International Journal of Medical and Pharmaceutical Research

Online ISSN-2958-3683 | Print ISSN-2958-3675
Frequency: Bi-Monthly
Available online on: https://ijmpr.in/

Original Article

Serum Bilirubin as a Marker of Appendicular Perforation: A Prospective Observational Study at a Tertiary care Hospital in Kashmir

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OPEN ACCESS

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Received: 04-05-2026
Accepted: 02-06-2026
Available online: 08-07-2026

ABSTRACT

Background: Acute appendicitis is a common surgical emergency, and delayed diagnosis may result in appendicular perforation with increased morbidity. Serum bilirubin has been suggested as a simple and routinely available biochemical marker for complicated appendicitis. Aim: The study aimed to evaluate serum bilirubin as a marker of appendicular perforation. **Material and Methods**: This retrospective observational study included 200 patients with confirmed appendicular perforation treated at Government Medical College Srinagar. Demographic, clinical, laboratory, intraoperative and postoperative data were analysed from hospital records. **Results**: The mean age was 32.5 ± 17.0 years, and 60.0% of patients were males. Raised serum total bilirubin >1.0 mg/dL was observed in 184 patients. Patients with raised bilirubin had longer hospital stay and higher postoperative morbidity compared with those with normal bilirubin levels. **Conclusion**: Hyperbilirubinaemia was commonly observed in patients with appendicular perforation and may serve as a useful adjunctive marker for complicated appendicitis when interpreted with clinical findings, inflammatory markers and imaging.

Keywords: *Acute appendicitis, appendicular perforation, hyperbilirubinaemia, Serum bilirubin, Government medical college, Srinagar.*

INTRODUCTION

Acute appendicitis is one of the most common causes of acute abdomen requiring emergency surgical intervention. It usually results from obstruction of the appendiceal lumen, followed by bacterial overgrowth, progressive inflammation, venous congestion, ischemia and, if untreated, gangrene or perforation. Although appendicitis is a frequently encountered surgical emergency, timely diagnosis remains clinically important because delayed recognition may lead to appendicular perforation, abscess formation, peritonitis, prolonged hospital stay and increased postoperative morbidity. The 2020 World Society of Emergency Surgery guidelines also emphasize that diagnosis and severity assessment in acute appendicitis remain challenging in many clinical settings (1).

Appendicular perforation represents a complicated form of acute appendicitis and is associated with greater inflammatory burden, increased risk of sepsis, wound infection, intra-abdominal collection and longer duration of treatment. Early identification of patients at risk of perforation is therefore essential for timely operative decision-making and appropriate perioperative management. Conventional diagnostic assessment relies on clinical history, physical examination, inflammatory markers such as total leucocyte count and C-reactive protein, and imaging modalities including ultrasonography or computed tomography. However, clinical findings may be atypical, laboratory markers may lack specificity, and imaging may not always be immediately available, affordable or conclusive, especially in resource-limited settings (1). In recent years, serum bilirubin has gained attention as a simple, inexpensive and routinely available biochemical marker that may help in predicting complicated appendicitis, particularly appendicular perforation. Several studies have reported that hyperbilirubinaemia is more frequently observed in gangrenous or perforated appendicitis than

in uncomplicated appendicitis. Emmanuel et al. observed that hyperbilirubinaemia was a useful marker in acute appendicitis and that patients with raised bilirubin were more likely to have appendiceal perforation or gangrene (2). Similarly, Ramu et al. reported that hyperbilirubinaemia, particularly above their study cut-off, was predictive of appendicular perforation and could assist in early diagnosis (3).

The proposed mechanism for raised bilirubin in appendicular perforation is related to bacterial invasion, portal bacteraemia and endotoxaemia. Organisms such as *Escherichia coli* and other gram-negative bacteria may release endotoxins, which interfere with hepatic bilirubin excretion and produce cholestasis at the hepatocellular or canalicular level. This process may occur even without primary hepatobiliary disease and may lead to an isolated or predominant rise in serum bilirubin. Thus, hyperbilirubinaemia in acute appendicitis may reflect systemic inflammatory response and bacterial translocation, both of which are more likely in complicated disease (4). Evidence from systematic reviews and meta-analyses supports the potential role of serum bilirubin as an adjunctive marker for appendiceal perforation. Burcharth et al. reviewed studies evaluating hyperbilirubinaemia for predicting appendiceal perforation and reported that elevated serum bilirubin showed moderate-to-high specificity, although sensitivity varied across studies (5).

Therefore, serum bilirubin estimation may provide additional diagnostic value when interpreted along with clinical findings, inflammatory markers and imaging. Since bilirubin testing is inexpensive, widely available and routinely included in preoperative biochemical evaluation, it may be particularly useful in identifying patients at higher risk of appendicular perforation. With this background, the present study was undertaken to evaluate the association between serum bilirubin levels and appendicular perforation among patients presenting with acute appendicitis attending a tertiary care hospital in Kashmir.

MATERIAL AND METHODS

Study Design, setting and period

It was a retrospective observational study that was conducted in the Department of General Surgery. Government Medical college Srinagar over a period of 6 months from

Study Population

The study population comprised patients diagnosed with appendicular perforation who underwent surgical management during the study period. Relevant hospital records, operative findings, laboratory investigations and discharge summaries were reviewed.

Inclusion Criteria

1. Patients diagnosed with acute appendicitis with appendicular perforation.
2. Patients whose diagnosis of perforation was confirmed intraoperatively and/or histopathologically.
3. Patients with available preoperative serum bilirubin levels, as liver function tests are routinely performed in all admitted surgical patients.

Exclusion Criteria

1. Known hepatobiliary disease.
2. History of jaundice or chronic liver disease.
3. Viral hepatitis or obstructive jaundice.
4. Haemolytic disorders.
5. Incomplete hospital records.
6. Missing preoperative serum bilirubin values.

Data Collection

Data was collected retrospectively from the hospital records of patients diagnosed and treated for appendicular perforation during the study period. Case files, admission records, laboratory reports, operative notes, histopathology reports and discharge summaries were reviewed. Demographic details such as age, gender, residence clinical details including presenting symptoms and duration of illness, and relevant laboratory parameters were recorded. Since liver function tests are routinely performed in admitted surgical patients, preoperative serum bilirubin values, including total, direct and indirect bilirubin wherever available, were obtained from laboratory records. Operative findings were reviewed to confirm appendicular perforation and to document associated findings such as gangrenous appendix, periappendicular abscess, purulent peritoneal contamination or generalized peritonitis. Information regarding duration of hospital stay and postoperative complications was also recorded wherever available. All data were entered in a structured proforma while maintaining patient confidentiality.

Study outcome

The primary outcome of the study was to assess the association between elevated serum bilirubin levels and appendicular perforation

Statistical Analysis
Data was entered into Microsoft Excel and analysed using appropriate statistical software IBM SPSS version 27. Categorical variables were expressed as frequency and percentage. Continuous variables were expressed as mean ± standard deviation.

RESULTS:
The mean age was 32.5 ± 17.0 years, with the majority belonging to the 21–30 years age group (32.0%), followed by 12–20 years (29.5%). Males were more commonly affected, comprising 60.0% of cases. Most patients were from rural areas (58.0%). Pain abdomen was present in all patients (100.0%), followed by vomiting (64.5%), guarding (62.0%), fever/history of fever (39.0%), and right iliac fossa tenderness (99.0%). Table 2 presents the biochemical and inflammatory parameters. The mean TLC was 15.8 ± 4.9 $\times 10^3/\mu L$, and the mean neutrophil count was 84.0 ± 7.0%, indicating marked leukocytosis and neutrophilia. The mean direct and indirect bilirubin levels were 0.72 ± 0.13 mg/dL and 0.66 ± 0.14 mg/dL, respectively. The mean AST and ALT levels were 32.88 ± 3.38 U/L and 32.77 ± 2.75 U/L, while the mean CRP was 77.0 ± 87.0 mg/L.

Figure 1 shows the distribution of serum total bilirubin levels. Raised total bilirubin >1.0 mg/dL was observed in 91.0% of patients, while 9.0% had bilirubin levels ≤1.0 mg/dL, indicating that hyperbilirubinaemia was common among patients with appendicular perforation. The most common appendix position was retrocaecal (54.5%), followed by pelvic (35.5%). The body of the appendix was the most common perforation site (57.5%), followed by the tip (39.0%). Generalised peritonitis was present in 20.0%, gangrene in 8.5%, and fecolith in 10.5%. The mean hospital stay was 7.3 ± 5.0 days. Postoperative complications occurred in 72.0% of patients, with surgical site infection being the most common (42.0%). Mortality was reported in 5.0% of cases.Table 4 shows postoperative outcomes according to serum bilirubin status. Patients with bilirubin >1.0 mg/dL had a longer mean hospital stay (7.4 ± 5.1 days) compared with those having bilirubin ≤1.0 mg/dL (5.8 ± 2.4 days). Postoperative complications were more frequent in the raised bilirubin group (73.9%) compared with the normal bilirubin group (50.0%). Surgical site infection was also higher among patients with raised bilirubin (43.5% vs 25.0%). All cases of intra-abdominal collection, re-exploration and mortality occurred in the hyperbilirubinaemia group.

Table 1: Baseline and clinical characteristics of study participants.

Variable	Frequency (n=200)	Percentage
Age, mean ± SD, years		32.5 ± 17.0
12–20	59	29.5
21–30	64	32.0
31–40	25	12.5
41–50	16	8.0
51–60	14	7.0
>60	22	11.0
Gender		
Male	120	60.0
Female	80	40.0
Residence		
Rural	116	58.0
Urban	84	42.0
Presenting symptoms		
Pain abdomen	200	100.0
Vomiting	129	64.5
Fever/history of fever	78	39.0
Right iliac fossa tenderness	198	99.0
Guarding	124	62.0

Table 2: Biochemical and Inflammatory Parameters among Patients with Appendicular Perforation

Parameter	Mean ± S.D
TLC, $\times 10^3/\mu L$	15.8± 4.9
Neutrophils, %	84.0 ± 7.0
Direct bilirubin, mg/dL	0.72 ± 0.13
Indirect bilirubin, mg/dL	0.66 ± 0.14
AST, U/L	32.88 ± 3.38

ALT, U/L	32.77 ± 2.75
CRP, mg/L	77.0 ± 87.0

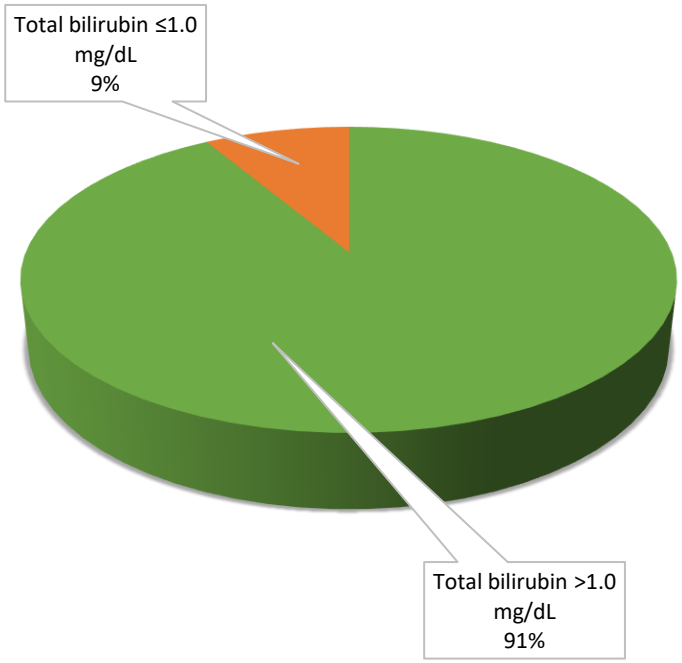

Figure 1: Distribution of Serum Total Bilirubin Levels among Patients with Appendicular Perforation

Table 3: Intraoperative and postoperative complications among study participants.

Variable	**Frequency n=200**	**Percentage %**
Intraoperative findings		
Appendix position		
Retrocaecal	109	54.5
pelvic	71	35.5
ileal	6	3.0†
post-ileal	8	4.0
subhepatic	6	3.0
Perforation site		
Tip	78	39.0
Body	115	57.5
Base	7	3.5
Gangrene present	17	8.5
Localised abscess present	12	6.0
Generalised peritonitis present	40	20.0
Fecolith present	21	10.5
Contamination <50 mL	156	78.0
Contamination 50–150 mL	25	12.5

Contamination >150 mL	19	9.5
Postoperative outcomes		
Length of stay, days, mean ± SD	7.3 ± 5.0	
Any postoperative complication	144	72.0
Surgical site infection	84	42.0
Intra-abdominal collection	3	1.5
Ileus / postoperative bowel obstruction	8	4.0
Re-exploration	4	2.0
Mortality	10	5.0

Table 4: Postoperative Outcomes According to Serum Total Bilirubin Status.

Postoperative outcome	**Total bilirubin ≤1.0 mg/dL (n=16)**	**Total bilirubin >1.0 mg/dL (n=184)**
Length of hospital stay, days, mean ± SD	5.8 ± 2.4	7.4 ± 5.1
Any postoperative complication	8 (50.0%)	136 (73.9%)
Surgical site infection	4 (25.0%)	80 (43.5%)
Intra-abdominal collection	0 (0.0%)	3 (1.6%)
Ileus / postoperative bowel obstruction	1 (6.3%)	7 (3.8%)
Re-exploration	0 (0.0%)	4 (2.2%)
Mortality	0 (0.0%)	10 (5.4%)

DISCUSSION

Acute appendicitis remains one of the most frequently encountered surgical emergencies, and timely recognition of complicated disease is essential to reduce morbidity. Appendicular perforation is particularly important because it is associated with greater inflammatory burden, postoperative complications and prolonged hospital stay. Therefore, evaluating serum bilirubin in the clinical setting of acute appendicitis may provide a simple and readily available adjunct for identifying patients at risk of appendicular perforation. In our study, the baseline and clinical profile of study population reflects the usual demographic and clinical pattern of acute appendicitis. In the present study, the mean age was 32.5 ± 17.0 years, with most of participants belonging to the 21–30 years age group, followed by the 12–20 years age group. Males were more commonly affected than females, and a slightly higher proportion of patients were from rural areas. Pain abdomen was present in all cases, while right iliac fossa tenderness, vomiting, guarding and fever were the other common clinical features. These findings are consistent with the established clinical presentation of acute appendicitis, which commonly affects adolescents and young adults and usually presents with abdominal pain, right iliac fossa tenderness, vomiting and signs of localized peritoneal irritation (1).

In our study, raised serum total bilirubin was observed in a large proportion of patients with appendicular perforation, supporting the role of hyperbilirubinaemia as an adjunctive biochemical marker of complicated appendicitis. Among 200 patients with confirmed appendicular perforation, 92% had total bilirubin levels >1.0 mg/dL. This finding is consistent with previous studies which have shown that hyperbilirubinaemia is more commonly associated with gangrenous or perforated appendicitis than with uncomplicated appendicitis (2,3,5-7). The biological explanation for this association is related to bacterial invasion, portal bacteraemia and endotoxaemia in complicated appendicitis. Gram-negative organisms such as Escherichia coli may release endotoxins, which impair hepatic uptake and canalicular excretion of bilirubin, resulting in cholestasis and raised serum bilirubin even in the absence of primary hepatobiliary disease (7,8).

Further in our study, AST and ALT levels were only mildly elevated, suggesting that the rise in bilirubin was not primarily due to hepatocellular injury but was more likely related to systemic inflammation, bacterial translocation and sepsis associated with perforated appendicitis. Our findings are comparable with those of Emmanuel et al., who reported that hyperbilirubinaemia was a valuable marker in acute appendicitis and that patients with raised bilirubin were more likely to have appendiceal perforation or gangrene (2). Similarly, Ramu et al. observed that hyperbilirubinaemia was significantly

associated with appendicular perforation and reported that a bilirubin cut-off of >1.3 mg/dL had a sensitivity of 80%, specificity of 89%, positive predictive value of 93% and negative predictive value of 96% for perforation (3). Chaudhary et al. also concluded that isolated hyperbilirubinaemia, particularly in the absence of marked elevation of liver enzymes, may serve as a useful predictor of gangrenous or perforated appendicitis (6). The high frequency of hyperbilirubinaemia in our cohort is in agreement with these observations and reinforces the clinical value of serum bilirubin as an easily available marker of disease severity. Systematic reviews have also supported the association between raised bilirubin and appendiceal perforation, although they emphasize that bilirubin should not be used as a standalone diagnostic test. Burcharth et al., in a systematic review, reported that elevated serum bilirubin showed value as a predictor of appendiceal perforation, particularly because of its relatively high specificity (5). A later diagnostic meta-analysis by Gavriilidis et al. concluded that hyperbilirubinaemia alone has limited diagnostic accuracy for ruling in or ruling out perforation but may be useful when interpreted along with clinical findings, inflammatory markers and imaging (9). This is clinically relevant in resource-limited settings, where bilirubin estimation is inexpensive, routinely available and may help identify patients requiring urgent operative management when imaging is delayed or inconclusive.

The inflammatory profile of our patients further supports the diagnosis of complicated appendicitis. The mean total leucocyte count and neutrophil percentage were markedly elevated, and the mean CRP was also high. Previous studies have shown that leukocytosis, neutrophilia and CRP are useful markers of inflammation but may lack specificity when used alone for predicting perforation (9,10). Kaser et al. reported that hyperbilirubinaemia was significantly associated with perforation, although CRP showed superior predictive performance (10). Therefore, bilirubin should be interpreted as part of a combined assessment rather than as an isolated diagnostic marker.

Postoperative morbidity was also higher among patients with raised bilirubin in our study. Patients with bilirubin >1.0 mg/dL had a longer mean hospital stay, higher overall postoperative complication rate and higher surgical site infection rate compared with those with normal bilirubin. All cases of intra-abdominal collection, re-exploration and mortality occurred in the hyperbilirubinaemia group. These findings suggest that raised bilirubin may reflect not only the presence of perforation but also the severity of inflammatory and septic burden. Complicated appendicitis is known to be associated with increased postoperative morbidity, wound infection, intra-abdominal collection and prolonged hospitalization (1,11-14).

Overall, our study supports the existing evidence that hyperbilirubinaemia is frequently associated with appendicular perforation. Serum bilirubin should be interpreted as an adjunct rather than a replacement for clinical assessment, inflammatory markers and imaging. In patients presenting with features of acute appendicitis, raised bilirubin may alert the surgeon to the possibility of perforation and help guide timely operative decision-making.

Limitations:

Our study has certain limitations. First, it was a retrospective observational study from a single tertiary care centre, which may limit the generalizability of the findings to other populations and healthcare settings. Second, the study included only patients with appendicular perforation and did not include a comparison group of uncomplicated appendicitis; therefore, diagnostic parameters such as sensitivity, specificity, positive predictive value and negative predictive value of serum bilirubin could not be calculated. Third, although patients with known hepatobiliary disease were excluded, other factors that may influence bilirubin levels, such as subclinical liver dysfunction, dehydration or severity of sepsis, could not be fully assessed due to the retrospective nature of the study. Further prospective, multicentre studies including both uncomplicated and complicated appendicitis cases are warranted to validate serum bilirubin as a predictive marker and to determine its optimal diagnostic cut-off for appendicular perforation.

CONCLUSION:

Our study showed that hyperbilirubinaemia was commonly observed among patients with appendicular perforation, with most patients having serum total bilirubin levels >1.0 mg/dL. Patients with raised bilirubin also had longer hospital stay and higher postoperative morbidity, including increased surgical site infection and overall complication rates. These findings suggest that serum bilirubin, being a simple, inexpensive and routinely available biochemical marker, may serve as a useful adjunct in identifying patients at risk of appendicular perforation. However, it should be interpreted along with clinical findings, inflammatory markers and imaging rather than as a standalone diagnostic test. Further prospective comparative studies are warranted to validate its diagnostic utility and determine an optimal predictive cut-off.

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