⁵ The exact cause behind this difference in incidence among male and female is still unknown.

The diagnosis of acute appendicitis is clinical. Presenting features of acute appendicitis may mimic with the symptoms of other conditions adding challenge to coming to a diagnosis mainly in pediatric population, elderly people and females of reproductive age group.¹⁶ The typical clinical presentation of acute appendicitis is noted in less than half of the patients with appendicitis.¹⁷ This can lead to delay in diagnosis with increase in morbidity and mortality. The decision to keep the patient under observation till definitive diagnosis or to operate immediately to prevent undesired complications including perforation, peritonitis and sepsis represents a serious dilemma for a surgeon.¹⁸ However, early surgery may lead to negative appendectomy resulting in removal of normal appendix and might contribute to unnecessary cost and morbidity to the patient.¹⁹ The availability of laboratory investigations and technological advances in radiological modalities have helped in the successful diagnosis of patients with acute appendicitis.^{20,21} However, easy and cost-effective availability of advanced radiological modalities is not possible in our setup. Simple laboratory parameters that can support the clinical diagnosis of acute appendicitis and prediction of complicated appendicitis have always been a matter of interest for surgeons.

Moderate leukocytosis is a persistent laboratory finding in cases of acute appendicitis.²² An elevated WBC count has no predictive value in differentiating simple and complicated appendicitis.^{23,24} Our study has also shown that WBC count cannot predict complicated appendicitis (p-value 0.269). However, the increased neutrophil count has shown a significant association with complicated appendicitis (p-value 0.012) in our study.

The neutrophil count indicates active and ongoing inflammation, while the lymphocyte count indicates the regulatory pathway.⁷ Lymphocyte counts can decrease in appendicitis with a significant decrease occurring in gangrenous appendicitis.²⁵ Neutrophilia and lymphocytopenia are components of the cellular response in systemic inflammation. Increase in the difference between neutrophil and lymphocyte counts reflects severity of inflammatory response.²⁶ Neutrophil to Lymphocyte ratio (NLR) is a simple and more sensitive parameter than leucocytosis.²⁷ It is shown that preoperative NLR is an independent predictor of positive appendicitis histology.²⁸

Kahramanca et al. determined a cutoff value of 5.74 for NLR to differentiate complicated appendicitis from simple appendicitis with a sensitivity of 70.8% and specificity of 48.5%.²⁹ Ishizuka et al. have shown NLR > 8 has a significant association with gangrenous appendicitis in patients undergoing an appendectomy.³⁰

A systematic review and meta-analysis by Hajibandeh et al. has shown NLR of 4.7 was the cut-off value of acute

appendicitis with a sensitivity of 88.89% and specificity of 90.91% with an AUC of 0.96 and an NLR of 8.8 was a cut-off value for complicated appendicitis with a sensitivity of 76.92% and specificity 100% with AUC of 0.91.⁴

Our results show that NLR value for complicated appendicitis is 12.6 with a sensitivity of 48.9% and specificity of 82.1% with AUC of 0.63. This value is higher than the numbers suggested by previous reports.^{4,29,30}

Despite variations in recommendations regarding cut-off values, we believe that NLR is a simple yet significant and useful for diagnosing acute appendicitis and identifying complicated appendicitis.

This study was a single-center study which can be a limitation of the study, a multiple-center study with a

larger patient population would yield better outcomes. Patients suspected of having acute appendicitis who did not undergo surgery were not included.

CONCLUSION

Simple, cost-effective, and yet perfect test is not available for identifying complicated appendicitis. Increased Neutrophil count and NLR can indicate complicated appendicitis. Elevated WBC counts alone has no role in differentiating complicated appendicitis. According to the results of our study, an NLR of 12.6 can help to differentiate complicated from uncomplicated appendicitis.

REFERENCES

- Storm-Dickerson TL, Despite. What have we learned over the past 20 years of appendicitis in the elderly? *Am J Surg.* 2003 Mar;185(3):198-201.
- Flum DR, Koepsell TD. Evaluating diagnostic accuracy in appendicitis using administrative data. *J Surg Res.* 2005 Feb;123(2):257-61.
- Kanumba ES, Mabula JB, Rambau P, Chalya PL. Modified Alvarado Scoring System as a diagnostic tool for acute appendicitis at Bugando Medical Centre, Mwanza, Tanzania. *BMC Surg.* 2011 Feb 17;11:4.
- Hajibandeh S, Hajibandeh S, Hobbs N, Mansour M. Neutrophil-to-lymphocyte ratio predicts acute appendicitis and distinguishes between complicated and uncomplicated appendicitis: A systematic review and meta-analysis. *Am J Surg.* 2020 Jan;219(1):154-163. doi: 10.1016/j.amjsurg.2019.04.018. Epub 2019 Apr 27. PMID: 31056211.
- Alvarado A. A practical score for the early diagnosis of acute appendicitis. *Ann Emerg Med.* 1986 May;15(5):557-64. doi: 10.1016/s0196-0644(86)80993-3. PMID: 3963537.
- N N, Mohammed A, Shanbhag V, Ashfaque K, S A P. A Comparative Study of RIPASA Score and ALVARADO Score in the Diagnosis of Acute Appendicitis. *J Clin Diagn Res.* 2014 Nov;8(11):NC03-5. doi: 10.7860/JCDR/2014/9055.5170. Epub 2014 Nov 20. PMID: 25584259; PMCID: PMC4290278.
- Acarturk G, Acay A, Demir K, Ulu MS, Ahsen A, Yuksel S. Neutrophil-to-lymphocyte ratio in inflammatory bowel disease - as a new predictor of disease severity. *Bratisl Lek Listy.* 2015;116(4):213-7. doi: 10.4149/bll_2015_041. PMID: 25773946.
- Juric I, Primorac D, Zagar Z, Biocić M, Pavić S, Furlan D, et al. Frequency of portal and systemic bacteremia in acute appendicitis. *Pediatr Int.* 2001 Apr;43(2):152-6.
- Lowsby R, Gomes C, Jarman I, Lisboa P, Nee PA, Vardhan M, et al. Neutrophil to lymphocyte count ratio as an early indicator of blood stream infection in the emergency department. *Emerg Med J.* 2015 Jul 1;32(7):531-4.
- Käser SA, Fankhauser G, Willi N, Maurer CA. C-reactive protein is superior to bilirubin for anticipation of perforation in acute appendicitis. *Scand J Gastroenterol.* 2010 Aug;45(7-8):885-92.
- Khairy G. Acute appendicitis: is removal of a normal appendix still existing and can we reduce its rate? *Saudi J Gastroenterol.* 2009 Jul-Sep;15(3):167-70. doi: 10.4103/1319-3767.51367. PMID: 19636177; PMCID: PMC2841415.
- Almaramhy HH. Acute appendicitis in young children less than 5 years: review article. *Ital J Pediatr.* 2017 Jan 26;43(1):15. doi: 10.1186/s13052-017-0335-2. PMID: 28257658; PMCID: PMC5347837.
- Humes DJ, Simpson J. Acute appendicitis. *BMJ.* 2006 Sep 9;333(7567):530-4. doi: 10.1136/bmj.38940.664363.AE. PMID: 16960208; PMCID: PMC1562475.
- Tsioplis C, Brockschmidt C, Sander S, Henne-Bruns D, Kornmann M. Factors influencing the course of acute appendicitis in adults and children. *Langenbecks Arch Surg.* 2013 Aug;398(6):857-67. doi: 10.1007/s00423-013-1096-z. Epub 2013 Jul 7. PMID: 23832465.
- Shrestha R, Ranabhat SR, Tiwari M. Histopathologic analysis of appendectomy specimens. *J pathol Nepal.* 2012;2(3):215-9.
- Kanumba ES, Mabula JB, Rambau P, Chalya PL. Modified Alvarado Scoring System as a diagnostic tool for acute appendicitis at Bugando Medical Centre, Mwanza, Tanzania. *BMC Surg.* 2011 Feb 17;11:4. doi: 10.1186/1471-2482-11-4. PMID: 21329493; PMCID: PMC3050681.
- Nshuti R, Kruger D, Luvhengo TE. Clinical presentation of acute appendicitis in adults at the Chris Hani Baragwanath academic hospital. *Int J Emerg Med.* 2014 Feb 17;7(1):12. doi: 10.1186/1865-1380-7-12. PMID: 24533851; PMCID: PMC3938026.
- Wray CJ, Kao LS, Millas SG, Tsao K, Ko TC. Acute appendicitis: controversies in diagnosis and management. *Curr Probl Surg.* 2013 Feb;50(2):54-86. doi: 10.1067/j.cpsurg.2012.10.001. PMID: 23374326.
- Bijnen CL, Van Den Broek WT, Bijnen AB, De Ruiter P, Gouma DJ. Implications of removing a normal appendix. *Dig Surg.* 2003;20(2):115-21. doi: 10.1159/000069386. PMID: 12686778.
- Atema JJ, van Rossem CC, Leeuwenburgh MM, Stoker J, Boermeester MA. Scoring system to distinguish uncomplicated from complicated acute appendicitis. *Br J Surg.* 2015 Jul;102(8):979-90. doi: 10.1002/bjs.9835. Epub 2015 May 12. PMID: 25963411.
- Xiong B, Zhong B, Li Z, Zhou F, Hu R, Feng Z, et al. Diagnostic Accuracy of Noncontrast CT in Detecting Acute Appendicitis: A Meta-analysis of Prospective Studies. *Am Surg.* 2015 Jun;81(6):626-9. PMID: 26031278.
- Farooqui W, Pommergaard HC, Burcharth J, Eriksen JR. The diagnostic value of a panel of serological markers in acute appendicitis. *Scand J Surg.* 2015 Jun;104(2):72-8. doi: 10.1177/1457496914529273. Epub 2014 Apr 15. PMID: 24737847.

23. Coleman C, Thompson JE Jr, Bennion RS, Schmit PJ. White blood cell count is a poor predictor of severity of disease in the diagnosis of appendicitis. *Am Surg.* 1998 Oct;64(10):983-5. PMID: 9764707.
24. Sand M, Bechara FG, Holland-Letz T, Sand D, Mehnert G, Mann B. Diagnostic value of hyperbilirubinemia as a predictive factor for appendiceal perforation in acute appendicitis. *Am J Surg.* 2009 Aug;198(2):193-8. doi: 10.1016/j.amjsurg.2008.08.026. Epub 2009 Mar 23. PMID: 19306980.
25. Raftery AT. The value of the leucocyte count in the diagnosis of acute appendicitis. *Br J Surg.* 1976 Feb;63(2):143-4. doi: 10.1002/bjs.1800630215. PMID: 1252716.
26. Zahorec R. Ratio of neutrophil to lymphocyte counts--rapid and simple parameter of systemic inflammation and stress in critically ill. *Bratisl Lek Listy.* 2001;102(1):5-14. English, Slovak. PMID: 11723675.
27. Goodman DA, Goodman CB, Monk JS. Use of the neutrophil:lymphocyte ratio in the diagnosis of appendicitis. *Am Surg.* 1995 Mar;61(3):257-9. PMID: 7887542.
28. Markar SR, Karthikesalingam A, Falzon A, Kan Y. The diagnostic value of neutrophil: lymphocyte ratio in adults with suspected acute appendicitis. *Acta Chir Belg.* 2010 Sep-Oct;110(5):543-7. PMID: 21158332.
29. 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 Travma Acil Cerrahi Derg.* 2014 Jan;20(1):19-22. doi: 10.5505/tjtes.2014.20688. PMID: 24639310.
30. Ishizuka M, Shimizu T, Kubota K. Neutrophil-to-lymphocyte ratio has a close association with gangrenous appendicitis in patients undergoing appendectomy. *Int Surg.* 2012 Oct-Dec;97(4):299-304. doi: 10.9738/CC161.1. PMID: 23294069; PMCID: PMC3727267.