

HYPERBILIRUBINEMIA: A POTENTIAL BIOMARKER FOR DIAGNOSING AND PREDICTING COMPLICATED APPENDICITIS

Ankush Banotra¹, Akshita Yadav², Sarvesh Singh Lobana³, Himanshi Dingra⁴

Received : 09/12/2024
Received in revised form : 21/01/2025
Accepted : 07/02/2025

Keywords:
Complicated appendicitis,
hyperbilirubinemia in appendicitis,
appendicular perforation..

Corresponding Author:
Dr. Sarvesh Singh Lobana,
Email: lobanasarvesh@gmail.com

DOI: 10.47009/jamp.2025.7.1.100

Source of Support: Nil,
Conflict of Interest: None declared

Int J Acad Med Pharm
2025; 7 (1); 520-524



¹Assistant Professor, Department of General Surgery, GMC, Kathua, Jammu and Kashmir, India
²DNB Resident, Department of General Surgery, GMC, Kathua, Jammu and Kashmir, India
³Post Graduate Resident, Department of Anesthesiology, SMVD Narayana Superspeciality Hospital, Jammu and Kashmir, India.
⁴Junior Resident, PGI Chandigarh, India

Abstract

Background: Recent studies have looked at the correlation between an increase in blood total bilirubin concentration and the progression to complicated acute appendicitis in an effort to identify a diagnostic marker for this condition.^[17,18] Serum bilirubin elevations can be accounted for by the spread of Gram-negative bacteria from the appendix into the portal system
Materials and Methods: A prospective observational study was conducted on patients admitted with clinical diagnosis of acute appendicitis. The study's participants were divided into two groups: uncomplicated appendicitis and complicated appendicitis. **Result:** Off the 53% patients that had complicated appendicitis, 75% patients had raised bilirubin levels, while only 25% patients with uncomplicated appendicitis had raised bilirubin levels. **Conclusion:** Total serum bilirubin should be used along with clinical examination and other laboratory investigations in the assessment of patients suspected of appendicitis.

INTRODUCTION

Acute appendicitis is one of the leading causes of acute abdomen. Around 7% of the population may contract this condition at some point in their lives, and up to 20% of those affected will suffer a perforation as a result.^[1] Although anyone is susceptible to acute appendicitis, it often strikes between 10 and 20 years of age, with males being disproportionately affected by this condition.^[2] Even well experienced surgeons make their diagnosis based on history, clinical Examination and findings, and laboratory investigations which are only 80% positive.^[3] As ultrasonography and CT is unavailable in the rural areas and with an intention to reduce negative appendicectomies and delay in diagnosis of complicated appendicitis, there arises a gap for available diagnostic markers. Even Though Alvarado scoring, WBC count and CRP are used as laboratory markers. Recent studies on rise in bilirubin value suggest high specificity and comparable sensitivity than former it can be easily done laboratory marker.^[4,5]

Acute Appendicitis is mostly polymicrobial in nature, causes bacterial translocation into the gut. There bacteria in turn releases endotoxins and stimulates production of pro inflammatory cytokines like TNF and IL1. These molecules reach the liver via portal

venous system leading to hepatocyte dysfunction and prevent the release of bilirubin and produces cholestatic type of jaundice. Based on these observation, present study was done to empathize the predictive value of hyperbilirubinemia in appendicitis and potential to detect complicated appendicitis.^[6-8]

Review of Literature

Misdiagnosis of appendicitis is 15.3% even in the hands of an experienced surgeon.^[9] There are 36 negative appendicectomies done globally to prevent one case of appendicitis per se as per main got. And it can be potentially life threatening to the patient if the diagnosis is late or delayed leading to perforation, peritonitis, abscess, sepsis. Hence appendicitis should be diagnosed early and negative appendicectomies have to be avoided to prevent unnecessary surgical morbidity.

In most cases, symptoms and physical examination results are all that are needed to make a diagnosis of acute appendicitis. Many other scoring systems have been developed to aid in the diagnosis; the most well-known of them is called the Alvarado score, which takes into account both clinical symptoms and laboratory findings. Diagnostic scores for appendicitis include special emphasis on patient history, physical examination findings, and laboratory results (such as white blood cell count

[WCC] and/or C-reactive protein [CRP]),^[10,11] Recently, imaging techniques such as ultrasound and computed tomography (CT) have been incorporated into the diagnostic process, increasing sensitivity but also bringing their own set of limitations with them. Contrasted with the widespread use of CT, which would increase costs and lead to excessive radiation exposure, ultrasonic scan results require an experienced diagnostician for accurate, thorough interpretation.^[12,13]

Because of this, a simple, affordable, and readily available test that is diagnostic for acute appendicitis and its consequences, in addition to clinical symptoms, is required for making the diagnosis, anticipating its extent and severity, and deciding on appropriate care. Previous research has already established the importance of certain blood markers such as CRP and WCC.^[14,15] However, there is no correlation between a higher WCC and the likelihood of developing complications from uncomplicated versus complicated appendicitis.^[16]

Recent studies have looked at the correlation between an increase in blood total bilirubin concentration and the progression to complicated acute appendicitis in an effort to identify a diagnostic marker for this condition.^[17,18] Serum bilirubin elevations can be accounted for by the spread of Gram-negative bacteria from the appendix into the portal system and liver, where they cause endotoxin-mediated disruptions of bile duct bilirubin excretion.^[19,20] In addition, further research has found that septic-induced hemolysis is a major factor contributing to the elevation of serum bilirubin in acute complicated appendicitis.^[21]

Aim

This study aims to evaluate total blood bilirubin levels as a preoperative diagnostic measure of acute complicated appendicitis in cohort of patients with diagnosed acute appendicitis who subsequently underwent emergency appendectomy.

MATERIALS AND METHODS

A prospective observational study was conducted on patients admitted with clinical diagnosis of acute appendicitis and planned for emergency surgery in the department of general surgery at Government Medical College, Kathua during the period of 2nd January 2024- 2nd January 2025

A total of 150 patients with pre-operative clinical diagnosis of appendicular pathology were included.

Selection criteria

Inclusion

All patients clinically diagnosed as acute appendicitis and gangrenous appendicitis which were taken up for emergency surgery in surgical department. In both the group histopathological report were considered.

Exclusion

- Prior history of jaundice
- Prior history of liver disease
- Prior history of pancreatitis
- Chronic alcoholism

- Patients with hepatitis B, A and C
- Patients taking drugs increasing liver parameters like rifampicin.

Procedure

The study was conducted after obtaining ethical committee clearance. Based on the criteria patient admitted and underwent emergency appendectomy. All eligible patients were informed about the purpose and usefulness of study. Then after obtaining informed consent as per consent form submitted in annexure.

Histopathological examination of all appendectomy specimens was conducted at the pathology lab. At the time of admission, venous blood samples were taken for analysis of CRP, white blood cell count (WBC), total serum bilirubin (TB), alanine transaminase (ALT) levels, aspartate aminotransferase (AST) levels, and alkaline phosphatase (ALP) levels. An individual's age and gender were among the clinical and demographic details we submitted.

The study's participants were divided into two groups: those with uncomplicated appendicitis and those with complicated appendicitis, as determined by the final pathology reports, and radiological, and surgical findings.

Definition

The established definition of uncomplicated appendicitis was the existence of histopathological or radiological proof of simple, localized, or purulent appendicitis. Patients with periappendiceal abscess development, peritonitis, gangrenous appendicitis, or radiologically proven gangrenous appendicitis are all considered to be part of the complicated group.

Statistical analysis

The collected data were analysed with IBM.SPSS statistics software 23.0 Version. To describe about the data descriptive statistics frequency analysis, percentage analysis were used for categorical variables and the mean & S.D were used for continuous variables. In all the above statistical tools the probability value .05 is considered as significant level.

RESULTS

150 cases of acute appendicitis undergoing emergency appendectomy were included in our study. Patients included in our study were resuscitated adequately before taken up for study. Patient's details were collected and documented using the standard proforma.

Of the included patient population, 28% were female and 72% were male.

Ultrasound showed that 53% patients had complicated appendicitis, 40% had inflamed appendix and 6% had a normal appendix.

Total frequency of patients with increased bilirubin levels was 66% and frequency with normal bilirubin level was 33%

Off the 53% patients that had complicated appendicitis, 75% patients had raised bilirubin levels,

while only 25% patients with uncomplicated appendicitis had raised bilirubin levels.

Table 1: Sex distribution.

Sex distribution		
	Frequency	Percent
Female	42	28
Male	108	72
Total	150	100

Table 2: Ultrasonogram finding.

Ultrasound	Frequency	Percent
Complicated appendicitis	80	53
Inflamed appendix	60	40
Normal Appendix	10	6
Total	150	

Table 3: Total bilirubin levels.

	Frequency	Percent
>1 mg/dl	100	66
<=1 mg/dl	50	33
Total	150	

Table 4: Descriptive stats of deranged LFTs

Descriptive Statistics	N	Minimum	Maximum
Total bilirubin	150	0.4	5.5
Direct Bil	150	0.4	3.6
Indirect Bil	150	0.1	1.1
SGOT	150	10	59
SGPT	150	11	45
ALP	150	33	141

Table 5: Total leucocyte count.

Total count		
	Frequency	Percent
< 10000	120	80
>= 10000	30	20
Total	150	150

Table 6

	Patients with Complicated appendicitis	Patients with Uncomplicated Appendicitis
% Patients with raised Bilirubin	75%	25%

DISCUSSION

As far as appendicitis is concerned, bilirubin is not a generally recognized marker. Raised bilirubin levels have been shown in prior studies to be a good and specific marker for perforated appendicitis.^[22,23] Among the adult surgical population, elevated bilirubin levels are frequently the consequence of liver or gallbladder disorders.^[24] Hepatic dysfunction caused by sepsis has been extensively studied.^[25] In acute appendicitis, the rise of serum bilirubin is thought to be caused by microorganisms and bacterial toxins migrating via the portal vein and eventually being metabolized by the liver.^[26] The dysfunctionality of the hepatocytes, driven by the toxic nature of the bacterial products and the products of the inflammatory response, influences bilirubin excretion.^[27] When the appendix wall is damaged, microorganisms and endotoxins can migrate out of the appendix lumen and into the portal system. After that, the inflammatory cytokines potentially end up in

the liver, where they could trigger intrahepatic cholestasis. Our findings of rising bilirubin levels with increasing appendicitis severity are consistent with previous studies showing that *Escherichia coli* endotoxin produces dose-dependent cholestasis.^[28] Hyperbilirubinemia and vermiform appendix inflammation have been studied extensively in recent years, with some research identifying bilirubin as a unique marker for appendiceal perforation. Elevated bilirubin levels have been linked to complicated appendicitis, as reported by many studies.^[22,29,30] Among those trials, TB sensitivity ranged from 49 to 70%, with specificity hovering between 70% and 86%. The pooled sensitivity and specificity of this study were 73.3%, and 61%, respectively. It is still the clinical presentation of the patient and the discretion of the emergency surgeon that determine whether or not the patient has appendicitis. Blood tests (including WBC and CRP) and imaging are the most typical ancillary diagnostic techniques. Although imaging tests such as CT scans improve

diagnosis accuracy, they are underutilized because of safety concerns about ionizing radiation for young patients who tend to suffer from appendicitis.^[31] Affordability might be an issue as well. This study confirms that increased bilirubin levels can indicate complicated appendicitis

CONCLUSION

Surgeons often have difficulty making an accurate diagnosis of acute appendicitis; nevertheless, our results suggest that a serum bilirubin level is a strong indicator in patients likely to have complicated (gangrenous or perforated) appendicitis therefore, Total serum bilirubin should be used along with clinical examination and other laboratory investigations in the assessment of patients suspected of appendicitis.

REFERENCES

- Hyperbilirubinemia as a predictor of gangrenous/perforated appendicitis: a prospective study. Chaudhary P, Kumar A, Saxena N, Biswal UC. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3959475/> Ann Gastroenterol. 2013;26:325–331. [PMC free article] [PubMed] [Google Scholar]
- Acute appendicitis. Humes DJ, Simpson J. BMJ. 2006;333:530–534. doi: 10.1136/bmj.38940.664363.AE. [DOI] [PMC free article] [PubMed] [Google Scholar]
- <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3950177/>
- Vesalius A. De humani corporis fabrica liber v basel, Switzerland: Johannes Oporinu 1543.
- Fitz RH. Perforating inflammation of the vermiform appendix with special reference to its early diagnosis and treatment. Am J Med Sci 1886; 321.
- D'Alia C, Lo Schiavo MG, Tonante A, et al. Amayand 's hernia: Case report and review of the literature. Hernia 2003; 7:89-91.
- McBurney C. The incision made in the abdominal wall in cases of appendicitis, with a description of a new method of operating. Ann Surg 1894; 20:38-43.
- Meade RH. An Introduction to the History of General Surgery. Philadelphia, PA: Saunders; 1968.
- Deutsch AA, Shani N, Reiss R. Are some some appendectomies unnecessary? An analysis of 319 white appendices. J Royal College Surg Edinburgh 1983; 28:35-40
- Acute appendicitis: modern understanding of pathogenesis, diagnosis, and management. Bhanu A, Soreide K, Di Saverio S, Assarsson JH, Drake FT. Lancet. 2015;386:1278–1287. doi: 10.1016/S0140-6736(15)00275-5. [DOI] [PubMed] [Google Scholar]
- A practical score for the early diagnosis of acute appendicitis. Alvarado A. Ann Emerg Med. 1986;15:557–564. doi: 10.1016/s0196-0644(86)80993-3. [DOI] [PubMed] [Google Scholar]
- How to diagnose acute appendicitis: ultrasound first. Mostbeck G, Adam EJ, Nielsen MB, et al. Insights Imaging. 2016;7:255–263. doi:10.1007/s13244-016-0469-6. [DOI] [PMC free article] [PubMed] [Google Scholar]
- The accuracy rate of Alvarado score, ultrasonography, and computerized tomography scan in the diagnosis of acute appendicitis in our center. Ozkan S, Duman A, Durukan P, Yildirim A, Ozbakan O. Niger J Clin Pract. 2014;17:413–418. doi: 10.4103/1119-3077.134001. [DOI] [PubMed] [Google Scholar]
- Meta-analysis of the clinical and laboratory diagnosis of appendicitis. Andersson RE. Br J Surg. 2004;91:28–37. doi: 10.1002/bjs.4464. [DOI] [PubMed] [Google Scholar]
- Correlation of white cell count and CRP in acute appendicitis in paediatric patients. Withers AS, Grieve A, Loveland JA. <https://pubmed.ncbi.nlm.nih.gov/31773931/> S Afr J Surg. 2019;57:40. [PubMed] [Google Scholar]
- White blood cell count is a poor predictor of severity of disease in the diagnosis of appendicitis. Coleman C, Thompson JE, Jr. Jr., Bennion RS, Schmit PJ. <https://www.proquest.com/openview/fad2e8dc75a555f26d58f37386a43169/1?pq-origsite=gscholar&cbl=49079>. Am Surg. 1998;64:983–985. [PubMed] [Google Scholar]
- Elevated serum bilirubin in acute appendicitis :a new diagnostic tool. Khan S. <http://chrome-extension://efaidnbmnnnibpcajpcglclefindmkaj/https://www.kumj.com.np/issue/22/161-165.pdf>. Kathmandu Univ Med J (KUMJ). 2008;6:161–165. [PubMed] [Google Scholar]
- Elevated serum bilirubin in assessing the likelihood of perforation in acute appendicitis: a diagnostic meta-analysis. Giordano S, Pääkkönen M, Salminen P, Grönroos JM. Int J Surg. 2013;11:795–800. doi: 10.1016/j.ijso.2013.05.029. [DOI] [PubMed] [Google Scholar]
- The value of serum bilirubin level and of white blood cell count as severity markers for acute appendicitis. Socca B, Carap A, Rac-Albu M, Constantin V. http://chrome-extension://efaidnbmnnnibpcajpcglclefindmkaj/https://www.researchgate.net/profile/Bogdan-Socca/publication/259316603_The_Value_of_Serum_Bilirubin_in_Level_and_of_White_Blood_Cell_Count_as_Severity_Markers_for_Acute_Appendicitis/links/5b31f17eaca2720785e8540b/The-Value-of-Serum-Bilirubin-Level-and-of-White-Blood-Cell-Count-as-Severity-Markers-for-Acute-Appendicitis.pdf. Chirurgia (Bucur) 2013;108:829–834. [PubMed] [Google Scholar]
- Hyperbilirubinaemia: its utility in non-perforated appendicitis. Sandstrom A, Grieve DA. ANZ J Surg. 2017;87:587–590. doi: 10.1111/ans.13373. [DOI] [PubMed] [Google Scholar]
- Diagnostic accuracy of hyperbilirubinaemia in anticipating appendicitis and its severity. Muller S, Falch C, Axt S, Wilhelm P, Hein D, Königsrainer A, Kirschniak A. Emerg Med J. 2015;32:698–702. doi: 10.1136/emered-2013-203349. [DOI] [PubMed] [Google Scholar]
- Preoperative diagnostic role of hyperbilirubinaemia as a marker of appendix perforation. Atahan K, Üreyen O, Aslan E, et al. J Int Med Res. 2011;39:609–618. doi: 10.1177/147323001103900230. [DOI] [PubMed] [Google Scholar]
- The value of hyperbilirubinaemia in the diagnosis of acute appendicitis. Emmanuel A, Murchan P, Wilson I, Balfe P. Ann R Coll Surg Engl. 2011;93:213–217. doi: 10.1308/147870811X566402. [DOI] [PMC free article] [PubMed] [Google Scholar]
- Berg CL, Crawford J, Gollan JL. Schiff's Disease of the Liver. Philadelphia, PA: Lippincott-Raven; 1999. Bilirubin metabolism and the pathophysiology of jaundice. [Google Scholar]
- The causes of obvious jaundice in South West Wales: perceptions versus reality. Whitehead MW, Hainsworth I, Kingham JG. Gut. 2001;48:409–413. doi: 10.1136/gut.48.3.409. [DOI] [PMC free article] [PubMed] [Google Scholar]
- Studies on the effects of C. coli endotoxin on canalicular bile formation in the isolated perfused rat liver. Utili R, Abernathy CO, Zimmerman HJ. <https://pubmed.ncbi.nlm.nih.gov/320281/> J Lab Clin Med. 1977;89:471–482. [PubMed] [Google Scholar]
- Mechanisms of disease: mechanisms and clinical implications of cholestasis in sepsis. Geier A, Fickert P, Trauner M. Nat Clin Pract Gastroenterol Hepatol. 2006;3:574–585. doi: 10.1038/ncpgasthep0602. [DOI] [PubMed] [Google Scholar]
- Cholestatic effects of Escherichia coli endotoxin on the isolated perfused rat liver. Utili R, Abernathy CO, Zimmerman HJ. Gastroenterology. 1976;70:248–253. [PubMed] [Google Scholar]
- Diagnostic value of hyperbilirubinemia as a predictive factor for appendiceal perforation in acute appendicitis. Sand M, Bechara FG, Holland-Letz T, Sand D, Mehnert G, Mann B. Am J Surg. 2009;198:193–198. doi: 10.1016/j.amjsurg.2008.08.026. [DOI] [PubMed] [Google Scholar]

30. Bilirubin; a diagnostic marker for appendicitis. D'Souza N, Karim D, Sunthareswaran R. *Int J Surg*. 2013;11:1114–1117. doi: 10.1016/j.ijso.2013.09.006. [DOI] [PubMed] [Google Scholar]
31. An international survey of opinion regarding investigation of possible appendicitis and laparoscopic management of a macroscopically normal appendix. Jaunoo SS, Hale AL, Masters JP, Jaunoo SR. *Ann R Coll Surg Engl*. 2012;94:476–480. doi: 10.1308/003588412X13373405385377. [DOI] [PMC free article] [PubMed] [Google Scholar]