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# Preoperative neutrophil-to-lymphocyte ratio in predicting the severity of appendicitis: A retrospective cohort study in a tertiary rural hospital

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**Abstract**
Acute appendicitis (AA) is one of the most common acute surgical conditions of the abdomen, and has a lifetime risk of approximately 7%. Although urgent appendectomy is still considered the gold standard treatment, recent evidence has shown that AA can be treated conservatively without surgery. However, conservative treatment is likely inconvenient in cases of perforated AA. Therefore, any factor that allows for prediction of perforation in AA contributes significantly to patient-specific treatment. Furthermore, relatively troublesome operation, including the selection of laparoscopy or laparotomy, etc.
The Neutrophil-to-Lymphocyte ratio is derived from the counts of circulating neutrophils and lymphocytes, both of which are major leukocyte subpopulations. The inflammation-triggered release of arachidonic acid metabolites and platelet-activating factors results in neutrophilia, and cortisol-induced stress results in relative lymphopenia, and thus, the Neutrophil-to-Lymphocyte ratio accurately represents the underlying inflammatory process.
**AIM:** The aim of the present study was to evaluate the predictive value of simple laboratory parameters including white cell count (WCC), NLR in the diagnosis of acute appendicitis and its complications.
**Materials and Methods:** Records of 514 patients who underwent open or laparoscopic appendectomy between March 2013 and July 2013 at R L Jalappa hospital, Tamaka, kolar were reviewed retrospectively. Demography, recorded anamneses, histopathological findings, and preoperative NLR was calculated.
**Results:** White cell count (WCC) and NLR were significant parameters for the diagnosis of acute appendicitis. Cut-off values were 11900/mm3 for WCC (sensitivity: 71.2%; specificity: 67.2%; OR: 5.13) and 3.0 for NLR (sensitivity: 81.2%; specificity: 53.1%; OR: 4.27). NLR was an independent variable for the diagnosis of perforated appendicitis. Cut-off value was 4.8 for NLR (sensitivity: 81.2%; specificity: 53.1%; OR: 2.6).
**Conclusion:** In conclusion, it was demonstrated that no simple yet perfect test currently exists for diagnosing acute appendicitis and recognizing perforation. However, increases in WCC, serum bilirubin level, and NLR can be considered moderately reliable indicators for the diagnosis of acute appendicitis. Serum bilirubin level and NLR are useful indicators for the recognition of perforated appendicitis.

**Keywords:** NLR; WCC; acute appendicitis; inflammation

## Introduction
In addition to so-called "leukocytosis," many laboratory parameters have been used to diagnose or determine severity of infectious or inflammatory diseases such as acute appendicitis. As diversity of such parameters increases, attendant problems arise, including availability, accuracy, intelligibility, time-effectiveness, and cost-effectiveness. When the relatively high incidence of acute appendicitis is considered, these problems take on great importance. Radiological modalities, particularly ultrasonography and computed tomography, have been widely and successfully used in the diagnosis of acute appendicitis and its complications [1, 2]. However, because these modalities require special equipment and experienced radiologists, surgeons seek simpler means of definitive diagnosis.
In the last decade, simple parameters included in a standard complete blood count and routine preoperative tests, including neutrophil count, neutrophil ratio [3], Neutrophil-to-lymphocyte ratio (NLR) [4-7], platelet count (PLT) [8, 9], mean platelet volume (MPV) [8-13], and serum bilirubin level [14-20], have been studied for potential value in diagnosis of acute appendicitis and prediction of possible complications. However, reported results widely vary, and the number of patients studied has been relatively small. The aim of the present study is to evaluate the

predictive value of NLR in the diagnosis of acute appendicitis and its complications in a very large case series.

## Materials and Methods

Records of 514 patients who underwent open or laparoscopic appendectomy between March 2013 and July 2017 at R L Jalappa hospital, Tamaka, kolar were reviewed retrospectively. Demography, recorded anamneses, histopathological findings, and preoperative NLR was calculated.

Patients were divided into 2 groups according to histopathological evaluation; Group 1 included patients with normal or inflamed appendix and Group 2 included patients with perforated or gangrenous appendix. Basic demographic data (age, gender) and preoperative laboratory findings were compared between Groups 1 and 2 providing reliable results regarding the diagnosis of acute appendicitis and the prediction of perforation, respectively.

Exclusion criteria were age younger than 15 years, presence of malignant diseases, current course of chemotherapy or radiotherapy, pregnancy, intraoperative diagnosis of intraabdominal pathology other than appendicitis, and presence of known liver diseases.

## Statistical Analysis

SPSS software (version 20.0; SPSS Inc., Chicago, IL, USA) was used for statistical analysis. In univariate analysis, normally distributed continuous variables were expressed as mean± SD and compared using t-test. Variables not normally distributed were expressed as median (range) and compared using Mann-Whitney U test. Nominal data were expressed as case numbers and percentages, and were compared using Fisher's exact test. Logistic regression analysis was performed as multivariate analysis on parameters with significant differences observed in univariate analysis. Diagnostic accuracy was evaluated using receiver operating characteristic (ROC) curve analysis. Appropriate cut-off values were identified, and sensitivity, specificity, positive predictive value, negative predictive value, positive likelihood ratio, and negative likelihood ratio were calculated for parameters with an area under the curve (AUC) of above 0.600. All tests were two-sided. A value of $p<0.05$ was considered statistically significant.

## Results

White cell count (WCC) and NLR were significant parameters for the diagnosis of acute appendicitis. Cut-off values were 11900/mm3 for WCC (sensitivity: 71.2%; specificity: 67.2%; OR: 5.13) and 3.0 for NLR (sensitivity: 81.2%; specificity: 53.1%; OR: 4.27). NLR Wasan independent variable for the diagnosis of perforated appendicitis. Cut-off value was 4.8 for NLR (sensitivity: 81.2%; specificity: 53.1%; OR: 2.6).

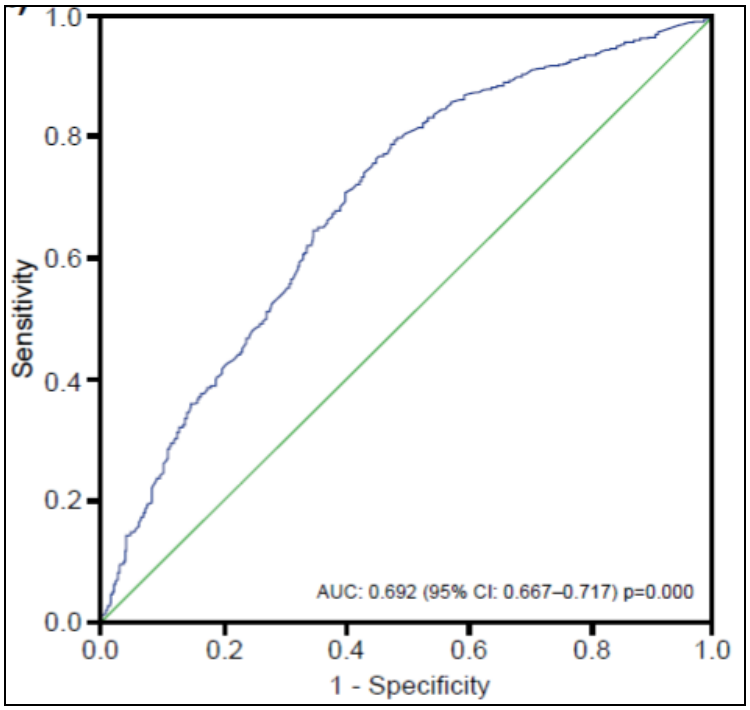


**Fig 1:** ROC curve analysis of NLR

Proposed cut-off values for significant parameters in diagnosis of acute appendicitis

| | Cut-off value | Sensitivity (%) | Specificity (%) | PPV | NPV | OR | pLLR | nLLR | AUC |
|---|---|---|---|---|---|---|---|---|---|
| WCC (/mm³) | 11,900 | 71.2 | 67.2 | 0.92 | 0.30 | 5.13 | 2.15 | 0.43 | 0.748 |
| Bilirubin (mg/dl) | 1.0 | 19.1 | 92.4 | 0.93 | 0.17 | 2.96 | 2.5 | 0.87 | 0.621 |
| NLR | 3.0 | 81.2 | 53.1 | 0.89 | 0.36 | 4.87 | 1.72 | 0.35 | 0.692 |

WCC: White cell count; NLR: Neutrophil-to-lymphocyte ratio; PPV: Positive predictive value; NPV: Negative predictive value; OR: Odds ratio; pLLR: Positive likelihood ratio; nLLR: Negative likelihood ratio; AUC: Area under the curve.

**Fig 2:** cut-off values in diagnosis of acute appendicitis

Proposed cut-off values for significant parameters in prediction of perforation

| | Cut-off value | Sensitivity (%) | Specificity (%) | PPV | NPV | OR | pLLR | nLLR | AUC |
|---|---|---|---|---|---|---|---|---|---|
| Bilirubin (mg/dl) | 1.0 | 34.4 | 81.4 | 0.11 | 0.94 | 2.6 | 1.84 | 0.80 | 0.594 |
| NLR | 4.8 | 78.4 | 41.7 | 0.08 | 0.96 | 2.6 | 1.34 | 0.51 | 0.624 |

WCC: White cell count; NLR: Neutrophil-to-lymphocyte ratio; PPV: Positive predictive value; NPV: Negative predictive value; OR: Odds ratio; pLLR: Positive likelihood ratio; nLLR: Negative likelihood ratio; AUC: Area under the curve.

**Fig 3:** cut-off values in prediction of perforation

## Discussion

Acute appendicitis is one of the most common causes of emergency surgery. Diagnosis is based on physical examination and presence of specific anamnesis. With technological advances in radiological modalities, successful diagnosis is more easily achieved [1, 2]. However, availability, intelligibility, time-effectiveness, and cost-effectiveness of these modalities remain disadvantageous, particularly to relatively small hospitals. Thus the potential of simple laboratory parameters to aid in diagnosis of acute appendicitis and prediction of perforations has attracted interest of surgeons. In the present study, simple, well-studied parameters were given particular consideration, and comprehensive and reliable data from a very large case series was provided.

Moderate leukocytosis is an expected laboratory finding in cases of acute appendicitis [15].

According to the present results, WCC is a significant parameter for the diagnosis of acute appendicitis. However, it is not a perfect indicator, due to relatively low sensitivity and specificity [21, 22].

Neutrophilia and lymphocytopenia are components of the cellular response in systemic inflammation [23]. Increase in the difference between neutrophil and lymphocyte counts reflects severity of inflammatory response. Hence, neutrophil-to-lymphocyte ratio has long been used as a marker for many pathologies, including malignancies, chronic inflammatory diseases, and postoperative complications [23, 24]. Use of NLR for diagnosis of acute appendicitis is not a new idea.

The argument that NLR is a more sensitive parameter than the number of leukocytes was put forth 20 years earlier by Goodman *et al*. [25-30]. Four studies have been published in the last 5 years regarding this issue [4-7]. Shimizu *et al*. [7] suggest a NLR cut-off value of 5.0 for the diagnosis of acute appendicitis, with 44% sensitivity and 22% specificity. Ishizuka *et al*. [5] determined a cut-off value of 8.0 for NLR to differentiate gangrenous appendicitis from catarrhal appendicitis, with 73% sensitivity and 39% specificity. Kahramanca *et al*. [6] reported 2 NLR cut-off values of 4.68 (65% sensitivity, 55% specificity) and 5.74 (71% sensitivity, 49% specificity) to distinguish acute appendicitis from normal appendix, and complicated appendicitis from non-complicated appendicitis, respectively. According to the present results, NLR cut-off values were 3.0 (81% sensitivity, 53% specificity) and 5.5 (78.4% sensitivity, 41.7% specificity) for the diagnosis of acute appendicitis and perforated appendicitis, respectively (Tables 2 and 4). In spite of conflicting suggestions regarding cut-off values, the authors believe that NLR is a significant parameter for diagnosing acute appendicitis and differentiating complicated cases.

The primary limitation of the present study was its retrospective nature. Only patients who underwent appendectomy were included; data did not reflect patients suspected of having acute appendicitis who did not undergo surgery. However, the patient population was very large, and the authors believe that comprehensive data is provided regarding diagnostic accuracy of simple laboratory parameters in cases of suspected acute appendicitis. An additional limitation was lack of data regarding patients with suspicious abdominal findings who did not undergo surgery. However, the authors believe that in spite of these limitations, the present study provides comprehensive results and contributes valuable reference data.

## Conclusion

In conclusion, it was demonstrated that no simple yet perfect test currently exists for diagnosing acute appendicitis and recognizing perforation. However, increases in WCC, serum bilirubin level, and NLR can be considered moderately reliable indicators for the diagnosis of acute appendicitis. Serum bilirubin level and NLR are useful indicators for the recognition of perforated appendicitis.

## References


1. Atema JJ, van Rossem CC, Leeuwenburgh MM, Stoker J, Boermeester MA. Scoring system to distinguish uncomplicated from complicated acute appendicitis. Br J Surg. 2015; 102:979-90.
2. Xiong B, Zhong B, Li Z, Zhou F, Hu R, Feng Z *et al*. Diagnostic Accuracy of Noncontrast CT in Detecting Acute Appendicitis: A Metaanalysis of Prospective Studies. Am Surg. 2015; 81:626-9.
3. Şahbaz NA, Bat O, Kaya B, Ulukent SC, İlkgül Ö, Özgün MY, *et al*. The clinical value of leucocyte count and neutrophil percentage in diagnosing uncomplicated (simple) appendicitis and predicting complicated appendicitis. Ulus TravmaAcilCerrahiDerg. 2014; 20:423-6.
4. 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; 110:543-7.
5. 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.
6. 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.
7. Shimizu T, Ishizuka M, Kubota K. A lower neutrophil to lymphocyte ratio is closely associated with catarrhal appendicitis versus severe appendicitis. Surg Today. 2016; 46:84-9.
8. Erdem H, Aktimur R, Cetinkunar S, Reyhan E, Gokler C, Irkorucu O, *et al*. Evaluation of mean platelet volume as a diagnostic biomarker in acute appendicitis. Int J Clin Exp Med. 2015; 8:1291-5.

9. Tanrikulu CS, Tanrikulu Y, Sabuncuoglu MZ, Karamercan MA, Akkapulu N, Coskun F. Mean platelet volume and red cell distribution width as a diagnostic marker in acute appendicitis. Iran Red Crescent Med J. 2014; 16:e10211.
10. Dinc B, Oskay A, Dinc SE, Bas B, Tekin S. New parameter in diagnosis of acute appendicitis: platelet distribution width. World J Gastroenterol. 2015; 21:1821-6.
11. Albayrak Y, Albayrak A, Albayrak F, Yildirim R, Aylu B, Uyanik A, *et al*. Mean platelet volume: a new predictor in confirming acute appendicitis diagnosis. Clin Appl Thromb Hemost. 2011; 17:362-6.
12. Bilici S, Sekmenli T, Göksu M, Melek M, Avci V. Mean platelet volume in diagnosis of acute appendicitis in children. Afr Health Sci. 2011; 11:427-32.
13. Narci H, Turk E, Karagulle E, Togan T, Karabulut K. The role of mean platelet volume in the diagnosis of acute appendicitis: a retrospective case-controlled study. Iran Red Crescent Med J. 2013; 15:11934.
14. D'Souza N, Karim D, Sunthareswaran R. Bilirubin; a diagnostic marker for appendicitis. Int J Surg. 2013; 11:1114-7.
15. Farooqui W, Pommergaard HC, Burcharth J, Eriksen JR. The diagnostic value of a panel of serological markers in acute appendicitis. Scand J Surg. 2015; 104:72-8.
16. Hong YR, Chung CW, Kim JW, Kwon CI, Ahn DH, Kwon SW, *et al*. Hyperbilirubinemia is a significant indicator for the severity of acute appendicitis. J Korean Soc Coloproctol. 2012; 28:247-52.
17. Sand M, Bechara FG, Holland-Letz T, Sand D, Mehnert G, Mann B *et al.* Diagnostic value of hyperbilirubinemia as a predictive factor for appendicealperforation in acute appendicitis. Am J Surg. 2009; 198:193-8.
18. Atahan K, Üreyen O, Aslan E, Deniz M, Çökmez A, Gür S, *et al*. Preoperative diagnostic role of hyperbilirubinaemia as a marker of appendix perforation. J Int Med Res. 2011; 39:609-18.
19. 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; 45:885-92.
20. Emmanuel A, Murchan P, Wilson I, Balfe P. The value of hyperbilirubinaemiain the diagnosis of acute appendicitis. Ann R Coll Surg Engl. 2011; 93:213-7.
21. Rafiq MS, Khan MM, Khan A, Ahmad B. Total leukocyte and neutrophil count as preventive tools in reducing negative appendectomies. Ulus Travma Acil Cerrahi Derg. 2015; 21:102-6.
22. Kamran H, Naveed D, Asad S, Hameed M, Khan U. Evaluation of modified Alvarado score for frequency of negative appendicectomies. J Ayub Med Coll Abbottabad. 2010; 22:46-9.
23. Zahorec R. Ratio of neutrophil to lymphocyte counts-rapid and simple parameter of systemic inflammation and stress in critically ill. BratislLekListy. 2001; 102:5-14.
24. Grivennikov SI, Greten FR, Karin M. Immunity, inflammation, and cancer. Cell. 2010; 140:883-99.
25. Goodman DA, Goodman CB, Monk JS. Use of the neutrophil: lymphocyteratio in the diagnosis of appendicitis. Am Surg. 1995; 61:257-9.
26. Mihajlovic D, Lendak D, Mitic G, Cebovic T, Draskovic B, Novakov A *et al*. Prognostic value of hemostasis-related parameters for prediction of organ dysfunction and mortality in sepsis. Turk J Med Sci. 2015; 45:93-8.
27. Kim CH, Kim SJ, Lee MJ, Kwon YE, Kim YL, Park KS *et al*. An increase in mean platelet volume from baseline is associated with mortality in patients with severe sepsis or septic shock. PLoS One. 2015; 10:e0119437.
28. Kisacik B, Tufan A, Kalyoncu U, Karadag O, Akdogan A, Ozturk MA, *et al*. Mean platelet volume (MPV) as an inflammatory marker in ankylosing spondylitis and rheumatoid arthritis. Joint Bone Spine. 2008; 75:291-4.
29. Leader A, Pereg D, Lishner M. Are platelet volume indices of clinical use? A multidisciplinary review. Ann Med. 2012; 44:805-16.
30. Miller DF, Irvine RW. Jaundice in acute appendicitis. Lancet. 1969; 94:201-6.