

Diagnostic Accuracy of Serum Bilirubin in Predicting Appendiceal Perforation: A Prospective Study in a Tertiary Care Hospital

Azharur Rahman^{1*}, Nasima Akhter², Ashik Mahmud³, Mohammad Golam Masum⁴, Ehsan-Ul-Bari⁵, Abdul Jabbar⁶, Gazi Gias Uddin⁷, A B M Mahbubur Rahman⁸, Mizanur Rahman Shikder⁹

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*Corresponding author



ABSTRACT

Introduction: Among patients with acute appendicitis, early identification of appendiceal perforation is important for appropriate clinical decision-making. Because hyperbilirubinemia has been associated with complicated appendicitis, serum bilirubin may provide a simple adjunctive marker for predicting perforation. **Aim of the study:** To evaluate the diagnostic accuracy of serum bilirubin for predicting appendiceal perforation among patients with acute appendicitis. **Methods & Materials:** In this prospective observational study, 72 patients aged ≥ 15 years with suspected acute appendicitis who underwent appendectomy at 250 Bedded General Hospital, Brahmanbaria, from July 2023 to June 2024 were included. Before surgery, total serum bilirubin and alanine aminotransferase were measured, and hyperbilirubinemia was defined as serum bilirubin ≥ 1.1 mg/dL. Following appendectomy, histopathological examination was used to classify patients as having uncomplicated or complicated appendicitis. Receiver operating characteristic analysis was used to assess the diagnostic performance of serum bilirubin. **Results:** Among 72 patients, 49, 68.06%, had uncomplicated acute appendicitis and 23, 31.94%, had appendiceal perforation or complicated appendicitis. A significantly higher mean serum bilirubin level was observed in the complicated group compared with the uncomplicated group, 1.59 ± 0.61 versus 0.95 ± 0.29 mg/dL, $p < 0.001$. Hyperbilirubinemia was present in 73.91% of complicated cases compared with 20.41% of uncomplicated cases and was associated with higher odds of complicated appendicitis, OR 11.05, 95% CI 3.46–35.30, $p < 0.001$. At a bilirubin cutoff of ≥ 1.17 mg/dL, sensitivity was 73.91%, specificity 89.80%, positive predictive value 77.27%, and negative predictive value 88.00%. Receiver operating characteristic analysis demonstrated an AUC of 0.84, 95% CI 0.735–0.945, $p < 0.001$. **Conclusion:** Serum bilirubin showed good discriminatory ability for appendiceal perforation and may be useful as a readily available adjunctive marker for identifying complicated acute appendicitis.

Keywords: Acute Appendicitis; Appendiceal Perforation; Hyperbilirubinemia; Serum Bilirubin; Diagnostic Accuracy

1. Senior Consultant, Department of Surgery, 250 Bedded General Hospital, Brahmanbaria, Bangladesh (ORCID: 0009-0009-6350-9246)
2. Associated Professor, Department of Obstetrics & Gynaecology, Brahmanbaria Medical College Hospital, Brahmanbaria, Bangladesh
3. Associated Professor, Department of Surgery, Brahmanbaria Medical College Hospital, Brahmanbaria, Bangladesh
4. Associate Professor, Department of Surgery, Kumudini Women's Medical College, Tangail, Bangladesh
5. Associate Professor, Department of Surgery, Anwer Khan Modern Medical College Hospital, Dhaka, Bangladesh
6. Associate Professor, Department of Anaesthesiology, SICU & Pain Medicine, BIRDEM General Hospital, Dhaka, Bangladesh
7. Assistant Professor, Department of Surgery, Bangladesh Medical College, Dhaka, Bangladesh
8. Professor (CC), Department of Surgery, Khwaja Yunus Ali Medical College & Hospital, Sirajganj, Bangladesh
9. Assistant Professor, Department of surgery, Brahmanbaria Medical College Hospital, Brahmanbaria, Bangladesh

INTRODUCTION

Among patients presenting with acute abdominal pain, acute appendicitis remains one of the most frequent surgical emergencies, and timely recognition of disease progression is important because perforation is associated with greater operative complexity, postoperative morbidity, and risk of intra-abdominal infection. In routine practice, differentiation between uncomplicated and perforated appendicitis is based on the combined interpretation of clinical findings, laboratory parameters, imaging, operative assessment, and histopathology; however, no single preoperative marker consistently identifies perforation with adequate certainty. Because severe appendiceal inflammation may be accompanied by bacterial translocation and endotoxin-mediated disturbance of hepatic bilirubin handling, serum bilirubin has been investigated as a simple biochemical marker of complicated disease. Across recent studies, higher bilirubin concentrations have repeatedly been observed among patients

with perforated or complicated appendicitis, although the magnitude and diagnostic performance of this association have varied between populations and thresholds. In a 2025 diagnostic validation study involving 96 patients, hyperbilirubinemia was found to have a sensitivity of 63.64% and specificity of 76.92% for appendiceal perforation, with positive and negative predictive values of 70.00% and 71.43%, respectively [1]. In another 2025 study of 122 patients, serum bilirubin was reported to have low sensitivity but high specificity for complicated appendicitis, with sensitivity of 28.6%, specificity of 90.8%, positive predictive value of 55.6%, and negative predictive value of 75.9%; in the same study, C-reactive protein showed substantially higher sensitivity but lower specificity [2]. In a 2024 case-control study of 100 patients, significantly higher preoperative bilirubin levels were observed among patients with complicated appendicitis, and total bilirubin remained a significant variable in regression analysis together with leukocytosis and symptom

duration [3]. In a Saudi Arabian study of 158 patients, elevated total bilirubin was found to be independently associated with complicated appendicitis, with an adjusted odds ratio of 3.79; at a cutoff of at least 15 $\mu\text{mol/L}$, sensitivity of 57.6%, specificity of 73.6%, and an area under the receiver operating characteristic curve of 0.69 were reported [4]. Among 333 patients undergoing emergency appendectomy, hyperbilirubinemia was observed in 70.59% of perforated cases compared with 19.03% of non-perforated cases, and an odds ratio of 10.21 was reported for perforation [5]. In a prospective study of 125 patients, total serum bilirubin above 1.1 mg/dL was reported to have sensitivity of 89.29%, specificity of 53.49%, positive predictive value of 38.46%, and negative predictive value of 93.88% for perforated or complicated appendicitis [6]. In an earlier retrospective cohort of 221 patients, elevated bilirubin was again found to be more specific than sensitive for perforation, with sensitivity of 50.0% and specificity of 80.73% [7]. At the evidence-synthesis level,

bilirubin was found to have only moderate discriminatory value in a systematic review of biomarkers for appendicitis, with pooled sensitivity of 0.52, specificity of 0.76, and an area under the curve of approximately 0.71 for perforated appendicitis [8]. In a separate diagnostic meta-analysis, hyperbilirubinemia alone was concluded to be insufficiently reliable as a standalone predictor of appendiceal perforation, supporting its use as an adjunct rather than an isolated diagnostic test [9]. Taken together, the available evidence suggests that serum bilirubin may provide clinically useful information about the likelihood of appendiceal perforation, particularly because specificity and negative predictive value are often moderate to high, but substantial heterogeneity remains across study populations, bilirubin thresholds, and reference standards. Within this context, further prospective evaluation in tertiary-care settings remains relevant. Therefore, the present study was conducted to assess the diagnostic accuracy of serum bilirubin for predicting appendiceal perforation among patients with acute appendicitis, using histopathological diagnosis as the reference standard.

METHODS & MATERIALS

This prospective observational study was conducted in the Department of Surgery, 250 Bedded General Hospital, Brahmanbaria, from July 2023 to June 2024. Patients aged 15 years or older who were admitted with suspected acute appendicitis and underwent appendectomy were purposively enrolled after applying predefined inclusion and exclusion criteria. Patients with HBsAg positivity, previous jaundice or liver disease, viral hepatitis, biliary or hemolytic disorders associated with hyperbilirubinemia, negative appendectomy on histopathology, or unwillingness to participate were excluded. Before surgery, venous blood was collected for measurement of total serum bilirubin and alanine aminotransferase (ALT). Serum bilirubin <1.1 mg/dL was considered normal, while a level ≥1.1 mg/dL was defined as hyperbilirubinemia. Following appendectomy, resected specimens were examined histopathologically. Based on histopathological findings, patients were classified as having uncomplicated acute appendicitis or complicated appendicitis, including perforation, ulceration, necrosis, or gangrenous appendicitis. Data were analyzed using SPSS. Continuous variables

were compared between groups using the independent-samples t test, while categorical variables were assessed using the chi-square test, as appropriate. Receiver operating characteristic analysis was performed to evaluate the diagnostic performance of serum bilirubin for predicting appendiceal perforation, including estimation of sensitivity, specificity, positive predictive value, negative predictive value, and area under the curve. A p-value <0.05 was considered statistically significant.

RESULTS

The mean age of the participants was 24.50 ± 9.39 years, and 46 (63.89%) were male. The mean duration of abdominal pain before presentation was 46.65 ± 30.41 hours. The overall mean serum bilirubin concentration was 1.16 ± 0.51 mg/dL, while the mean serum ALT level was 30.736 ± 4.9305 U/L. Hyperbilirubinemia, defined as serum bilirubin ≥1.1 mg/dL, was present in 27 (37.50%) patients. Histopathological examination demonstrated acute appendicitis in 49 (68.06%) patients and appendiceal perforation or complicated appendicitis in 23 (31.94%) (Table I).

Table I
Baseline demographic, clinical, and laboratory characteristics of the study participants (n=72).

Characteristic	RESULT
Age, years	24.50 ± 9.39
Male sex	46 (63.89%)
Female sex	26 (36.11%)
Duration of pain, hours	46.65 ± 30.41
Serum bilirubin, mg/dL	1.16 ± 0.51
Serum ALT, U/L	30.736 ± 4.9305
Bilirubin ≥1.1 mg/dL	27 (37.50%)
Bilirubin <1.1 mg/dL	45 (62.50%)
Histopathology: acute appendicitis	49 (68.06%)
Histopathology: appendiceal perforation / complicated appendicitis	23 (31.94%)

Data are mean ± SD or n (%), as appropriate. ALT: alanine aminotransferase.

The mean serum bilirubin level was significantly higher among patients with appendiceal perforation or complicated appendicitis than among those with uncomplicated acute appendicitis, 1.59 ±

0.61 mg/dL versus 0.95 ± 0.29 mg/dL, respectively, p<0.001. A similar difference was observed for serum ALT, with a mean level of 33.478 ± 6.0443 U/L in the complicated group compared with 29.449 ±

3.7308 U/L in the acute appendicitis group, p=0.004 (Table II).

Table II
Serum bilirubin and ALT according to histopathological diagnosis.

Laboratory parameter	Acute appendicitis (n=49)	Appendiceal perforation / complicated appendicitis (n=23)	p-value
Serum bilirubin, mg/dL	0.95 ± 0.29	1.59 ± 0.61	<0.001
Serum ALT, U/L	29.449 ± 3.7308	33.478 ± 6.0443	0.004

The histopathological 'appendiceal perforation' group included perforation, ulceration, necrosis, or gangrenous appendicitis.

Hyperbilirubinemia was considerably more frequent among patients with appendiceal perforation or complicated appendicitis. Serum bilirubin ≥1.1 mg/dL was observed in 17 of 23 patients, 73.91%, with complicated appendicitis compared with 10

of 49 patients, 20.41%, with uncomplicated acute appendicitis. Conversely, normal serum bilirubin levels were present in 79.59% of uncomplicated cases but only 26.09% of complicated cases. Based on these frequencies, hyperbilirubinemia was

associated with approximately 11-fold higher odds of complicated appendicitis, OR=11.05, 95% CI 3.46–35.30, p<0.001 (Table III).

Table III
Association between hyperbilirubinemia and histopathological diagnosis.

Serum bilirubin	Acute appendicitis (n=49)	Appendiceal perforation / complicated appendicitis (n=23)	Total
≥1.1 mg/dL	10 (20.41%)	17 (73.91%)	27
<1.1 mg/dL	39 (79.59%)	6 (26.09%)	45
Total	49 (100%)	23 (100%)	72

odds ratio 11.05, 95% CI 3.46 to 35.30; Fisher's exact $p < 0.001$.

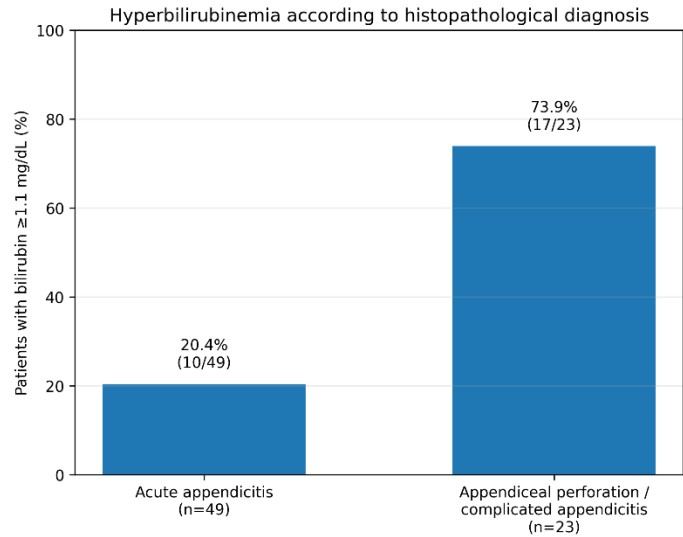


Figure 1 Proportion of patients with hyperbilirubinemia according to histopathological diagnosis.

The distribution of hyperbilirubinemia according to histopathological diagnosis is illustrated in *Figure 1*. Only 20.41% of patients with uncomplicated acute appendicitis had serum bilirubin ≥ 1.1 mg/dL, whereas the corresponding proportion among patients with appendiceal

perforation or complicated appendicitis was 73.91%.

At a serum bilirubin cutoff of ≥ 1.01 mg/dL, sensitivity and specificity for detecting appendiceal perforation were 78.26% and 75.50%, respectively. The corresponding positive predictive value was 60.00%, while the negative predictive value was 88.10%.

Increasing the cutoff to ≥ 1.17 mg/dL reduced sensitivity slightly to 73.91% but increased specificity to 89.80%. At this threshold, the positive predictive value increased to 77.27%, while the negative predictive value remained similar at 88.00% (*Table IV*).

Table IV
Diagnostic performance of serum bilirubin thresholds for appendiceal perforation.

Cutoff	TP	FP	FN	TN	Sensitivity	Specificity	PPV	NPV
≥1.01 mg/dL	18	12	5	37	78.26%	75.50%	60.00%	88.10%
≥1.17 mg/dL	17	5	6	44	73.91%	89.80%	77.27%	88.00%

Histopathology was used as the reference standard. TP, true positive; FP, false positive; FN, false negative; TN, true negative; PPV, positive predictive value; NPV, negative predictive value.

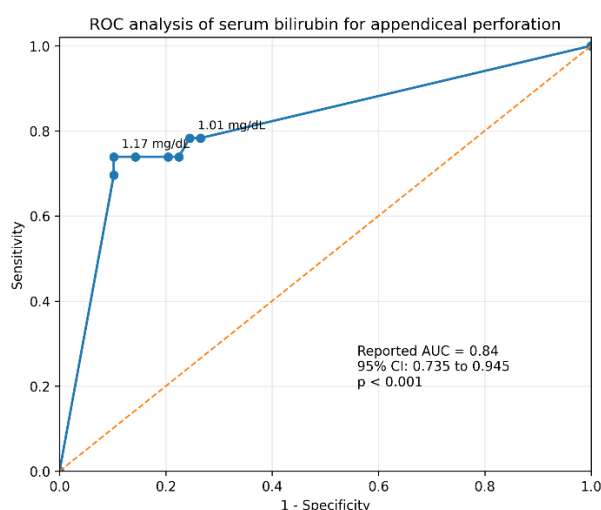


Figure 2 Receiver operating characteristic analysis of serum bilirubin for predicting appendiceal perforation.

Receiver operating characteristic analysis demonstrated an area under the curve of 0.84, standard error 0.053, with a 95% confidence interval of 0.735–0.945, $p < 0.001$. The AUC of 0.84 indicates that serum bilirubin showed good discriminatory ability for differentiating patients with appendiceal perforation or complicated appendicitis from those with uncomplicated acute appendicitis (Figure 2).

DISCUSSION

In the present study, serum bilirubin demonstrated a strong association with appendiceal perforation or complicated appendicitis and showed good overall discriminatory performance. A significantly higher mean serum bilirubin concentration was observed in patients with complicated appendicitis than in those with uncomplicated acute appendicitis, 1.59 ± 0.61 mg/dL versus 0.95 ± 0.29 mg/dL, respectively, $p < 0.001$. Comparable findings have been reported in several prospective and retrospective studies. In the study by Bakshi and Mandal, mean bilirubin was reported as 1.39 ± 0.26 mg/dL in complicated appendicitis compared with 0.79 ± 0.16 mg/dL in uncomplicated disease [10]. Similarly, in the prospective study by Goudar and Kanchan, mean serum bilirubin was reported as 1.9 ± 1.13 mg/dL in histopathologically proven appendicular perforation compared with 1.0 ± 0.4 mg/dL in uncomplicated acute appendicitis [11]. Higher bilirubin concentrations in complicated disease were also reported by Sardoo et al., Alfehaid et al., and Halaseh et al [3,4,12]. Taken together, these findings support a consistent relationship between increasing appendiceal disease severity and bilirubin elevation, although the absolute concentrations differ among study populations. A particularly notable finding was the marked difference in the prevalence of hyperbilirubinemia between the two histopathological groups. Serum bilirubin

≥ 1.1 mg/dL was present in 73.91% of patients with complicated appendicitis compared with only 20.41% of uncomplicated cases. A strikingly similar distribution was reported in the study by Khalid and Elamin, in which hyperbilirubinemia was observed in 70.59% of perforated cases compared with 19.03% of non-perforated appendicitis [5]. Likewise, in the study by Goudar and Kanchan, elevated bilirubin was identified in 31 of 41 perforated cases, 75.6%, compared with 17 of 59 uncomplicated cases, 28.8% [11]. More pronounced differences were reported by Bakshi and Mandal, with hyperbilirubinemia occurring in 91.42% of complicated cases and 12.0% of uncomplicated cases [10]. These differences in magnitude may reflect variations in bilirubin thresholds, definitions of complicated disease, timing of laboratory assessment, and underlying population characteristics. In the present analysis, hyperbilirubinemia was associated with approximately 11-fold increased odds of complicated appendicitis, OR 11.05, 95% CI 3.46–35.30, $p < 0.001$. Very similar evidence was reported by Khalid and Elamin (2023), where an odds ratio of 10.21 was observed for the association between hyperbilirubinemia and appendiceal perforation. Smaller independent associations have also been demonstrated. In the study by Alfehaid et al., elevated total bilirubin was associated with complicated appendicitis after adjustment, with an adjusted OR of 3.79, while an OR of 3.184 was reported for total bilirubin in the study by Yamazaki et al [4,14]. Direct numerical comparison of these odds ratios should be undertaken cautiously because different bilirubin thresholds, endpoint definitions, and statistical models were applied. At a bilirubin cutoff of ≥ 1.01 mg/dL, sensitivity and specificity in the present study were 78.26% and 75.50%, respectively, with a positive predictive value of 60.00% and negative predictive value of 88.10%.

Closely comparable sensitivity and specificity, 75.6% and 71.2%, were reported by Goudar and Kanchan [11]. Greater sensitivity but lower specificity was reported by Kar et al., where bilirubin > 1.1 mg/dL yielded sensitivity of 89.29% and specificity of 53.49% [6]. These findings illustrate the substantial threshold-dependent trade-off between identifying most complicated cases and minimizing false-positive classifications. When the cutoff was increased to ≥ 1.17 mg/dL, sensitivity decreased modestly to 73.91%, while specificity increased to 89.80%; PPV and NPV were 77.27% and 88.00%, respectively. A particularly comparable pattern was reported by Ramasamy Ramu et al., where a cutoff > 1.3 mg/dL produced sensitivity of 80% and specificity of 89% [14]. In the study by Raza et al., specificity was similarly high at 90.8%, although sensitivity was considerably lower at 28.6% [2]. Conversely, in the study by Shuaib et al. (2022), bilirubin > 20 $\mu\text{mol/L}$, approximately 1.17 mg/dL, yielded sensitivity of 65.6%, specificity of 75.4%, and NPV of 93.6%. Such variability reinforces that a universally applicable bilirubin threshold has not yet been established. Receiver operating characteristic analysis in the present study showed an AUC of 0.84, 95% CI 0.735–0.945, $p < 0.001$, indicating good discrimination between uncomplicated and complicated appendicitis. Lower AUC values have been reported in several verified studies, including 0.79 by Shuaib et al., 0.739 by Halaseh et al., 0.723 by Yamazaki et al., and 0.69 by Alfehaid et al [4,12,13,15]. In contrast, stronger discrimination was reported by Bakshi and Mandal, with an AUC of 0.958 at an optimized cutoff of 1.06 mg/dL [10]. At the evidence-synthesis level, an AUC of approximately 0.71 was reported for bilirubin in predicting perforated appendicitis in the systematic review by Acharya et al., with substantial between-study heterogeneity [8]. More recently,

considerable variation in bilirubin thresholds and diagnostic estimates was again identified in the systematic review by Czyszczon et al., supporting the interpretation of bilirubin as an adjunctive rather than standalone diagnostic marker [16]. A secondary finding was the significantly higher ALT level in complicated appendicitis, 33.478 ± 6.0443 U/L versus 29.449 ± 3.7308 U/L, $p=0.004$. This finding has not been reproduced consistently. No significant ALT difference was reported by Halaseh et al., while ALT was not significantly associated with complicated appendicitis in the study by Alfehaid et al [4,12]. However, more frequent ALT elevation with increasing pathological severity was observed by MoulaBux et al [17]. Therefore, although hepatic biochemical alterations may accompany complicated appendicitis, bilirubin appears to have a more consistent relationship with disease severity than ALT. Overall, the findings support serum bilirubin as a readily available adjunct for preoperative risk assessment of appendiceal perforation. Its comparatively high specificity at the higher threshold may be particularly useful for strengthening suspicion of complicated disease when interpreted alongside clinical findings, inflammatory markers, and imaging. Nevertheless, variation across studies in cutoff values, disease definitions, reference standards, and prevalence limits the use of bilirubin as an isolated diagnostic test.

LIMITATIONS

Because this was a single-center study with a relatively small sample size and purposive sampling, the findings may have limited generalizability to other populations and healthcare settings. In addition, serum bilirubin was evaluated as an adjunctive biochemical marker without direct comparison with established clinical scoring systems or imaging-based diagnostic approaches.

CONCLUSION

In this prospective study, serum bilirubin was significantly higher among patients with appendiceal perforation or complicated appendicitis than among those with uncomplicated acute appendicitis. Hyperbilirubinemia was strongly associated with complicated disease, while serum bilirubin demonstrated good overall discriminatory ability with an AUC of 0.84. At a cutoff of ≥ 1.17 mg/dL, relatively high specificity of 89.80% was achieved while maintaining a sensitivity of 73.91%. Therefore, serum bilirubin may serve as a simple, readily available adjunctive marker for identifying patients at increased risk of appendiceal perforation, although it should be interpreted together with clinical assessment and other diagnostic findings rather than used as a standalone test.

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CONFLICT OF INTEREST

None declared

ETHICAL APPROVAL

The study was approved by the Institutional Ethics Committee

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