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Original Research Article

Hyperbilirubinemia as a predictive factor for appendicular perforation in acute appendicitis: a prospective observational study

Souliyh Majeed[1]*, Shams ul Bari[2], Ajaz A. Malik[3]

[1]Department of General and Minimal Invasive Surgery, SKIMS Soura, Srinagar, Jammu and Kashmir, India
[2]Department of General Surgery, SKIMS Medical College and Hospital, Bemina, Srinagar, Jammu and Kashmir, India
[3]Department of General and Minimal Invasive Surgery, SKIMS Soura, Srinagar, Jammu and Kashmir, India

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***Correspondence:**
Dr. Souliyh Majeed,
E-mail: majidsouliha@gmail.com

ABSTRACT

Background: Acute appendicitis is one of the most common surgical emergencies worldwide. Delay in diagnosis may lead to complications such as appendicular perforation. Identifying simple laboratory markers that predict perforation may assist in early intervention. Hyperbilirubinemia has been proposed as a potential indicator of complicated appendicitis. The objective was to evaluate the role of elevated serum bilirubin levels as a predictive factor for appendicular perforation in patients with acute appendicitis.
Methods: This prospective observational study was conducted in the Department of General Surgery at Sher-i-Kashmir Institute of Medical Sciences (SKIMS), Soura and SKIMS Medical College Hospital, Bemina, Srinagar, India from March 2023 to February 2025. A total of 198 patients with clinically or radiologically diagnosed acute appendicitis were included. Serum bilirubin levels measured at admission were correlated with operative and histopathological findings. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and odds ratio were calculated.
Results: The majority of patients belonged to the 20–30-year age group (50.5%). Males constituted 53% of the study population. Hyperbilirubinemia (>1.2 mg/dl) was observed in 74.2% of patients. Among patients with appendicular perforation, 90.2% had elevated bilirubin levels compared with 70.1% of patients with uncomplicated appendicitis. Sensitivity, specificity, positive predictive value, negative predictive value and odds ratio were 90.2%, 29.9%, 36.4%, 87.2% and 3.92 respectively.
Conclusion: Hyperbilirubinemia is significantly associated with appendicular perforation in patients with acute appendicitis. Serum bilirubin estimation is a simple, inexpensive and widely available investigation that may aid in early detection of complicated appendicitis when interpreted alongside clinical findings.

Keywords: Acute appendicitis, Hyperbilirubinemia, Appendicular perforation, Serum bilirubin, Diagnostic marker

INTRODUCTION

Acute appendicitis is one of the most common causes of acute abdomen requiring emergency surgical intervention. It accounts for a significant proportion of emergency surgical admissions worldwide. Despite advances in diagnostic imaging and laboratory investigations, early diagnosis of appendicitis, particularly complicated appendicitis, remains a clinical challenge. Delayed diagnosis may lead to complications such as gangrene and perforation, which significantly increase patient morbidity and postoperative complications.[1]

The diagnosis of acute appendicitis is primarily based on clinical evaluation supported by laboratory investigations and imaging modalities such as ultrasonography and computed tomography. However, these investigations may

not always provide definitive diagnosis, especially in atypical cases.

Therefore, the search for simple and reliable biochemical markers that can assist in early diagnosis and prediction of complicated appendicitis continues to be an important area of research.[2]

Recent studies have suggested that hyperbilirubinemia may be associated with complicated appendicitis, particularly gangrenous and perforated forms. Elevated serum bilirubin levels have been reported in patients with severe appendiceal inflammation and may serve as a useful marker in predicting appendicular perforation.[3-5]

The pathophysiological mechanism behind hyperbilirubinemia in acute appendicitis is thought to involve bacterial translocation and endotoxemia resulting from appendiceal inflammation. Endotoxins produced by gram-negative bacteria may impair hepatocellular uptake and excretion of bilirubin, resulting in elevated serum bilirubin levels.[6]

Several clinical studies have demonstrated a significant association between hyperbilirubinemia and complicated appendicitis.[7-9] Early identification of patients at risk of appendicular perforation is essential for prompt surgical management and prevention of complications. Serum bilirubin estimation is a simple, inexpensive and widely available laboratory test that may provide additional diagnostic value when combined with clinical findings and imaging studies.

The present study was undertaken to evaluate the role of serum bilirubin levels in patients with acute appendicitis and to determine its association with appendicular perforation. The aim of this study was to assess whether hyperbilirubinemia can serve as a reliable predictive marker for complicated appendicitis.

METHODS

Study design and setting

This prospective observational study was conducted in the Department of General Surgery at Sher-i-Kashmir Institute of Medical Sciences (SKIMS), Soura and SKIMS Medical College Hospital, Bemina, Srinagar, India.

Study period

The study was carried out over a two-year period from March 2023 to February 2025.

Ethical approval

Ethical approval was obtained from the Institutional Ethics Committee of SKIMS Srinagar prior to commencement of the study (approval no. #164/2023). Written informed consent was obtained from all participants.

Study population

All patients admitted with a clinical or radiological diagnosis of acute appendicitis or appendicular perforation were evaluated.

Inclusion criteria

Patients diagnosed with acute appendicitis clinically or radiologically; patients diagnosed with appendicular perforation, and histopathological confirmation of appendicitis following surgery were included.

Exclusion criteria

Patients managed conservatively, patients with appendicular lump, patients with chronic liver disease, hemolytic disorders, hepatitis or biliary tract disease, and history of hepatotoxic drug intake were excluded.

Sample size and sampling technique

The sample size was calculated using the formula, where Z=1.96 for 95% confidence interval, p=assumed prevalence of 50%, q=1-p and margin of error (d)=10%.

$$n = Z^2 \times p \times q/d^2$$

Based on this calculation the minimum required sample size was 96. However, a total of 198 patients were included during the study period using convenience sampling.

Data collection

Detailed clinical history and physical examination findings were recorded. Laboratory investigations at admission included complete blood count, liver function tests, serum bilirubin, renal function tests and viral markers.

Serum bilirubin levels were measured using an automated biochemical analyzer.

Statistical analysis

Data were entered in Microsoft Excel and analyzed using standard statistical methods.

Sensitivity, specificity, positive predictive value, negative predictive value and odds ratio were calculated using a 2×2 contingency table.

RESULTS

A total of 198 patients with a clinical diagnosis of acute appendicitis or appendicular perforation admitted to the Department of General Surgery at SKIMS Soura and SKIMS Medical College and Hospital, Bemina were included in this study.

Age distribution

The age distribution of the study population is shown in Table 1. Most patients were young adults (21–30 years, 47.5%), with a slight male predominance. There was no statistically significant association between age and gender.

Table 1: Age and gender distribution of study patients.

Age group (years)	Female, N (%)	Male, N (%)	Total (N, %)
15–20	13 (6.6)	15 (7.6)	28 (14.1)
21–30	47 (23.7)	47 (23.7)	94 (47.5)
31–40	28 (14.1)	35 (17.7)	63 (31.8)
≥41	4 (2.0)	8 (4.0)	12 (6.1)
Total	93 (47.0)	105 (53.0)	198 (100)

Mean bilirubin was 1.22±0.58 mg/dl. A large proportion (74.2%) of patients had elevated serum bilirubin, suggesting a possible association between hyperbilirubinemia and appendicitis (Table 2).

Nearly one-third (30.8%) of patients presented with appendicular perforation, indicating a substantial burden of complicated appendicitis (Table 3).

Elevated bilirubin was more frequent in perforation (90.2%) compared to uncomplicated appendicitis (70.1%), indicating a strong association with disease severity (Table 4).

Table 2: Serum bilirubin levels among study patients.

Serum bilirubin (mg/dl)	Number (N)	Percentage (%)
≤1.2	51	25.8
>1.2	147	74.2
Total	198	100

Table 3: Distribution of acute appendicitis and appendicular perforation.

Diagnosis	Number (N)	Percentage (%)
Acute appendicitis	137	69.2
Appendicular perforation	61	30.8
Total	198	100

Most patients had TLC within normal limits, suggesting that leukocytosis alone may not be a reliable marker for appendicitis severity (Table 5).

Neutrophil predominance was observed, consistent with acute inflammatory process such as appendicitis (Table 6).

Table 4: Association of serum bilirubin with type of appendicitis.

Serum bilirubin (mg/dl)	Acute appendicitis (N, %)	Perforation (N, %)	Total (N, %)
≤1.2	41 (29.9)	6 (9.8)	47 (23.7)
>1.2	96 (70.1)	55 (90.2)	151 (76.3)
Total	137 (100)	61 (100)	198 (100)

Ultrasonography identified acute appendicitis in the majority of cases (~70%), supporting its role as a useful initial imaging modality (Table 7). Histopathology confirmed the diagnosis in all cases and served as the gold standard for comparison (Table 8).

Table 5: Distribution of total leukocyte count.

TLC (/mm³)	Number (N)	Percentage (%)
≤11,000	129	65.2
>11,000	69	34.8
Total	198	100

Table 6: Mean differential leukocyte count.

Parameter	Mean	Standard deviation
Total count (/mm³)	10030	3712
Neutrophils (%)	71.7	11.5
Lymphocytes (%)	23.7	10.7
Monocytes (%)	3.6	2.6
Eosinophils (%)	1.0	1.4

Serum bilirubin showed high sensitivity and negative predictive value, indicating its usefulness in ruling out appendicular perforation (Table 9).

Table 7: Ultrasonographic findings.

Finding	Number (N)	Percentage (%)
Normal	34	17.2
Acute appendicitis	138	69.7
Appendicular perforation	26	13.1
Total	198	100

Table 8: Histopathological diagnosis.

Diagnosis	Number (N)	Percentage (%)
Acute appendicitis	136	68.7
Appendicular perforation	62	31.3
Total	198	100

Table 9: Diagnostic accuracy of serum bilirubin.

Parameter	Value (%)
Sensitivity	90.2
Specificity	29.9
Positive predictive value	36.4
Negative predictive value	87.2
Odds ratio	3.92

Hyperbilirubinemia was strongly associated with appendicular perforation, supporting its role as a potential predictor of complicated appendicitis (Table 10).

Table 10: Association of clinical parameters with appendicular perforation.

Parameter	Perforation present (N, %)	Perforation absent (N, %)	Total (N)
Bilirubin >1.2 mg/dl	55 (90.2)	96 (70.1)	151
Bilirubin ≤1.2 mg/dl	6 (9.8)	41 (29.9)	47

DISCUSSION

Acute appendicitis remains one of the most frequently encountered surgical emergencies worldwide. Although the diagnosis is largely clinical, laboratory investigations and imaging techniques are commonly used to support clinical findings. Identifying reliable biochemical markers that can predict the severity of appendicitis and the likelihood of complications remains an important area of clinical research.

In the present study, the mean age of patients was 29.55±9.33 years, with the majority belonging to the 20–30-year age group. These findings are consistent with epidemiological studies reported by Addiss et al and Bhangu et al, which demonstrated that acute appendicitis most commonly affects adolescents and young adults.[1,10]

A slight male predominance (53%) was observed in the present study. Similar findings have been reported in previous literature, where appendicitis has been shown to occur more frequently in males than females. Andersson also reported a higher incidence of appendicitis among males.[11] However, the absence of a statistically significant association between age and gender in the present study (p=0.624) suggests that the disease affects both genders across various age groups.

Hyperbilirubinemia was observed in 74.2% of patients in the present study. The elevation of serum bilirubin in appendicitis is believed to occur due to bacterial endotoxins released during appendiceal infection. These endotoxins can impair hepatocellular function and interfere with bile excretion, resulting in cholestasis and subsequent elevation of serum bilirubin levels. Similar mechanisms have been described in previous studies investigating the relationship between hyperbilirubinemia and complicated appendicitis.[6]

A key finding of the present study was that 90.2% of patients with appendicular perforation had elevated bilirubin levels, compared with 70.1% of patients with uncomplicated appendicitis. These findings suggest a significant association between hyperbilirubinemia and appendicular perforation. Similar results were reported by Sand et al, who demonstrated significantly higher bilirubin levels in patients with perforated appendicitis.[12]

In another study, Estrada et al reported that patients with hyperbilirubinemia had a significantly increased risk of appendiceal perforation.[13] Likewise, Emmanuel et al found that elevated serum bilirubin levels had diagnostic value in predicting complicated appendicitis.[4]

The diagnostic performance of serum bilirubin in the present study showed high sensitivity (90.2%) but relatively low specificity (29.9%). These findings are consistent with the systematic review conducted by Burcharth et al, which concluded that serum bilirubin is a sensitive but not highly specific marker for appendiceal perforation.[5] Therefore, elevated bilirubin levels should be interpreted in conjunction with clinical examination and other diagnostic investigations.

Ultrasonography diagnosed acute appendicitis in 69.7% of cases in the present study, supporting its role as an initial imaging modality in the evaluation of suspected appendicitis. However, the sensitivity of ultrasonography for detecting appendicular perforation remains variable, as reported in previous studies.[14]

Overall, the findings of the present study support the role of serum bilirubin as a useful adjunctive laboratory marker for predicting appendicular perforation. When interpreted alongside clinical evaluation, laboratory parameters, and imaging studies, serum bilirubin estimation may assist clinicians in early identification of complicated appendicitis and facilitate timely surgical intervention.

Limitations

The present study had certain limitations. First, it was conducted at a single tertiary care center, which may limit generalizability. Second, the sample size was relatively modest. In addition, other inflammatory markers such as C-reactive protein were not evaluated in combination with serum bilirubin levels. Larger multicenter studies are required to further validate the role of hyperbilirubinemia as a predictive marker for complicated appendicitis.

CONCLUSION

Hyperbilirubinemia is significantly associated with appendicular perforation in patients with acute appendicitis. Elevated serum bilirubin levels demonstrate

high sensitivity and negative predictive value in predicting complicated appendicitis. Serum bilirubin estimation is a simple and widely available investigation that may assist surgeons in identifying patients at higher risk of appendicular perforation when interpreted alongside clinical findings and imaging studies.

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