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Serum Bilirubin as a Potential Marker in Diagnosing the Severity of Acute Appendicitis: A Retrospective Study

Sanjay Bikram Shrestha[1], **Jay Prakash Thakur**[2], **Manisha Pradhan**[3], **Rupa Jha**[4], **Shanti Tamang**[5]

[1]Department of General Surgery, Nepal Police Hospital, Maharajgunj, Kathmandu, Nepal, [2]Department of Anesthesiology and Intensive Care, National Academy of Medical Sciences, Bir Hospital, Kathmandu, Nepal, [3]Department of Anesthesiology, Patan Academy of Health Sciences, Lalitpur, Nepal, [4]Department of Obstetrics and Gynaecology, [5]Registered Nurse, Green City Hospital, Kathmandu, Nepal.

ABSTRACT

Background

Acute appendicitis ranks among the leading causes of emergency abdominal surgeries. Although clinical assessments and imaging techniques are crucial for diagnosis, a straightforward and economical biomarker to evaluate severity is yet to be identified. Recent research indicates that serum bilirubin might act as a surrogate indicator of disease severity. The objective of this study was to analyse the relationship between serum bilirubin concentrations and the severity of acute appendicitis.

Methods

A retrospective case-control study was performed on patients who underwent appendectomy at Green City Hospital from June 1, 2023 to May 31, 2025. Patients with chronic liver disease, haemolytic disorders, conditions that influence bilirubin metabolism, or those with alternative diagnoses post-surgery were excluded. Patients were classified into normal (≤1 mg/dL) and elevated (>1 mg/dL) groups based on serum bilirubin levels. Intraoperative findings of the appendix were categorized as normal, inflamed, or complicated (gangrenous, perforated). Pearson's correlation coefficient was utilized to evaluate the correlation between bilirubin levels and the severity of appendicitis.

Results

Among the 170 patients screened, 156 were included in the analysis. Four patients had normal appendices, and all had normal bilirubin levels. Out of 127 patients with inflamed appendices, 123(96.85%) exhibited normal bilirubin. Of the 25 patients with complicated appendicitis, 17(68%) had elevated bilirubin levels. A strong positive correlation ($r=0.650$, p-value<0.000) was established between bilirubin concentrations and disease severity.

Conclusions

Increased serum bilirubin levels demonstrate a significant association with the severity of acute appendicitis and may be a valuable additional marker in clinical assessments.

Keywords: appendicitis; gangrene; total bilirubin.

Correspondence: Dr. Jay Prakash Thakur, Department of Anesthesiology and Intensive Care, National Academy of Medical Sciences, Bir Hospital, Mahaboudha, Kathmandu, Nepal. Email: dr.jay2002@gmail.com, Phone: +977-9849001429. **Article received**: 2025-06-26. **Article accepted**: 2025-08-24. **Article published**: 2025-09-15.

INTRODUCTION

Acute appendicitis is a common cause of abdominal pain necessitating surgical intervention, but its diagnosis can be difficult due to varying presentations and overlapping symptoms with other conditions like ectopic pregnancy, Crohn's disease, endometriosis, and urinary tract infections.[1,2] While most diagnoses are based on classic symptoms, atypical cases can postpone treatment, raising the likelihood of complications such as perforation and peritonitis.[3] Typically, diagnosis is grounded in clinical evaluation, white blood cell (WBC) count, C-reactive protein (CRP), and imaging, yet these methods can lack specificity.[3] Many scoring systems (e.g., modified Alvarado score) are available. However, while useful for diagnosis, these scoring systems do not evaluate the risk of complications such as appendicular gangrene or perforation. There is increasing interest in finding dependable, cost-effective biomarkers to assist with diagnosis and severity. Serum bilirubin, which has traditionally been associated with liver function, has surfaced as a potential marker of inflammation in acute appendicitis.[4,5] Elevated levels of bilirubin, especially total and direct bilirubin, may correlate with severe manifestations like gangrenous or perforated appendicitis.[5] The suggested mechanism involves bacterial translocation and endotoxemia, hindering bilirubin excretion.[3,4,6] This retrospective analysis explores the connection between serum bilirubin levels and the severity of acute appendicitis.

METHODS

This retrospective case-control study was conducted at Green City Hospital, Kathmandu, Nepal, after obtaining ethical clearance from Nepal Health Research Council (NHRC Registration No. 411_2025). Patient records were analysed over a 2-year period from 1st June 2023 to 31st May 2025. Data were extracted from the Operation Theater (OT) register and hospital computerized database. The OT register contained the patients' names, age, sex, hospital number, diagnosis, and date of appendectomy. The hospital's computerized database contained the patients' total bilirubin levels and intraoperative appendix findings. The study included patients clinically confirmed acute appendicitis with or without radiological diagnosis, and who subsequently underwent appendectomy, and for whom preoperative serum bilirubin levels were available. Patients with incomplete data records, alternative diagnoses made after surgery, or patients having confounding diseases with high bilirubin levels (e.g., hepatitis, haemolytic disorders, liver cirrhosis, etc.) were excluded from the study.

Based on serum bilirubin values, patients were categorized into two groups: those with normal bilirubin levels (≤1 mg/dl) and those with elevated levels (>1 mg/dL).[7] The intraoperative morphological findings of the appendix were divided into 3 groups, as shown in Table 1.

Table 1. Intraoperative morphological findings of the appendix.[7]

Group	Intraoperative findings of the Appendix
1	Normal-looking Appendix
2	Inflamed appendix
3	Complicated appendix (gangrenous appendix or perforated appendix with localized or generalized peritoneal infiltrates)

Statistical analysis was performed using SPSS version 16. The association between elevated serum bilirubin levels and, their correlation with complications such as perforation or gangrene, was assessed using Pearson's correlation coefficient analysis test.

RESULTS

A total of 170 patient records were reviewed, out of which 156 met the inclusion criteria. The mean±SD age of the study population was 32.96±16.82 years, which ranges from 8 years to 85 years. The numbers of female patients were 68(43.59%) and the number of male patients were 88(56.41%). Elevated serum bilirubin levels (>1 mg/dl) were observed in 21(13.5%) of patients and normal bilirubin level were found in 135(86.5%) of patients. As per intraoperative morphological findings, normal-looking appendix were in 4(2.6%) patients, an inflamed appendix was in 127(81.4%) patients and a complicated (gangrenous/

perforated) appendix in 25(16%) of patients as shown in Table 2.

Table 2. Demographic data and bilirubin level of participants. (n=156)	
Variables	**Frequency (%)**
Age (years): Mean ± SD = 32.96 ± 16.82	
Sex	
Male	88(56.41)
Female	68(43.59)
Bilirubin level	
Low bilirubin level (≤1 mg/dl)	135(86.5)
High bilirubin level (>1 mg/dl)	21(13.5)
Morphology of appendix	
Group 1 (normal-looking appendix)	4(2.6)
Group 2 (Inflamed appendix)	127(81.4)
Group 3 (Complicated appendix)	25(16)

Normal looking appendix were found in 4 patients, and all of them had normal bilirubin levels. Inflamed appendix was found in 127 patients, out of which 123(91.11%) had normal bilirubin level. Complicated appendix was found in 25 patients, out of which 17(80.95%) had elevated bilirubin level (Table 3).

Table 3. Bilirubin level compared to morphology of appendix. (n=156)		
Morphology of appendix	**Bilirubin ≤1 mg/dl**	**Bilirubin >1 mg/dl**
Group 1 (normal-looking appendix)	4(2.96%)	0(0)
Group 2 (Inflamed appendix)	123(91.11%)	4(19.04%)
Group 3 (Complicated appendix)	8(5.92%)	17(80.95%)

The correlation table illustrated the linear relationship between the bilirubin level and the intraoperative morphology of the appendix, indicating the severity of inflammation. There was a strong positive correlation with r=0.650, p-value<0.000, indicating that the hyperbilirubinemia was associated with the severity of appendicitis. This relationship is statistically significant. The serum bilirubin levels in patients with complicated appendicitis were notably higher compared to those with uncomplicated cases (Table 4).

Table 4. Correlations between bilirubin group and morphology of appendix. (n=156)		
Correlations	**Bilirubin group**	**Morphology of appendix**
Bilirubin group		
Pearson correlation (r)	1	0.650**
p-value		0
Morphology of appendix		
Pearson correlation	0.650**	1
p-value	0	
**Correlation is significant at the 0.01 level.		

DISCUSSION

The findings of this study support the hypothesis that serum bilirubin levels are significantly elevated in patients with complicated appendicitis. Delays in the timely surgical management of appendicitis can lead to serious complications. These delays may result from late presentation (often seen in males with retrocecal or retroileal appendix positions) or from clinical misjudgement. When treatment is postponed, the appendix can become gangrenous or perforate, which in turn can cause further issues such as appendicular abscesses, localized or generalized peritonitis, fecal fistula, intestinal obstruction from adhesions, portal pyemia, and sepsis. Overall, these complications contribute to increased morbidity and longer hospital stays.[8]

Despite significant advances in diagnostic techniques over the past 125 years, acute appendicitis still poses a diagnostic challenge for surgeons and is primarily a clinical diagnosis. While various tools can aid in assessment-such as laboratory tests, scoring systems, ultrasonography (with a sensitivity of 0.86 and specificity of 0.81 in experienced hands), multidetector computed tomography (MDCT, with sensitivity and specificity of 0.94 and 0.95, respectively), scintigraphy, MRI (especially useful during pregnancy), and diagnostic laparoscopy-these are generally used to support, rather than replace, clinical judgment.[9-12]

Several diagnostic scoring systems are commonly used to evaluate suspected cases of appendicitis.

These include the Alvarado score (scale 0-10), the modified Alvarado score, the Pediatric Appendicitis Score (PAS; scale 0-10), the Rajalsteri Pengiran Anak saleha Appendicitis (RIPASA) score-designed specifically for Asian populations (scale 0-14), and the Appendicitis Inflammatory Response Score (AIRS; scale 0-12).[13-16] However, while useful for diagnosis, these scoring systems do not evaluate the risk of complications such as appendicular gangrene or perforation. Notably, none of them incorporate hyperbilirubinemia as a marker. Some studies have shown that patients with total serum bilirubin levels above 1 mg/dL have a threefold increased risk of appendiceal perforation.[17] Rodriguez et al.,[18] had concluded that total bilirubin had a positive predictive value of severity in patients with acute appendicitis. Alfehaid et al.,[19] found elevated total and direct bilirubin are associated with acute complicated appendicitis.

The findings of this study support the growing body of evidence suggesting that serum bilirubin can serve as a useful adjunctive marker in diagnosing acute appendicitis, particularly in identifying more severe forms such as perforation or gangrene. The significant correlation between elevated bilirubin levels and complicated appendicitis highlights the potential role of this parameter in clinical decision-making. Its elevation may reflect systemic inflammatory response and hepatic dysfunction secondary to bacterial translocation and endotoxemia, leading to impaired conjugation and excretion of bilirubin. Sardoo et al.[20] found that patients with complicated appendicitis had significantly (p-value<0.01) higher total bilirubin levels than patients with uncomplicated appendicitis. Pattnaik et al.,[7] found that out of 39 patients with complicated appendicitis, 38 patients had raised bilirubin which was statistically significant (p-value<0.001).

While WBC count and CRP remain useful, they may not always differentiate between simple and complicated cases. In contrast, a rise in bilirubin, particularly when >1.0 mg/dL, should raise suspicion of a more severe underlying pathology. This study reinforces that even modest increases in bilirubin could warrant closer clinical attention, especially in ambiguous cases.

Limitations

It is important to note the limitations of this study, including its retrospective design, single-center data, and exclusion of potential confounding factors beyond liver or hemolytic disorders. Larger prospective studies are recommended to validate serum bilirubin as a routine diagnostic marker and to establish standardized cut-off values for clinical use. Nevertheless, the data suggest that bilirubin level, when interpreted in conjunction with clinical findings, can enhance early risk stratification.

CONCLUSIONS

The present study demonstrates that elevated serum bilirubin levels are significantly associated with complicated acute appendicitis, particularly in cases with perforation or gangrene. While hyperbilirubin should not replace imaging or clinical judgment, it can serve as a simple, cost-effective, valuable and readily available adjunct in predicting the severity of acute appendicitis, particularly in resource-limited settings. Hyperbilirubinemia can aid in early identification of complicated cases, and facilitate timely surgical intervention. Further large-scale prospective studies are recommended to validate its predictive value and establish standardized cutoff levels.

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