Original Article

Validation of Neutrophil to Lymphocyte Ratio as A Predictor of Acute Appendicitis

Dr. Ajita Pandey[1], Dr. Bhimanagouda V Goudar[2], Dr. Rajendra Benkatti[3], Dr. Neelu Patil[4]

[1]Junior Resident, Department of General Surgery, SNMC & HSK Hospital, Bagalkot, Karnataka, India
[2]Professor, Department of General Surgery, SNMC & HSK Hospital, Bagalkot, Karnataka, India
[3]Professor, Department of General Surgery, SNMC & HSK Hospital, Bagalkot, Karnataka, India
[4]Senior Resident, Department of General Surgery, SNMC & HSK Hospital, Bagalkot, Karnataka, India

🔓 OPEN ACCESS

Corresponding Author:

Dr. Ajita Pandey
Junior Resident, Department of General Surgery, SNMC & HSK Hospital, Bagalkot, Karnataka, India

A B S T R A C T

Acute appendicitis is one of the most common causes of Abdominal surgical emergencies with lifetime prevalence of approximately 1 in 7 worldwide.1 The pooled incidence of appendicitis in the Indian subcontinent ranges from 100 to 105 cases per 100,000 person/year.2 This prospective Hospital based cross-sectional study was done in Department of General Surgery, SNMC & HSK Hospital, Bagalkot, Karnataka, India to compare the relation between Neutrophil to Lymphocyte Ratio for the diagnosis & to predict the severity of Acute Appendicitis. An average Neutrophil-to-Lymphocyte Ratio (NLR) of 5.42 (±5.33), indicating systemic inflammation in several patients. Patients with acute appendicitis had a significantly lower mean NLR (4.93 ± 5.56) compared to those with Appendicular perforation (7.15 ± 4.19). Thus, NLR is a promising marker that can predict both diagnosis and severity of appendicitis with acceptable sensitivity and specificity.

Keywords: Neutrophil to leukocyte ratio, Alvardo score, Modified Alvardo score, Negative appendicectomy, Acute Appendicitis.

INTRODUCTION

Acute appendicitis is one of the commonest surgical problems and though less common at the extremes of age, it can present classically or in an atypical manner in the very young and the elderly. Men and women have a lifetime risk of 8.6% and 6.7% of developing acute appendicitis respectively.[3] The most accurate means of diagnosing acute appendicitis is always debatable. A combination of history, physical examination, laboratory and radiological investigations is used to accurately diagnose and treat acute appendicitis, but none of them individually have high accuracy for diagnosis. Therefore, this study was undertaken to find out the effectiveness of Neutrophil to Lymphocyte Ratio for the diagnosis of acute appendicitis. This will hopefully lower the negative appendectomy rate.

MATERIALS AND METHODS

a) A Hospital based study was conducted among 50 clinically & radiologically confirmed acute appendicitis in HSK Hospital, S. Nijalingappa Medical College, Navanagar, Bagalkot.

b) **Inclusion criteria:**
   - All cases of clinically & radiologically confirmed acute appendicitis in SNMC Bagalkot
   - Age more than or equal to 13.
   - All the Patients consenting for the study.

c) **Exclusion criteria:**
   - Pregnant women
   - Post chemotherapy and other immunosuppressive status.

d) **Sampling Method:**
   - Sample size estimation was done using Medcalc software.

Dr. Ajita Pandey, *et al.* Validation Neutrophil to Lymphocyte Ratio as A Predictor of Acute Appendicitis. *Int. J Med. Pharm. Res., 6 (6): 675-681, 2025*

675

- At 95% confidence level, and 80% power of the study
- α (two-tailed) =0.050 and at 95% confidence level.
- 80% of power of the study
- The standard normal deviate for $\alpha = Z\alpha = 1.960$
- The standard normal deviate for $\beta = Z\beta = 0.842$
- Based on the study conducted by Asma A ()
- AUC of ROC=0.73, for Neutrophil-lymphocyte ratio for diagnosing Acute Appendicitis

e) METHODS

- This prospective non randomized study includes 50 patients admitted in the Department of General Surgery, S N MEDICAL COLLEGE HSK Hospital during the period of FEB 2023 to August 2024 with clinical suspicion of acute appendicitis and underwent Appendicectomy.
- After approval by local bioethics committees, informed consent was obtained
- All cases had undergone thorough history and detailed clinical examination at the time of admission as part of routine management.
- Total and differential leucocyte count was measured using an autoanalyzer.
- Neutrophil-to-lymphocyte ratio was taken out for these patients.
- As USG is technician dependent, only those patients who underwent abdominal USG by Consultant Radiologist were included in the study to exclude observer bias. He is blinded to the results of physical examination and blood report of the patients.
- Those with radiologist's opinion of findings suggestive of acute appendicitis, based on these criteria were taken as USG positive.
- Appendix was sent for Histopathology examination and patients whose HPR report was suggestive of acute appendicitis were considered for study.

RESULTS AND DISCUSSION

The results are based on the analysis of 50 patients who were diagnosed to have appendicitis and underwent appendectomy. The study population had a mean age of 31.84 years (±16.21), with a wide range from 13 to 84 years.

GENDER DISTRIBUTION

Over the 18 months study period (Feb 2023 to August 2024), 50 patients with a presumed diagnosis of acute appendicitis were admitted.

Among the 50 patients, 78% were male. Acute appendicitis was more common among males (30 of 39 males) and less frequent in females (9 of 11), though the Chi-square test did not reveal a statistically significant gender difference in diagnosis (p > 0.05).

Gender	Acute Appendicitis (AA)	Appendicular perforation	Total
Male	30	9	39
Female	9	2	11
Total	39	11	50

Gender Distribution Across Histopathological Diagnoses (Chi-Square Test)

DESCRIPTIVE STATISTICS OF STUDY POPULATION

The study population had a mean age of 31.84 years (±16.21), with a wide range from 13 to 84 years. Hematological parameters showed a mean WBC count of 11,318/μL and an average Neutrophil-to-Lymphocyte Ratio (NLR) of 5.42 (±5.33), indicating systemic inflammation in several patients. The mean Alvarado Score (AS) was 5.58, suggesting a moderate clinical suspicion for acute appendicitis in most cases.

Variable	Mean ± SD	Median (Min–Max)
Age (years)	31.84 ± 16.21	25.5 (13 – 84)
WBC (/μL)	11,318 ± 5,229	10,300 (2,800 – 28,500)
Neutrophil (%)	72.96 ± 11.67	71.5 (50 – 92)
Lymphocyte (%)	21.70 ± 11.10	22.0 (3 – 46)
N:L Ratio	5.42 ± 5.33	3.15 (1.0 – 30.6)
Alvarado Score	5.58 ± 2.32	5.0 (2 – 10)

NLR COMPARISON BETWEEN DIAGNOSIS GROUPS

Patients with acute appendicitis had a significantly lower mean NLR (4.93 ± 5.56) compared to those with Appendicular perforation (7.15 ± 4.19). This difference was statistically significant (p = 0.03), indicating that NLR could potentially help differentiate between acute appendicitis and other abdominal conditions.

Diagnosis	N	Mean N:L Ratio ± SD
Acute Appendicitis	39	4.93 ± 5.56
Appendicular perforation	11	7.15 ± 4.19
P VALUE	0.03*	
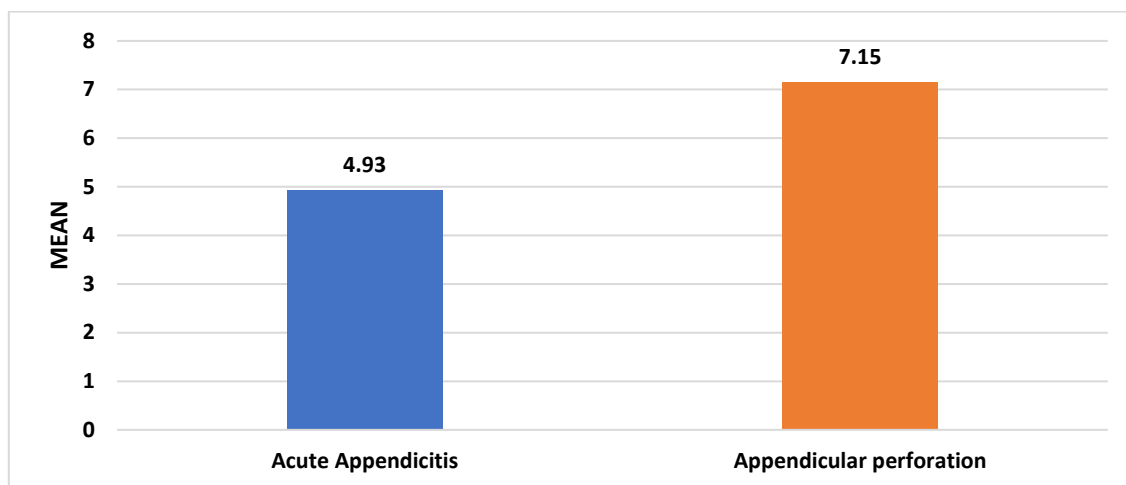
Variable	Acute Appendicitis (AA) (n=32)	Appendicular perforation (AP) (n=18)	p-value
Age (years)	29.5 ± 14.2	34.1 ± 17.3	0.28 (t-test)
Male Gender (%)	25 (78%)	14 (78%)	0.99 (Chi-square)
WBC (×10³/µL)	9,820 ± 4,210	14,500 ± 6,930	0.002 (t-test)
NLR	4.1 ± 3.8	7.9 ± 6.2	0.03 (t-test)

Although age and gender did not significantly differ between acute appendicitis and Appendicular perforation groups, WBC count and NLR were significantly higher in the Appendicular perforation (WBC: 14,500 vs. 9,820, p = 0.002; NLR: 7.9 vs. 4.1, p =0.03), implying more severe systemic inflammation in Appendicular perforation

CORRELATION OF NLR WITH ALVARADO SCORE
A strong positive correlation ($r = 0.62$, $p < 0.001$) was observed between NLR and Alvarado Score. This implies that higher NLR values are associated with more severe clinical presentations of appendicitis, supporting its utility in assessing disease severity.

Metric	Value
Pearson's r	0.62
p-value	<0.001
Conclusion	Strong positive correlation (Higher NLR predicts worse severity).

Dr. Ajita Pandey, *et al.* Validation Neutrophil to Lymphocyte Ratio as A Predictor of Acute Appendicitis*. Int. J Med. Pharm. Res., 6 (6): 675-681, 2025*

677
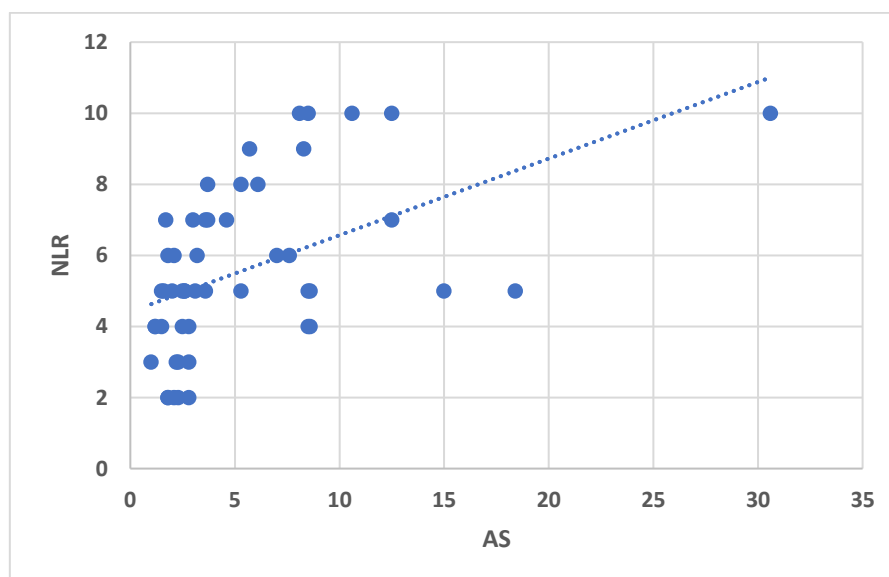
NLR STRATIFIED BY ALVARADO SEVERITY

When stratified by Alvarado Score, mean NLR values increased with severity: 2.9 for mild (AS 1–4), 5.6 for moderate (AS 5–7), and 9.3 for severe (AS 8–10). The Kruskal walis test showed a significant difference across these groups (p < 0.001), suggesting that NLR reliably reflects the clinical progression of appendicitis.

AS Group	Number of patients	Mean NLR ± SD	Clinical Implication
Mild (AS 1–4)	16	2.9 ± 1.8	Low likelihood of complications
Moderate (AS 5–7)	24	5.6 ± 3.4	Requires monitoring
Severe (AS 8–10)	10	9.3 ± 7.1	High risk of perforation

NLR ACROSS ALVARADO SEVERITY GROUPS

A Kruskal-Wallis test confirmed a significant difference in NLR among severity groups (p < 0.001), with Dunn's post-hoc analysis highlighting those severe cases significantly differed from both mild (p < 0.001) and moderate (p = 0.02). This further validates NLR as a severity marker in appendicitis.

Alvarado Score	NLR (Mean ± SD)	Median (IQR)	Kruskal-Wallis p-value
Mild (1–4)	2.9 ± 1.8	2.5 (1.8–3.6)	<0.001
Moderate (5–7)	5.6 ± 3.4	4.6 (3.1–7.0)	
Severe (8–10)	9.3 ± 7.1	8.5 (5.3–12.5)	

At a cutoff of ≥3.5, NLR demonstrated good diagnostic performance with 84% sensitivity and 72% specificity. Increasing the cutoff to ≥4.5 improved specificity to 85% while maintaining acceptable sensitivity (78%). At ≥6.0, specificity peaked at 89% but sensitivity dropped to 65%. Hence, an optimal balance between sensitivity and specificity appears around 4.5.

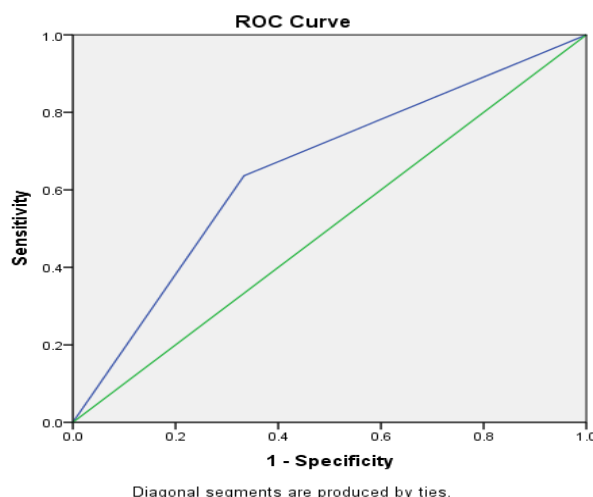| Cut-off	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
≥3.5	84	72	81	76	80
≥4.5	78	85	82	81	82
≥6.0	65	89	87	70	76

LOGISTIC REGRESSION ANALYSIS

Multivariate logistic regression showed that an NLR ≥6.0 was a strong independent predictor of severe appendicitis (AS ≥8), with an odds ratio of 4.8 (95% CI: 1.9–12.1, p = 0.001). Elevated WBC also predicted severity (OR: 3.2, p = 0.02), while age >50 was not statistically significant.

| Predictor	Odds Ratio (95% CI)	p-value
NLR ≥6.0	4.8 (1.9–12.1)	0.001
WBC >12,000	3.2 (1.2–8.5)	0.02
Age >50	1.5 (0.6–3.9)	0.38

ROC CURVE ANALYSIS

The ROC analysis of NLR yielded an AUC of 0.652 (95% CI: 0.465–0.838), indicating a modest discriminative ability for diagnosing acute appendicitis. Although the AUC did not reach statistical significance (p = 0.128), NLR still holds clinical value when used in conjunction with other parameters like WBC and Alvarado Score.

Diagonal segments are produced by ties.

Dr. Ajita Pandey, *et al.* Validation Neutrophil to Lymphocyte Ratio as A Predictor of Acute Appendicitis*. Int. J Med. Pharm. Res., 6 (6): 675-681, 2025*

678

Area Under the Curve				
Test Result Variable(s): NLRR				
Area	Std. Error[a]	Asymptotic Sig.[b]	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
.652	.095	.128	.465	.838

ASSOCIATION OF DIAGNOSIS WITH USG SIZE

The association between ultrasound (USG) appendix size and diagnosis based on histopathological reports (HPR) reveals a statistically significant pattern, with a p-value of 0.001, indicating a strong association between USG size and the type of appendiceal pathology. Among patients diagnosed with Acute Appendicitis (AA), the majority (56.4%) had a USG appendix diameter ranging from 5–8 mm, followed by 33.3% with a diameter of 9–12 mm, and only 10.3% with a size of 13–15 mm. In contrast, patients diagnosed with Appendicular Perforation (AP) showed a different distribution, with most cases (63.6%) having a USG size in the 9–12 mm range, 27.3% in the 5–8 mm range, and 9.1% in the 13–15 mm category. Overall, 50% of all patients had a USG appendix size between 5–8 mm, 40% between 9–12 mm, and only 10% between 13–15 mm. These results suggest that a USG diameter of 5–8 mm is more often associated with uncomplicated acute appendicitis, while a larger diameter, especially 9–12 mm, may be indicative of appendicular perforation.
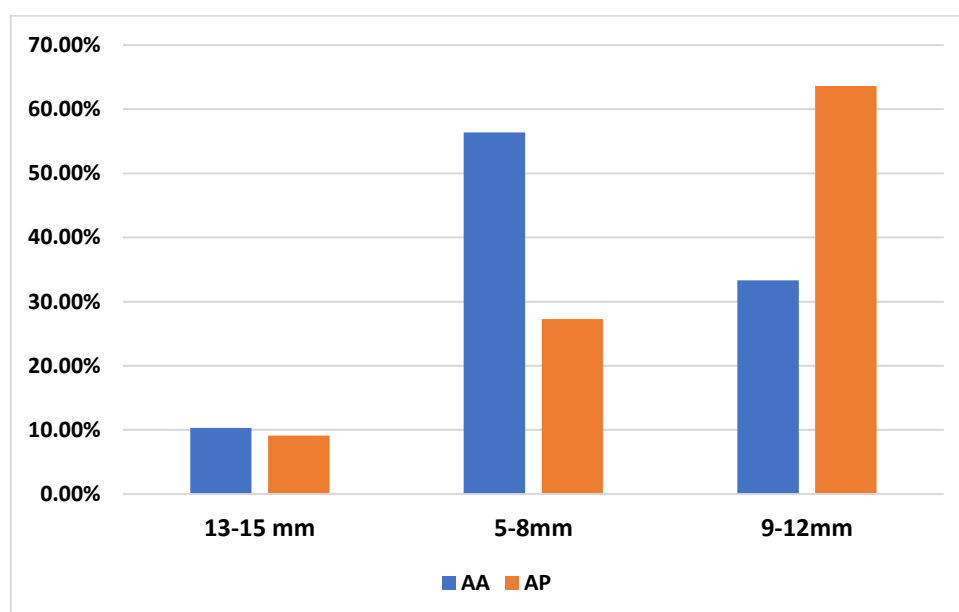
ANALYSIS OF THE STUDY

- The mean age of patients was 31.84 years with a standard deviation of 16.21 years.
- There was a slight male preponderance with 39 being males and 11 patients being females.
- 100% of patients have histologically proven acute appendicitis.
- Hematological parameters showed a mean WBC count of 11,318/µL. Elevated WBC also predicted severity (OR: 3.2, p = 0.02), while age >50 was not statistically significant.
- An average Neutrophil-to-Lymphocyte Ratio (NLR) of 5.42 (±5.33), indicating systemic inflammation in several patients.
- A strong positive correlation (r = 0.62, p < 0.001) was observed between NLR and Alvarado Score. This implies that higher NLR values are associated with more severe clinical presentations of appendicitis, supporting its utility in assessing disease severity.
- At a cutoff of ≥3.5, NLR demonstrated good diagnostic performance with 84% sensitivity and 72% specificity. Increasing the cutoff to ≥4.5 improved specificity to 85% while maintaining acceptable sensitivity (78%). At ≥6.0, specificity peaked at 89% but sensitivity dropped to 65%. Hence, an optimal balance between sensitivity and specificity appears around 4.5.
- Multivariate logistic regression showed that an NLR ≥6.0 was a strong independent predictor of severe appendicitis (AS ≥8), with an odds ratio of 4.8 (95% CI: 1.9–12.1, p = 0.001).
- Thus our study shows that Patients with acute appendicitis had a significantly lower mean NLR (4.93 ± 5.56) compared to those with Appendicular perforation (7.15 ± 4.19).
- This difference was statistically significant (p = 0.03), indicating that NLR could potentially help differentiate between acute appendicitis and complicated appendicitis.

- The mean Alvarado Score (AS) was 5.58, suggesting a moderate clinical suspicion for acute appendicitis in most cases.

CONCLUSIONS

Acute appendicitis is a common surgical emergency. Good clinical judgment aided by investigation scoring system can help to reduce the negative appendectomy rate. Ultrasound scan has now become easily available, even in developing countries and it can immensely aid the surgeon in diagnosis. Neutrophil-to-lymphocyte ratio is a simple, readily available adjunct in predicting severity of appendicitis.

NLR is a promising marker that can predict both diagnosis and severity of appendicitis with acceptable sensitivity and specificity. NLR may also have implications for patients who do not routinely undergo CT scan (pregnant or pediatric patients) and in countries or settings where "twenty-four seven" access to immediate CT is limited.

In conclusion, Acute appendicitis is a common surgical emergency. Good clinical judgment aided by an investigation scoring system can help to reduce the negative appendectomy rate. NLR Is one of the good investigation markers for diagnosis and predicting the severity of appendicitis.

Ethics approval and consent to participate
Ethical Clearance given by Institutional Ethics Committee on Human subjects (SNMC/IECHSR/2023/A-79/1.1)

List of abbreviations

AA	Acute Appendicitis
AP	Appendicular Perforation
USG	Ultrasonography
USG	Ultrasonogram
HPR	Histopathology report
NLR	Neutrophil to Lymphocyte Ratio

Authors' contributions
AP collected & analysed the patient data regarding the Clinical scores, blood & radiological investigations. Department of pathology performed the histological examination of the sent appendix specimen. RB and NP were a major contributor in writing the manuscript. BVG read and approved the final manuscript."

REFERENCES

1. Bhangu, Aneel; Søreide, Kjetil; Di Saverio, Salomone; Assarsson, Jeanette Hansson; Drake, Frederick Thurston . (2015). *Acute appendicitis: modern understanding of pathogenesis, diagnosis, and management. The Lancet, 386(10000), 1278–1287.* doi:10.1016/S0140-6736(15)00275-5
2. Al-Tarakji M, Zarour A, Singh R, Ghali MS. The Role of Alvarado Score in Predicting Acute Appendicitis and Its Severity in Correlation to Histopathology: A Retrospective Study in a Qatar Population. Cureus. 2022 Jul15;14(7):e26902.doi:10.7759/cureus.26902.
3. Krzyzak M, Mulrooney SM. Acute Appendicitis Review: Background, Epidemiology, Diagnosis, and Treatment. Cureus. 2020 Jun 11;12(6):e8562. doi: 10.7759/cureus.8562. PMID: 32670699; PMCID: PMC7358958.
4. Diagnostic Scores for Appendicitis: A Systematic Review of Scores' Performance. British Journal of Medicine and Medical Research. 2013;4(2).
5. Lee J, Jeong Y, Hwang J, Ham S, Yang S. Graded Compression Sonography with Adjuvant Use of a Posterior Manual Compression Technique in the Sonographic Diagnosis of Acute Appendicitis. American Journal of Roentgenology. 2002;178(4):863- 868.
6. Ohel R, O'Reilly F, O'Brien K, Fahey T, Dimitrov B. The Alvarado score for predicting acute appendicitis: a systematic review. BMC Medicine. 2011;9(1).
7. Singhania P. Diagnostic Accuracy of Ultrasonography in Cases of Acute Appendicitis. International Journal of Advanced and Integrated Medical Sciences. 2017;2(1):32-36.
8. Patil B, Makandar U. Study of Position, Length and Arterial Supply of Vermiform Appendix in South Indian Population. Medicolegal Update. 2014;14(2):109.
9. Stephens PL, Mazzucco JJ. Comparison of ultrasound and the Alvarado score for the diagnosis of acute appendicitis. Conn Med. 1999; 11:137–140.
10. Schwerk WB, Wichtrup B, Ruschoff J, Rothmund M. Acute and perforated appendicitis: current experience with ultrasound-aided diagnosis. World J Surg.1990; 14:271-276.

11. Jones K, Penna AA, Dunn EL, Nadalo L, Mangram AJ. Are negative appendectomies still acceptable Am J Surg. 2004; 188:748-754.

12. Yu SH, Kim CB, Park JW, et al. Ultrasonography in the diagnosis of appendicitis: evaluation by meta-analysis. Korean journal of Radiology. 2005; 6:267.

13. Hajibandeh, S., Hajibandeh, S., Hobbs, N., & Mansour, M. (2019). Neutrophil-tolymphocyte ratio predicts acute appendicitis and distinguishes between complicated and uncomplicated appendicitis: A systematic review and meta-analysis. The American Journal of Surgery. doi:10.1016/j.amjsurg.2019.04.018

14. Khan A, Riaz M, Kelly ME, Khan W, Waldron R, Barry K, Khan IZ. Prospective validation of neutrophil-to-lymphocyte ratio as a diagnostic and management adjunct in acute appendicitis. Ir J Med Sci. 2018 May;187(2):379-384. doi: 10.1007/s11845-0171667-z

15. Jayalal, J. A., Raj, S. E. K., Baghavath, P. R., & Dhayanithi, E. (2024). Surgical site infections after appendectomy in the Indian subcontinent: A meta-analysis. European Journal of Cardiovascular Medicine, 14(5), 557-562.

16. Duke, E., Kalb, B., Arif-Tiwari, H., Daye, Z. J., Gilbertson-Dahdal, D., Keim, S. M., & Martin, D. R. (2016). A Systematic Review and Meta-Analysis of Diagnostic Performance of MRI for Evaluation of Acute Appendicitis. American Journal of Roentgenology, 206(3), 508-517.doi:10.2214/ajr.15.14544

17. Al-Tarakji M, Zarour A, Singh R, Ghali MS. The Role of Alvarado Score in Predicting Acute Appendicitis and Its Severity in Correlation to Histopathology: A Retrospective Study in a Qatar Population. Cureus. 2022 Jul 15;14(7):e26902. doi:10.7759/cureus.26902

18. Gans SL, Atema JJ, Stoker J, Toorenvliet BR, Laurell H, Boermeester MA. C-reactive protein and white blood cell count as triage test between urgent and nonurgent conditions in 2961 patients with acute abdominal pain. Medicine (Baltimore). 2015 Mar;94(9): e569. doi: 10.1097/MD.0000000000000569

19. Beltrán, M. A., Almonacid, J., Vicencio, A., Gutiérrez, J., Cruces, K. S., & Cumsille, M. A. (2007). Predictive value of white blood cell counts and C-reactive protein in children with appendicitis. Journal of Pediatric Surgery, 42(7), 1208–1214. doi: 10.1016/j.jpedsurg.2007.02.010

20. Dueholm S, Bagi P, Bud M. Laboratory aid in the diagnosis of acute appendicitis. A blinded, prospective trial concerning diagnostic value of leukocyte count, neutrophil differential count, and C-reactive protein. Dis Colon Rectum. 1989 Oct;32(10):855-9. doi:10.1007/BF02554555.

21. Andersson RE. Meta-analysis of the clinical and laboratory diagnosis of appendicitis. Br J Surg. 2004 Jan;91(1):28-37. doi: 10.1002/bjs.4464

22. Sengupta, A., Bax, G., & Paterson-Brown, S. (2009). White Cell Count and C-Reactive Protein Measurement in Patients with Possible Appendicitis. The Annals of The Royal College of Surgeons of England, 91(2), 113–115. doi:10.1308/003588409x359330

23. Merlin MA, Shah CN, Shiroff AM. Evidence-based appendicitis: the initial work-up.Postgrad Med. 2010 May;122(3):189-95. doi: 10.3810/pgm.2010.05.2157

24. Ilves I, Paajanen HE, Herzig KH, Fagerström A, Miettinen PJ. Changing incidence of acute appendicitis and nonspecific abdominal pain between 1987 and 2007 in Finland. World J Surg. 2011 Apr;35(4):731-8. doi: 10.1007/s00268-011-0988-8

25. Kharbanda AB. Improving Appendicitis Care for All Patients. JAMA Netw Open. 2021 Aug 2;4(8):e2124523. doi: 10.1001/jamanetworkopen.2021.24523.