

## Evaluation of Importance of S Bilirubin Level in Cases of Simple and Complicated Acute Appendicitis

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### How to cite this article:

Sachin Murukanahalli Basavaraju, Akshatha Hebbale Srinivasa, Hanumantha Basappa Vaggara, et al. Evaluation of Importance of S Bilirubin Level in Cases of Simple and Complicated Acute Appendicitis. *New Indian J Surg.* 2020;11(4):509-514.

### Abstract

**Introduction:** Acute Appendicitis is the most common general surgical emergency and early surgical intervention improves outcomes. Despite the increased use of ultrasonography, computed tomography scanning and laparoscopy, the rate of misdiagnosis of appendicitis has remained constant (15.3%) and the rate of appendicular perforation. In an age, accustomed to early and accurate preoperative diagnosis, acute appendicitis remains an enigmatic challenge and a reminder of the art of surgical diagnosis. This study was done to conclude whether the Serum Bilirubin can be considered as a new laboratory marker to aid in the diagnosis of acute appendicitis.

**Aims:** To evaluate whether elevated Bilirubin level is important in predicting the diagnosis of acute appendicitis (simple and complicated appendicitis).

**Material and Methods:** This retrospective study was conducted in the department of general surgery, Adichunchanagiri institute of medical sciences, B. G. Nagara, Mandya (D), from August 2018 to February 2020. A total of 100 patients with clinical diagnosis of acute appendicitis or appendicular perforation were studied.

**Results:** In this study, males (68%) outnumbered females (32%) and overall mean age was 27±9.58 years. Of the 100 patients, 71% were confirmed as acute appendicitis while 29% were diagnosed with appendicular perforation. Of 71 patients with acute

appendicitis, 12.7% had raised bilirubin levels, while 87.3% had normal levels.

**Conclusion:** This scoring system is practical and reliable diagnostic modality for the accuracy in diagnosis of acute appendicitis and to avoid negative appendectomies.

**Keywords:** Pain abdomen; Acute Appendicitis; Appendicular perforation; Elevated Serum Bilirubin level; Negative Appendectomy.

### Introduction

Acute appendicitis is the commonest cause of "Acute Surgical abdomen".<sup>1,2</sup> The diagnosis of Appendicitis still remains a dilemma in spite of advances in the radiological and laboratory investigations. Experienced clinicians accurately diagnose appendicitis based on a combination of history, physical examination and laboratory studies about 80% of the time.<sup>3</sup> Although most patients with acute appendicitis can be easily diagnosed, in some cases the sign and symptoms are variable and a firm diagnosis can be difficult. This is particularly true where the appendix is retrocaecal or retroileal. The percentage of appendectomies performed where appendix subsequently found to be normal varies 15- 50%<sup>4</sup> and postoperative complications can occur in up to 50%<sup>5</sup> of these patients. Appendicitis is relatively rare in infants and becomes increasingly common in childhood. Delay in diagnosis of acute appendicitis leads to perforation and peritonitis and increased mortality. Perforation ranges 50-90% in various series.<sup>6,7</sup> To supplement the clinical diagnosis

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and to reduce the frequency of unnecessary appendectomy, the importance of laboratory investigations like White Blood Cell (WBC) counts and C-reactive protein (CRP) etc values has been stressed.<sup>8</sup> The use of Ultrasonography (USG) as a diagnostic tool for appendicitis has been widely known and studied.<sup>9-12</sup> Various scores combining clinical features and laboratory investigations have also been developed and are good enough to reach the diagnosis. These are the Alvarado score<sup>13</sup> and the Modified Alvarado score.<sup>14</sup> However up to date there is no confirmatory laboratory marker for the pre-operative diagnosis of acute appendicitis and appendicular perforation. Recently, elevation in serum bilirubin was reported, but the importance of the raised total bilirubin has not been stressed in acute appendicitis and appendicular perforation<sup>15</sup>. It is well established that when microbes invade the body, leukocytes defend it. This leads to increase in the leukocyte count. Bacterial invasion in the appendix leads to transmigration of bacteria and the release of pro-inflammatory cytokines such as TNF-alpha, IL6 and cytokines. These reach the liver via Superior mesenteric vein (SMV) and may produce inflammation, abscess or dysfunction of liver either directly or indirectly by altering the hepatic blood flow.<sup>16-22</sup> In view of the above context, the present study was undertaken to assess relationship between hyperbilirubinemia and acute appendicitis/perforated appendicitis and to evaluate its importance as a diagnostic marker.

*Objective of the study:* To evaluate whether elevated Bilirubin level is important in predicting the diagnosis of acute appendicitis (simple and complicated appendicitis).

*Study Period:* From August 2018 to February 2020.

*Inclusion Criteria:* All clinically diagnosed case with acute appendicitis (simple and complicated).

*Exclusion Criteria:*

1. Individuals with history of confirmed hepatitis or liver disease or HBsAg positive.
2. Individuals with age less than 13 years of age.
3. Patients with known congenital liver diseases like gilbert syndrome , Dubin - Johnson, Rotor's syndrome and Crigler -Najjar syndrome.
4. Individuals with intra or extra hepatic cholestasis.
5. Individuals with haemolytic anemia.
6. Chronic alcoholism (i.e. intake of alcohol of >40g/day for Men and >20g/day in Women for 10 years).

## Material and Methods

This study was conducted in the department of general surgery, Adichunchanagiri institute of medical sciences, B. G. Nagara, Mandya (D), from February 2018 to February 2020. A total of 100 patients with clinical diagnosis of acute appendicitis or appendicular perforation were studied. All patients data collected with respect to age, gender, duration of symptoms. surgical procedures were undertaken with the understanding and appropriate informed consent of each patient before surgery. The operations were performed under regional or General anesthesia.

The following tests report were collected.

- Routine blood investigations (Complete blood count, platelet count, reticulocyte count).
- Peripheral smear to rule out hemolytic anemia.
- Serum Bilirubin (Total and Direct bilirubin).
- Liver Function Tests(LFTs) which include
  - ▶ SGPT (Alanine transaminase).
  - ▶ SGOT (Aspartate transaminase).
  - ▶ ALP (Alkaline phosphatase).
- Seropositivity for HbsAg
- Urine analysis (routine and microscopy).
- Histopathological examination of the resected specimen of appendix.

*Statistical Analysis:* Statistical analysis was done using statistical software (SPSS version 16).

## Results

**Table1:** Distribution of patients by age.

Age	Frequency	Percent
<20	24	24.0
20-24	21	21.0
25-29	19	19.0
30-34	17	17.0
>35	19	19.0
Total	100	100.0

The age group <20years is most commonly affected (24%) followed by age group 20-24 (21%). The mean age was 27 years (Table 1).

**Table 2:** Sex distribution.

Sex	Frequency	Precent
Female	32	32.0
Male	68	68.0
Total	100	100

Out of 100 patients enrolled for the study, 68 patients (68%) were males while the remaining 32 patients (32%) were female (Table 2).

**Table 3:** Serum bilirubin levels in the study population.

Serum bilirubin levels	Frequency	Percent
Elevated	28	28.0
Normal	72	72.0
Total	100	100.0

Among the study group 28 patients had serum bilirubin levels >1mg% and 72 patients<1mg% (Table 3).

**Table 4:** Intra-operative findings in study population.

Intra operative finding	Frequency	Percent
Perforated	29	29.0
Simple	71	71.0
Total	100	100.0

Among the study population 29 patients were diagnosed of having perforated appendicitis (Table 4 and 5).

**Table 5:** Bilirubin levels in perforated and simple appendicitis.

	Serum bilirubin levels				Total	
	Elevated		Normal			
Intra-operative finding	N	%	N	%	N	%
Perforated	19	65.5	10	34.5	29	100.0
Simple	9	12.7	62	87.3	71	100.0
Total	28	28.0	72	72.0	100	100.0

$\chi^2=28.517$  df=1 p<0.001

**Table 6:** Accuracy of serum bilirubin as a marker in predicting Appendicular perforation.

Serum bilirubin levels	Intra-operative finding		Total
	Perforated	Simple	
Elevated	19	9	28
Normal	10	62	72
Total	29	71	100

From Table 6, following values were calculated as -

**Sensitivity:** sensitivity of bilirubin in predicting acute appendicitis and Appendicular perforation diagnosis was 65.5% (Table 6).

**Specificity:** Specificity of bilirubin in predicting acute appendicitis and appendicular perforation diagnosis was 87.3% (Table 6).

**Positive predictive value:** Positive predictive value of bilirubin in predicting acute appendicitis and

Appendicular perforation diagnosis was 67.9. (Table 6).

**Negative predictive value:** Negative predictive value of bilirubin in predicting acute appendicitis and Appendicular perforation diagnosis was 76.5%. (Table 6).

**Odds ratio:** Odds ratio is 13. (Table 6).

**Table 7:** Liver function tests in study population.

Parameters	Mean
Total bilirubin (mg/dL)	0.9
Direct bilirubin (mg/dL)	0.7
Indirect bilirubin (mg/dL)	0.2
SGOT (U/L)	27.9
SGPT (U/L)	25.9
ALP (U/L)	80.8

The mean Total bilirubin of all 100 patients was  $0.9 \pm 0.7$  mg/dL (range, 0.2 - 1.6 mg/dL) while the Direct bilirubin was  $0.7 \pm 0.4$  mg/dL (range, 0.3-1.1 mg/dL). The mean SGOT and SGPT were  $27.9 \pm 12.2$  U/L (range, 15.7-40.1 U/L) and  $25.9 \pm 11.0$  U/L (range, 14.9 - 35.9 U/L). The mean ALP values were  $80.8 \pm 21.6$  U/L (range, 59.2 -102.4 U/L) (Table 7).

**Total 8:** bilirubin in study population.

Total bilirubin (mg/dL)	Number	Percentage
< 1.0	72	72.0
≥ 1.0	28	28.0
Total	100	100.00

72 patients (72%) of all 100 patients were found to have normal bilirubin levels ( $\leq 1.0$  mg/dL), while 28 patients (28%) had raised bilirubin levels ( $> 1.0$  mg/dL) (Table 8).

**Table 9:** comparison of mean serum bilirubin levels in patients with appendicitis and Appendicular perforation.

Bilirubin levels (mg/dL)	Diagnosis	
	Acute appendicitis	Appendicular perforation
	Mean	Mean
Total bilirubin	0.7	1.9
Direct bilirubin	0.6	1.2
Indirect bilirubin	0.1	0.7

The mean bilirubin levels in patients diagnosed with Acute appendicitis was  $0.7 \pm 0.4$  mg/dL (range, 0.3 - 1.1 mg/dL) while in patients diagnosed with Appendicular perforation was  $1.9 \pm 1.16$  mg/dL (range, 0.74 - 3.06 mg/dL). The Direct bilirubin and Indirect bilirubin in patients diagnosed with Acute appendicitis were  $0.6 \pm 0.4$  mg/dL and  $0.1 \pm 0.2$  respectively. The Direct bilirubin and Indirect bilirubin in patients diagnosed with Appendicular perforation were  $1.2 \pm 1.06$  mg/dL and  $0.70 \pm 0.33$  mg/dL respectively (Table 9).

**Table 10:** Correlation of acute appendicitis and appendicular perforation with total serum bilirubin levels.

Serum bilirubin (mg/dL)	Final diagnosis (n=100)			
	Acute appendicitis (n=71)		Appendicular perforation (n=29)	
	Number	%	Number	%
>1.0	9	12.7	19	65.5
≤1.0	62	87.3	10	34.5
Total	71	100.00	29	100.00

9 patients (12.7%) of the total patients diagnosed with Acute appendicitis (n=71) were found to have elevated bilirubin levels (> 1.0 mg/dL) while 62 patients (87.3%) had normal bilirubin levels (≤ 1.0 mg/dL). Similarly, 19 patients (65.5%) of the total patients diagnosed with Appendicular perforation (n=29) were found to have elevated bilirubin levels (> 1.0 mg/dL) while 10 patients (34.5%) had normal bilirubin levels (≤ 1.0 mg/dL) (Table 10).

## Discussion

In this study of 100 patients, hyperbilirubinemia was found in 19 of 29 patients with gangrenous/perforated appendicitis. This hyperbilirubinemia was mixed in type (both conjugated and unconjugated) in most of the patients and at the same time there was no elevation or minimal elevation (<100 U/L) in ALT and AST in most of the cases. For gangrenous/perforated appendicitis, the P-value of SB was <0.001, specificity 87.3%, sensitivity 65.5%, positive predictive value 67.9% and negative predictive value was 86.1% and accuracy value of 81%. The level of Serum bilirubin was higher than 1 mg/dL in cases of gangrenous/perforated appendicitis while in cases with acute appendicitis it was lower than 1mg/dL (P<0.05). Broadly, we can say that it was predominantly isolated hyperbilirubinemia in the majority of cases. These findings are almost similar to another reported study. Since these findings were documented at the time of admission, it is unlikely that liver injury because of anesthetic agents, blood transfusion, or medication was the cause of elevated bilirubin levels. The most likely explanation of the rise in SB is therefore circulating endotoxemia as a result of appendiceal infection. It was demonstrated by Sisson et al in 1971 that in appendicitis mucosal ulceration occurs early and this facilitates invasion of bacteria into the muscularis

propria of the appendix thereby causing classical acute suppurative appendicitis. Subsequent events lead to edema, elevated intraluminal pressure and ischemic necrosis of mucosa, causing tissue gangrene and perforation. This process is associated with progressive bacterial invasion most likely facilitated by bacterial cytotoxins. The number of organisms isolated from patients with gangrenous appendicitis is five times greater than those with acute suppurative appendicitis. This elevated load of bacteria in appendicitis causes either direct invasion or translocation into the portal venous system. Direct invasion of bacteria into the hepatic parenchyma interferes with the excretion of bilirubin into the bile canaliculi by a mechanism that is thought to be caused by the bacterial endotoxin and is biochemical in nature rather than obstructive. Indirect evidence of bacterial translocation from inflamed gastrointestinal tract or peritonitis to the liver via the portal vein and the development of hepatitis and pyogenic liver abscess was observed by Dieulafoy. Two classical findings were described: firstly, simultaneous inflammation of the intestine (e.g. appendix), peritoneum and development of pyogenic liver abscesses and secondly, bacteriological similarities of the gastrointestinal tract and pyogenic liver abscesses. These bacteria commonly reach liver from intra-abdominal organs, commonly from the appendix.<sup>23</sup> Recently, in one study, blood samples from the superior mesenteric vein in acute appendicitis showed bacteria in 38% of patients. These findings suggest that bacteria may transmigrate and produce portal bacteremia, hepatocellular dysfunction or pyogenic liver abscess. Thus, it is concluded that hepatocellular function is depressed during the early stage of sepsis despite the increased cardiac output and hepatic blood flow and decreased peripheral resistance. The depression of hepatocellular function in the early, hyper-dynamic stage of sepsis does not appear to be due to reduction in hepatic perfusion but is associated with elevated levels of circulating pro-inflammatory cytokines such as TNF and IL-6. Thus up regulation of TNF and/or IL-6 may be responsible for producing hepatocellular dysfunction during the early hyper-dynamic stage of sepsis.

Our study shows that isolated hyperbilirubinemia without much elevation in the liver enzymes is a significant predictor of appendiceal perforation. This was demonstrated by a study by Estrada et al and other studies showing nearly a threefold risk of perforated appendicitis in patients with total bilirubin levels greater than 1 mg/dL. The positive predictive value of Serum bilirubin in our study

is 67.9%, comparable to other published studies 80%. The negative predictive value of Serum bilirubin was 86% in our study as compared to 100% to other study. Therefore, in suspected cases of appendicitis elevation of Serum bilirubin can be used as a criterion to diagnose and manage acute appendicitis, especially when there is doubtful differential diagnosis were considered like right uretric colic, mesenteric adenitis, right salphingitis. Both sensitivity and specificity of elevated total Serum bilirubin level in acute appendicitis with perforation and/or gangrene is higher as compared to TLC and liver enzyme.

### Conclusion

This study suggests Serum bilirubin levels appears to be a promising new laboratory marker for diagnosing acute appendicitis. Patients with clinical signs and symptoms of appendicitis and with hyperbilirubinemia higher than the normal range should be identified as having a higher probability of Appendicular perforation. Since the rise in Serum bilirubin level was significantly higher in patients with appendiceal perforation in the study. Serum bilirubin has a definite predictive potential in these cases suggesting, serum bilirubin levels have a predictive potential for the diagnosis of Appendicular perforation. Therefore, obtaining Serum bilirubin values upon admission can be used in conjunction with more modern diagnostic tests such as CT scan, ultrasonography to help determine the presence of perforation and thus aid in prompt clinical management. Serum bilirubin levels may be considered as one more positive factor for strong suspicion of appendicitis or perforated appendix in differential diagnosis of right iliac fossa pain.

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