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Evaluation of Neutrophil Lymphocyte Ratio, Hyperbilirubinemia and Hyponatremia as a Predictive Marker of Complicated Appendicitis

Prabesh Joshi[1], **Sudip Poudel**[1], **Saroj Nayak**[1], **Surakshya Ghimire**[2], **Sarojini Sharma**[3]

[1]Department of Surgery, Bharatpur Hospital, Chitwan, Nepal, [2]Department of Pathology, Chitwan Medical College, Chitwan, Nepal, [3]B.P Koirala Memorial Cancer Hospital Nursing College, Chitwan, Nepal.

ABSTRACT

Background

Complicated appendicitis, including perforated and gangrenous forms, is associated with increased morbidity. This study evaluated the utility of NLR, hyperbilirubinemia, and hyponatremia as readily available preoperative biomarkers for predicting complicated appendicitis.

Methods

A prospective observational study was conducted between May 26, 2025, and December 25, 2025 among patients with clinically diagnosed acute appendicitis undergoing appendectomy. Preoperative laboratory parameters, including complete blood count, serum bilirubin, and serum sodium, were recorded, and NLR was calculated from absolute neutrophil and lymphocyte counts. Based on intraoperative findings, patients were classified as having uncomplicated or complicated appendicitis. Laboratory parameters were compared between groups, and statistical analyses were performed to assess their association with disease severity.

Results

A total of 91 patients were included, of whom 64 (70.3%) underwent appendectomy. The cohort comprised 41 males and 50 females, with a mean age of 30.75 ± 17.90 years and a mean BMI of 22.03 ± 5.79 kg/m². Among operated patients, 42 (65.6%) had non-complicated and 22 (34.4%) had complicated appendicitis. Mean NLR was higher in complicated cases (14.23 ± 17.5 vs. 7.7 ± 5.8), although the difference was not significant. Serum bilirubin was significantly elevated and serum sodium significantly lower in complicated appendicitis. ROC analysis identified hyponatremia as a strong predictor of complicated appendicitis.

Conclusions

Elevated NLR and serum bilirubin levels and reduced serum sodium levels are significantly associated with complicated appendicitis. These readily available laboratory markers, when used alongside clinical scoring systems such as the Alvarado score, can improve preoperative risk stratification and facilitate timely surgical intervention.

Keywords: Appendicitis; Serum Bilirubin; Serum Sodium

Correspondence: Dr. Prabesh Joshi, Department of Surgery, Bharatpur Hospital, Chitwan, Nepal. Email: prabeshjoshi53@gmail.com, Phone: +977-9845364100. **Article received**: 2026-02-20. **Article accepted**: 2026-05-24. **Article published**: 2026-06-30.

INTRODUCTION

Acute appendicitis is one of the most common surgical emergencies, with a morbidity rate of 1.5-1.9 per 10 million population and a 1.4-fold higher incidence in men than women.[1,2] Approximately 10% of individuals in developing countries experience acute appendicitis during their lifetime. Globally, appendicitis caused 33,400 deaths in 2019, while in Nepal it accounted for 220 deaths (0.14% of total mortality) in 2020. [3] Elderly patients are particularly susceptible to complicated appendicitis, with perforation and morbidity rates reported as high as 70% and 48%, respectively. [4] Overall, appendiceal perforation occurs in 17-30% of cases and is associated with increased morbidity and prolonged hospitalization. [1]

Based on pathology, appendicitis is classified as uncomplicated or complicated. Uncomplicated appendicitis may be managed conservatively with antibiotics, whereas surgery remains the standard treatment for complicated disease. [5] Early identification of complicated appendicitis is therefore essential to reduce complications and improve outcomes. Although several diagnostic tools are available, including laboratory markers, clinical scoring systems, ultrasonography, and computed tomography (CT), only about 60% of patients present with classical symptoms such as migratory right lower quadrant pain, fever, nausea, and vomiting. [1, 2, 6] Common inflammatory markers including C-reactive protein (CRP), white blood cell (WBC) count, and neutrophil percentage indicate the presence of infection but have limited value in predicting disease severity. [7, 8] While CT demonstrates high diagnostic accuracy, its cost and radiation exposure may restrict routine use.[9–11]

Recently, attention has focused on inexpensive and readily available laboratory markers that may predict complicated appendicitis. The neutrophil-to-lymphocyte ratio (NLR), derived from differential WBC counts, reflects systemic inflammatory response and has shown potential in assessing disease severity.[12] Hyperbilirubinemia may result from endotoxin-mediated hepatic dysfunction and septic hemolysis associated with appendiceal perforation. [13] Similarly, hyponatremia has been linked to complicated appendicitis, possibly through inflammatory cytokine-mediated vasopressin release. [14] Given the need for simple and accessible predictors of disease severity, this study aimed to evaluate the diagnostic value of NLR, serum bilirubin, and serum sodium levels in patients with complicated appendicitis.

METHODS

Study Design

A prospective, single-center observational study was conducted to evaluate the diagnostic value of neutrophil-to-lymphocyte ratio (NLR), serum bilirubin, and serum sodium in predicting complicated appendicitis.

Study Area

The study was carried out in the Department of General Surgery at Bharatpur Hospital, Chitwan, Nepal, between May 26, 2025, and December 25, 2025.

Study Population

All patients of either gender and any age admitted with a clinical diagnosis of acute appendicitis during the study period were eligible for inclusion. Patients with stump appendicitis and those undergoing appendectomy as part of another surgical procedure were excluded.

Sample Size

A total of 91 patients diagnosed with acute appendicitis were enrolled in the study.

Sampling Technique

Consecutive sampling was employed, whereby all eligible patients presenting during the study period were included until the study endpoint was reached.

Data Collection Tools and Technique

Data were collected prospectively using a structured proforma. Information recorded included demographic characteristics (age, sex, BMI), comorbidities, duration of symptoms, laboratory parameters (total leukocyte count, NLR, serum sodium, and total bilirubin), Alvarado score, operative findings, type of surgery, postoperative complications, and mortality. NLR was calculated by dividing the absolute neutrophil count by the

absolute lymphocyte count.

Variables/Measurements

The primary outcome variable was complicated appendicitis, defined by the intraoperative presence of perforation, gangrene, or purulent collection. Cases without these findings were categorized as non-complicated appendicitis. Hyperbilirubinemia was defined as a total bilirubin level >1.2 mg/dL, while hyponatremia was defined as a serum sodium level <135 mEq/L. Other variables included age, sex, BMI, total leukocyte count, Alvarado score, duration of symptoms, postoperative complications, and mortality.

Data Analysis

Data were analyzed using SPSS version 27. Continuous variables were expressed as means, while categorical variables were presented as frequencies and percentages. Normality testing was performed before analysis. Normally distributed continuous variables were compared using the unpaired t-test, whereas non-normally distributed variables were analyzed using the Mann–Whitney U test. Categorical variables were compared using the chi-square test or Fisher's exact test as appropriate. Receiver operating characteristic (ROC) curve analysis was performed to determine the area under the curve (AUC), sensitivity, specificity, and diagnostic accuracy of NLR, serum bilirubin, and serum sodium. A p-value <0.05 was considered statistically significant.

Ethical Consideration

Ethical approval was obtained from the Institutional Review Committee of Bharatpur Hospital (IRC No./Ref: 081/82-049). The study was conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all participants or their guardians before enrolment, and confidentiality of patient information was maintained throughout the study.

RESULTS

A total of 91 patients were included in the study among which 64 (70.3%) underwent appendectomy. Among the 91 patients there were 41 males (45.1%) and 50 females (54.9%), with a mean age of 30.75 ± 17.90 years. The mean age of female patients was 31.88 ± 16.27 years, while that of male patients was 29.37 ± 19.82 years. The maximum age of the patient was 76 years and the minimum age was 5 years. Mean body mass index (BMI) was 22.03 ± 5.79 kg/m². Among the operated patients, 42 (65.6%) had non-complicated appendicitis and 22 (34.4%) had complicated appendicitis. Appendectomy was performed laparoscopically in 7 patients (10.9%) whereas 57 patients underwent open appendectomy (89.1%). Mean TLC was higher in complicated appendicitis compared to non-complicated cases (14.24 ± 4.8 vs. 13.2 ± 4.5 x 10^3 cells/mm³), though this difference was not statistically significant (p > 0.05). Mean NLR was elevated in complicated appendicitis (14.23 ± 17.5) compared to non-complicated appendicitis (7.7 ± 5.8; p > 0.05). Mean serum bilirubin levels were significantly higher in complicated appendicitis (1.46 ± 0.76 mg/dL) than in non-complicated cases (1.03 ± 0.63 mg/dL; p < 0.05). Mean serum sodium level was significantly lower in complicated appendicitis (133.89 ± 1.60 mmol/L) compared to non-complicated appendicitis (136.83 ± 2.48 mmol/L; p < 0.05). (Table1)

Table 1. Demographic and clinical characteristics of patients

Variable	Non operated cases	Non complicated appendicitis	Complicated appendicitis
Cases	27 (29.7)	42 (46.2)	22 (24.2)
Age	35.6 ± 19.3	25.67 ± 14.67	34.54 ± 19.89
BMI	23.3 ± 4.4	22.0 ± 6.6	21.7 ± 5.0
Alvarado score	5.75 ± 2.1	7.46 ± 1.5	8.10 ± 1.4
TLC	9.16 ± 3.7 x 10^3	13.2 ± 4.5 x 10^3	14.24 ± 4.8 x 10^3
NLR	5.6 ± 9	7.7 ± 5.8	14.23 ± 17.5
TBIL (mg/dL)	1.09 ± 0.56	1.02 ± 0.63	1.45 ± 0.76

Operated patients had a significantly higher mean Alvarado score (7.68 ± 1.46) than those managed non-operatively (5.75 ± 2.1; p < 0.05). There

were 2 cases of surgical site infection (3.1%) after open appendectomy for complicated appendicitis however there was no mortality. Hyponatremia had sensitivity of 86.4% and specificity of 75% and PPV of 63.4%, NPV of 91.7%. Hyperbilirubinemia had sensitivity of 54.5% and specificity of 81.8%, PPV of 60% and NPV of 78.3%. Receiver operating characteristic (ROC) curve analysis demonstrated that serum sodium had excellent predictive ability for complicated appendicitis (AUC = 0.873), outperforming total bilirubin (AUC = 0.681) and neutrophil-to-lymphocyte ratio (AUC = 0.692). (Figure 1)

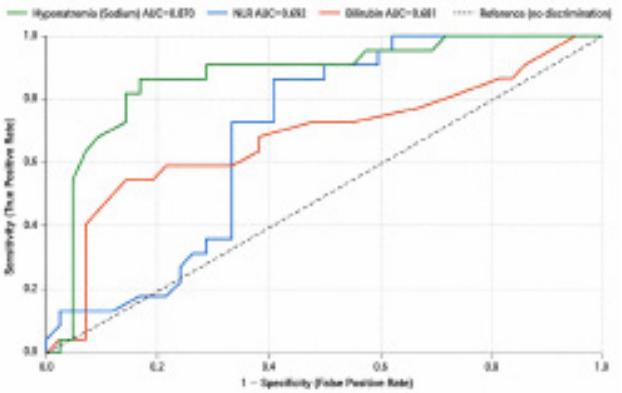

Figure 1. ROC curve to predict complicated appendicitis

DISCUSSION

In this study, we evaluated the clinical, laboratory, and operative characteristics of patients with acute appendicitis and analysed markers predictive of complicated appendicitis. A total of 91 patients were included, with a slight female predominance (54.9%) and a mean age of 30.75 ± 17.90 years. This is consistent with prior epidemiological studies, which report appendicitis as a disease of young adults with a slight male predominance in most cohorts, though some studies have reported similar female predominance in certain populations.[15] The age distribution in our study (range 5-76 years) highlights that acute appendicitis can affect both pediatric and elderly populations, aligning with observations from Andersson et al. and other large-scale appendicitis studies.[16]

Among the 64 patients who underwent appendectomy, 65.6% had non-complicated appendicitis, and 34.4% had complicated appendicitis. This proportion of complicated appendicitis is comparable to other studies, which have reported rates ranging from 20-40%. Open appendectomy predominated in our cohort (89.1%), with laparoscopic procedures accounting for only 10.9%, reflecting limited laparoscopic availability in our setting; globally, laparoscopic appendectomy is increasingly common and has been associated with reduced postoperative complications and faster recovery.[17]

Laboratory parameters were evaluated as potential predictors of complicated appendicitis. Mean total leukocyte count (TLC) was higher in complicated appendicitis (14.24 ± 4.8 x 10^3 cells/mm^3) compared to non-complicated cases (13.2 ± 4.5 x 10^3 cells/mm^3), although the difference did not reach statistical significance. This aligns with prior reports indicating that while leukocytosis is a hallmark of appendicitis, its predictive value for severity is limited. [18] Similarly, mean neutrophil-to-lymphocyte ratio (NLR) was elevated in complicated appendicitis (14.23 ± 17.5 vs. 7.7 ± 5.8), consistent with prior studies suggesting that NLR can reflect the systemic inflammatory response, but in our cohort, this difference was not statistically significant, possibly due to sample size limitations.[19]

Serum bilirubin and sodium levels emerged as significant discriminators of complicated appendicitis. Hyperbilirubinemia was observed in complicated appendicitis (1.46 ± 0.76 mg/dL vs. 1.03 ± 0.63 mg/dL, $p < 0.05$), supporting evidence that elevated bilirubin reflects bacterial translocation and hepatic inflammatory response in severe appendiceal infection.[20] Our findings on hyponatremia are particularly notable: mean serum sodium was significantly lower in complicated cases (133.89 ± 1.60 mmol/L vs. 136.83 ± 2.48 mmol/L, $p < 0.05$). Hyponatremia demonstrated high sensitivity (86.4%) and negative predictive value (91.7%), suggesting it is a reliable early marker for complicated appendicitis. These results are in line with emerging literature that highlights hyponatremia as an effective predictor of complicated intra-abdominal infections, likely mediated by systemic inflammation and antidiuretic hormone

dysregulation. [14] ROC analysis further supported the discriminative value of serum sodium (AUC 0.873), whereas NLR and bilirubin showed relatively low discriminative ability in our cohort in comparison to sodium level (AUC = 0.692 and 0.681, respectively). Finally, the Alvarado score was significantly higher in operated patients (7.68 ± 1.46) compared to those managed non-operatively (5.75 ± 2.1, $p < 0.05$), reaffirming its utility in guiding surgical decision-making. Our results are consistent with prior studies demonstrating that higher Alvarado scores correlate with increased likelihood of operative intervention and complicated appendicitis.[21]

Limitations

Limitations of our study include the single-center design and relatively small sample size, which may limit the generalizability of the findings. Additionally, the low proportion of laparoscopic procedures may influence postoperative outcomes. Future studies with larger multicenter cohorts and inclusion of additional biomarkers could strengthen the predictive model for complicated appendicitis.

Conclusions

Our study demonstrates that hyponatremia is a strong and reliable predictor of complicated appendicitis, outperforming traditional markers such as NLR and serum bilirubin in this cohort. Elevated Alvarado scores and hyperbilirubinemia remain supportive indicators. Incorporating serum sodium into routine preoperative evaluation may aid in early identification and timely surgical intervention for high-risk patients.

Conflicts of Interest: The authors declare that they have no conflict of interest.

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Ethical and Publication Integrity: Ethical approval was obtained from the Institutional Review Committee of Bharatpur Hospital (IRC No./Ref: 081/82-049)

Availability of data and materials: The datasets used and analyzed during the current study are available from the corresponding author upon reasonable request.

Authors' Contributions

Conceptualization: Prabesh Joshi, Sudip Poudel.
Data curation: Prabesh Joshi, Sudip Poudel, Saroj Nayak.
Formal analysis: Prabesh Joshi, Sudip Poudel.
Investigation: Prabesh Joshi, Sudip Poudel, Saroj Nayak, Surakshya Ghimire, Sarojini Sharma.
Methodology: Prabesh Joshi, Sudip Poudel, Saroj Nayak.
Supervision: Sarojini Sharma.
Writing-original draft: Prabesh Joshi.
Writing-review & editing: Sudip Poudel, Saroj Nayak, Surakshya Ghimire, Sarojini Sharma.

REFERENCES

1. Baird DL, Simillis C, Kontovounisios C, Rasheed S, Tekkis PP. Acute appendicitis. BMJ. 2017 Apr 19;357. [DOI]
2. Pogorelić Z, Mihanović J, Ninčević S, Lukšić B, Elezović Baloević S, Polašek O. Validity of appendicitis inflammatory response score in distinguishing perforated from non-perforated appendicitis in children. Children. 2021 Apr 19;8(4):309. [DOI]
3. Shakya YR. Epidemiological and Clinical Profiles of Cases of Appendicitis Managed At a Tertiary Hospital in Nepal. Journal of KIST Medical College. 2023;5(10):29-32. [DOI]
4. Weinandt M, Godiris-Petit G, Menegaux F, Chereau N, Lupinacci RM. Appendicitis is a severe disease in elderly patients: a twenty-year audit. JSLS: Journal of the Society of Laparoscopic & Robotic Surgeons. 2020 Jul;24(3). [DOI]
5. Pogorelić Z, Lukšić B, Ninčević S, Lukšić B, Polašek O. Hyponatremia as a predictor of perforated acute appendicitis in pediatric population: A prospective study. Journal of pediatric surgery. 2021 Oct 1;56(10):1816-21. [DOI]
6. Andersson RE. Meta-analysis of the clinical and laboratory diagnosis of appendicitis. Journal of

British Surgery. 2004 Jan;91(1):28-37. [DOI]
7. Di Saverio S, Birindelli A, Kelly MD, Catena F, Weber DG, Sartelli M, Sugrue M, De Moya M, Gomes CA, Bhangu A, Agresta F. WSES Jerusalem guidelines for diagnosis and treatment of acute appendicitis. World Journal of Emergency Surgery. 2016 Dec;11:1-25. [DOI]
8. Zhang Q, Zhao H, Wang F, Li W, Zhang P. Diagnostic value of laboratory parameters for complicated appendicitis: A two-center study. Biomedical Reports. 2024 May 1;20(5):1-6. [DOI]
9. Peixoto RD, Nunes TA, Gomes CA. Indices of diagnostic abdominal ultrasonography in acute appendicitis: influence of gender and physical constitution, time evolution of the disease and experience of radiologist. Revista do Colégio Brasileiro de Cirurgiões. 2011;38:105-11. [DOI]
10. Ramalingam V, Bates DD, Buch K, Uyeda J, Zhao KM, Storer LA, Roberts MB, Lebedis CA, Soto JA, Anderson SW. Diagnosing acute appendicitis using a nonoral contrast CT protocol in patients with a BMI of less than 25. Emergency radiology. 2016 Oct ;23:455-62. [DOI]
11. Nielsen JW, Boomer L, Kurtovic K, Lee E, Kupzyk K, Mallory R, Adler B, Bates DG, Kenney B. Reducing computed tomography scans for appendicitis by introduction of a standardized and validated ultrasonography report template. Journal of pediatric surgery. 2015 Jan 1;50(1):144-8. [DOI]
12. Ishizuka M, Shimizu T, Kubota K. Neutrophil-to-lymphocyte ratio has a close association with gangrenous appendicitis in patients undergoing appendectomy. International surgery. 2013 Jan 1;97(4):299-304. [DOI]
13. Halaseh SA, Kostalas M, Kopec C, Nimer A. Bilirubin as a Predictor of Complicated Appendicitis in a District General Hospital: A Retrospective Analysis. Cureus. 2022 Sep;14(9). [DOI]
14. Giannis D, Matenoglou E, Moris D. Hyponatremia as a marker of complicated appendicitis: A systematic review. The Surgeon. 2020 Oct 1;18(5):295-304. [DOI]
15. Mekakas A, Nagorni EA. Complicated Appendicitis: A Surgical Controversy Concerning. Doubts, problems and certainties about acute appendicitis. 2022 Jan 12:65. [DOI]
16. Segev L, Keidar A, Schrier I, Rayman S, Wasserberg N, Sadot E. Acute appendicitis in the elderly in the twenty-first century. Journal of Gastrointestinal Surgery. 2015 Apr 1;19(4):730-5. [DOI]
17. Ahmad J, Ali I, Akhtar H, Awan SU, Khan U, Ijaz F. Understanding Techniques, Risks, and Recovery for Enhanced Patient Care of Laparoscopic Appendectomy. Innovative Research in Applied, Biological and Chemical Sciences. 2024 Jun 30;2(1):133-8. [DOI]
18. Naser M, Nasr MM, Shehata LH. Biomarkers and Diagnosis of Acute Appendicitis in Children. Int. J. Progress. Sci. Technol.. 2024 Apr;44:127-41. URL: [Link]
19. Wang RH, Wen WX, Jiang ZP, Du ZP, Ma ZH, Lu AL, Li HP, Yuan F, Wu SB, Guo JW, Cai YF. The clinical value of neutrophil-to-lymphocyte ratio (NLR), systemic immune-inflammation index (SII), platelet-to-lymphocyte ratio (PLR) and systemic inflammation response index (SIRI) for predicting the occurrence and severity of pneumonia in patients with intracerebral hemorrhage. Frontiers in immunology. 2023 Feb 13;14:1115031. [DOI]
20. Khan S. Evaluation of hyperbilirubinemia in acute inflammation of appendix: a prospective study of 45 cases. Kathmandu Univ Med J. 2006 Jul 1;4(3):281-9. [PubMed]
21. Haak F, Kollmar O, Ioannidis A, Slotta JE, Ghadimi MB, Glass T, von Strauss Und Torney M. Predicting complicated appendicitis based on clinical findings: the role of Alvarado and Appendicitis Inflammatory Response scores. Langenbeck's archives of surgery. 2022 Aug;407(5):2051-7. [DOI]

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