

## Original Research Article

# A study on the role of raised serum bilirubin levels in acute appendicitis and its outcomes

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### ABSTRACT

**Background:** Acute appendicitis is the most common general surgical emergency and early surgical intervention improves outcomes. Despite the increased use of ultrasonography, computed tomography and laparoscopy, the rate of misdiagnosis of appendicitis has remained constant (15.3%) as has the rate of appendicular perforation. Thus, elevated serum bilirubin level will help in the early and accurate diagnosis of acute appendicitis and if so does it have the predictive capacity to warn us about appendicular perforation.

**Methods:** In this study 100 patients were selected as per satisfaction of the inclusion criteria. This study was carried out at SRM medical college hospital between July 2017 to October 2018. All the data findings were recorded and were analysed.

**Results:** In this study 100 patients were selected on satisfying the inclusion criteria. The serum bilirubin levels were recorded for all these patients. Based on the study it was found out that the serum bilirubin levels was elevated in majority of the cases of acute appendicitis and markedly elevated in case of perforated appendicitis. Though the results were not statistically significant the study seems to be clinically significant.

**Conclusions:** Serum bilirubin level seems to be a reliable diagnostic marker for predicting acute appendicitis and perforated or gangrenous appendicitis.

**Keywords:** Acute appendicitis, Perforated/gangrenous appendicitis, Serum bilirubin, Total counts

### INTRODUCTION

The most common cause of acute abdomen is Appendicitis. The diagnosis of acute appendicitis is based on clinical history and physical examination.<sup>1</sup> Appendectomy is the most commonly performed abdominal surgery. 15-30% of appendectomy specimen found to be normal.<sup>2</sup> In order to decrease the number of unnecessary appendectomy, significance of laboratory investigations like white blood cells, C-reactive protein, etc. have been emphasised. Ultrasonogram abdomen has been widely accepted as the diagnostic tool for appendicitis.<sup>3</sup> Many number of scoring system were

developed to arrive the diagnosis. These scoring systems are based on clinical features, laboratory investigations. Some examples are Alvarado, modified Alvarado, Ripasa.<sup>4</sup>

Still there is no definitive laboratory marker for acute appendicitis and appendicular perforations. Studies show that serum bilirubin is raised in acute appendicitis and appendicular perforations. But the significance of which is not stressed. On bacterial invasion of the appendix, there is transmigration of bacteria and release of pro-inflammatory cytokines like TNF  $\alpha$ , IL6. is difficult to diagnose in cases of retrocaecal or retroileal appendix.

The cytokines enter the superior mesenteric vein and reach the liver and produce inflammation, abscess and liver dysfunction.<sup>5</sup> Based on this background, the above said study was done in view of understanding the relation between acute appendicitis and raised serum bilirubin levels and to ascertain its use as a tool for diagnosing acute appendicitis and in that case, appendicular perforation can be accurately predicted using raised serum bilirubin levels.

- To know the relationship between raised serum bilirubin levels in acute appendicitis and its use as a tool for diagnosing acute appendicitis.
- To assess whether the diagnosis of perforated appendicitis be evaluated with increase in serum bilirubin levels.

## METHODS

A prospective study was undertaken in the Department of General Surgery, SRM Medical College Hospital & Research Centre, Kanchipuram District of Tamil Nadu for a period of 16 months from July 2017 to October 2018 on 100 patients. Approval from SRM Institutional Scientific and Ethical committee was obtained to conduct the study. The study population was patients admitted with diagnosis of acute appendicitis or perforated appendicitis on admission.

### Selection of cases

The method of selection was to select 100 patients as per the inclusion and exclusion criteria in the order date of their admission admitted in general surgery ward within the study period, without any other methods of randomization. The case selection was made based on clinical diagnosis of acute appendicitis or perforated appendicitis on admission.

### Inclusion criteria

Inclusion criteria were patients who are diagnosed as acute appendicitis clinically on admission; patients who are diagnosed as appendicular perforation clinically on admission; only patients with histopathological report suggestive of acute appendicitis or appendicular perforation were included.

### Exclusion criteria

Exclusion criteria were patients with previous history of jaundice or liver pathology; patients with alcoholism (>40 g/day for men and >20 g/day in women for 10 years); hemolytic disease; acquired or congenital diseases of the biliary tree; patients who are HBsAg positive; patients who have gall stone disease; patients who have malignancy of hepato-biliary system.

Informed written consent was obtained from each of the cases. All subjects were interviewed and examined by the

single observer. History and clinical examination were done for all and recorded in the proforma.

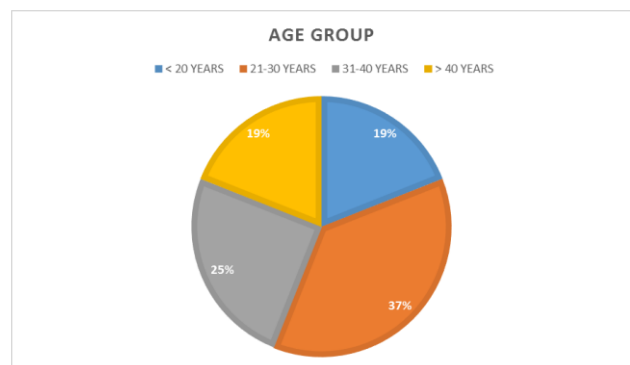
Following tests were carried out on admission.

- Routine blood investigations (Complete blood count, platelet count, reticulocyte count).
- Peripheral smear to rule out haemolytic anemia.
- Serum Bilirubin (Total and Direct bilirubin).
- Liver Function Tests (LFTs) which include SGPT /ALT, SGOT/AST, ALP.
- HbsAg screening.
- Urine routine.

Statistical analysis was done with SPSS software version 19. Univariate analysis was done for each parameter between the two groups. Chi square test and unpaired T test were done and p value was calculated. A p value of <0.05 was taken as significant.

## RESULTS

A total of 100 patients with clinical diagnosis of acute appendicitis or appendicular perforation admitted in the Department of General surgery, SRM medical college, Chennai were studied. As per the study, the age group 21-30 years is most commonly affected (37%) followed by age group 31-40 (25%) (Figure 1). The youngest patients of this study were of 15 years old while the oldest patient was a 59 years old. Out of the 100 patients included in the study 61 patients (61%) were males and the remaining 39 patients (39%) were females.



**Figure 1: Age distribution among cases.**

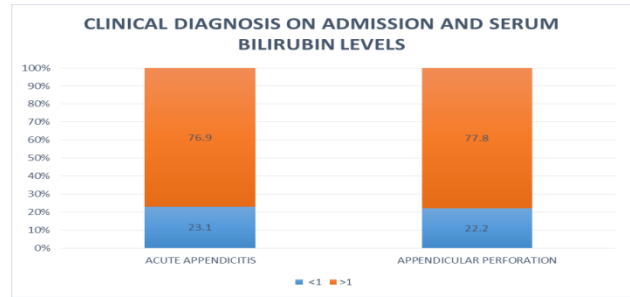
The mean Total bilirubin of all 100 patients was  $1.51 \pm 0.77$  mg/dL (range, 0.74–2.28 mg/dL) while the direct bilirubin was  $0.98 \pm 0.70$  mg/dL (range, 0.28–1.68 mg/dL). The mean SGOT and SGPT were  $27.70 \pm 12.51$  U/L (range, 15.19– 40.21 U/L) and  $26.32 \pm 11.75$  U/L (range, 14.57–38.07 U/L). The mean ALP values were  $79.90 \pm 25.06$  U/L (range, 54.84–104.96 U/L) (Table 1).

23 patients (23%) of all 100 patients were found to have normal bilirubin levels ( $\leq 1.0$  mg/dl), while 77 patients (77%) had raised bilirubin levels ( $> 1.0$  mg/dl) (Table 2). Of the 91 patients diagnosed as uncomplicated acute

appendicitis clinically on admission 70 patients (76.9%) had raised serum bilirubin levels (>1 mg/dl) and 21 patients (23.1%) had bilirubin levels (<1 mg/dl). Of the 9 patients diagnosed as appendicular perforation on admission 7 patients (77.8%) had raised serum bilirubin levels (>1 mg/dl) and 2 patients (22.2%) had bilirubin levels (<1 mg/dl) (Table 3) (Figure 2).

**Table 1: Mean values of different parameters among.**

	N	Min	Max	Mean
Age	100	15	59	31.07
Total count	100	1200	22540	9896.00
Total bilirubin	100	0.60	4.40	1.5119
Direct bilirubin	100	0.10	3.80	0.9855
Indirect bilirubin	100	01	1.4	.531
SGOT	100	10	91	27.75
SGPT	100	10	94	26.32
ALP	100	22	132	79.90
Valid N (listwise)	100			



**Figure 2: Comparison between clinical diagnosis on admission and serum bilirubin.**

**Table 2: Total bilirubin levels.**

	Freq	%	Valid percent	Cumulative percent
Valid	≥1	77	77.0	77.0
	<1	23	23.0	100.0
	Total	100	100.0	100.0

**Table 3: Clinical diagnosis on admission vs total bilirubin levels.**

		Total bilirubin		Total	
		≥1	< 1		
Clinical diagnosis on admission	Acute appendicitis	Count	70	21	91
		% within clinical diagnosis on admission	76.9%	23.1%	100.0%
	Appendicular perforation	Count	7	2	9
		% within clinical diagnosis on admission	77.8%	22.2%	100.0%
Total		Count	77	23	100
		% within clinical diagnosis on admission	77.0%	23.0%	100.0%

Intra operatively 62 patients (74.7%) diagnosed with acute appendicitis had elevated serum bilirubin levels (>1 mg/dl) and remaining 21 patients had serum bilirubin levels (<1 mg/dl) Intra operatively 15 patients (88.2%) diagnosed with appendicular perforation had elevated serum bilirubin levels (>1 mg/dl) and remaining 2 patients (11.8%) had serum bilirubin levels (<1 mg/dl).

**DISCUSSION**

Acute abdomen mostly occurring during childhood and in young adults is acute appendicitis. The most widely done emergency surgery is appendectomy which is mostly, first major operative procedure done by a trainee surgeon.<sup>1</sup> Close to 8% of the total western population might experience appendicitis once in their lifespan.<sup>5</sup> Acute appendicitis is most common during the second and third decades and is least encountered in infants, and has high incidence among children and young adults. Before puberty, both males as well as females are equally affected. Whereas in adolescents and in early adulthood, male are more commonly affected than females in the ration 3:2 around the age of 25. 12% of males and 25% of females have a lifetime risk of undergoing appendectomy.<sup>6,7</sup> Acute appendicitis is caused mainly due to luminal obstruction with faecoliths being the most

common cause of obstruction.<sup>5</sup> Other causes include lymphoid hypertrophy, malignancy, Worm infestations.<sup>8</sup>

The normal colon and the appendix have the same bacterial microorganisms. Escherichia Coli and Bacteroids fragilis are the most common microorganism present in both complicated appendicitis and in uncomplicated appendicitis. The flora may contain a broad spectrum of aerobic, facultative as well as anaerobic bacterium.<sup>8</sup>

The diagnosis of acute appendicitis is made out mainly by clinical examination; however, the decision to perform appendectomy on the basis of clinical suspicion only can lead to negative appendectomy in 15-50% of cases.<sup>9</sup> Moreover it is wise to operate on a normal appendix rather than delaying the diagnosis which may lead on to complications in 50% cases.<sup>10</sup> Even with the advent of variety of lab tests and imaging modalities, a new diagnostic tool which aids in diagnosing acute appendicitis would be welcomed.

Elevated levels of bilirubin help in accurately supporting the diagnosis of uncomplicated appendicitis and predicting the complications of appendicitis.

The present study was undertaken with the concept that bilirubin levels can be added to diagnose acute appendicitis and in that case if helpful, does it have the credibility to even give us an idea about the complications of appendicitis.

The significance of raised serum bilirubin levels and its relation to acute appendicitis has been hypothesized only of late. Till date very few case reports are available in writing which describe the role of elevated serum bilirubin levels in acute appendicitis.<sup>11</sup>

It is also being postulated that there is a relation which exists between raised serum bilirubin levels and complications of appendicitis.<sup>11</sup> This study was taken up to evaluate the role of raised serum bilirubin levels in acute appendicitis and to evaluate its credibility as a new diagnostic marker in a case of acute appendicitis and, to know whether they can accurately predict the diagnosis of perforated appendicitis.

The present study was undertaken in, General Surgery department, SRM medical college hospital and research centre, Chennai over a period of 16 months from July 2017 to October 2018 on a total of 100 patients who are diagnosed with acute appendicitis or perforated appendicitis.

Of the 100 patients who were enrolled for the study 61 patients (61%) were males while 39 patients (39%) were females. Mean age of the study group of 100 patients was found to be  $31.07 \pm 10.86$  years (range 20.21-41.93). As per the literature, the incidence of appendicitis are most commonly encountered in patients in second to fourth decade of life.<sup>6,7</sup>

In our study hyperbilirubinemia ( $>1.0$  mg/dL) was seen in 77 (77%) of the 100 patients who were enrolled, while the other 23 patients (23%) had normal levels of bilirubin ( $\leq 1.0$  mg/dl) while Estrada et al had registered raised serum bilirubin levels in 59 (38%) of 157 patients enrolled with appendicitis.<sup>11</sup>

Of all 100 patients, the mean serum bilirubin value was  $1.51 \pm 0.77$  mg/dl (range 0.74–2.28 mg/dl), much above the normal value ( $\leq 1.0$  mg/dl) which was considered for the study, hence indicating the occurrence of raised serum bilirubin levels.

Mean direct bilirubin was  $0.98 \pm 0.70$  mg/dl (range 0.28–1.68 mg/dl) and the mean indirect bilirubin was  $0.53 \pm 0.25$  mg/dl (range, 0.28–0.78 mg/dL). The findings of our study was consistent with hyperbilirubinemia which was documented by Khan S, where he found that average serum bilirubin levels in his study was around 2.38 mg/dL.<sup>12</sup>

The SGOT and SGPT of all the patients were well under the normal limits, thus underlying liver pathology was excluded as per the exclusion criteria. The mean levels of

SGOT and SGPT were  $27.70 \pm 12.51$  U/L (range 15.19 - 40.21 U/L) and  $26.32 \pm 11.75$  U/L (range 14.57–38.07 U/L) respectively. Mean values of ALP were  $79.90 \pm 25.06$  U/L (range, 54.84–0.96 U/L).

Of the 100 patients enrolled for the study population, 91 (91%) were diagnosed to have acute appendicitis preoperatively while the remaining 09 (9%) were diagnosed to have perforated appendicitis.

The clinical diagnosis was later confirmed post-surgery with the help of histopathological examination (HPE) and others with different preoperative diagnosis were excluded. Among those patients who were diagnosed with uncomplicated appendicitis (n=77), 62 (80.5%) of them had elevated bilirubin ( $>1.0$  mg/dL) while remaining 15 patients (19.5%) had normal bilirubin levels ( $\leq 1.0$  mg/dL).

Among those patients who were diagnosed with Appendicular perforation (n=23), 21 (91.3%) of them had raised serum bilirubin levels ( $>1.0$  mg/dL), and remaining 2 (8.7%) had normal levels ( $>1.0$  mg/dL). Thus concluding that, raised serum bilirubin levels was seen in majority of the patients who were diagnosed as acute appendicitis (80.5%) and appendicular perforation (91.3%).

The WBC count which was increased in 35 patients (35%) out of 100 enrolled patients. Mean WBC count of all patients enrolled was  $10030 \pm 3721$ /mm<sup>3</sup> (range 6319–13741/mm<sup>3</sup>).

On ultrasonographic examination, 73 patients (73%) were diagnosed to have acute appendicitis, while 14 patients (14%) diagnosed to have Appendicular perforation and remaining 13 patients (13%) had normal sonographic recordings. The sonography was 87% sensitive for acute appendicitis and perforated appendicitis, therefore sonography is a useful diagnostic imaging modality for appendicitis and its complications.

Mean serum bilirubin levels in all patients with acute appendicitis was found to be  $1.45 \pm 0.69$  mg/dl (range 0.76–2.14 mg/dl) and in patients with perforated appendicitis was found to be  $2.05 \pm 1.28$  mg/dl (range 0.77–3.33 mg/dl). Therefore, 65 patients with perforated appendicitis had relatively raised serum bilirubin level compared to those of acute appendicitis. So we conclude that, in patients with acute appendicitis with raised bilirubin levels, are at more risk of having perforated appendicitis rather than those with moderate or no increase in bilirubin levels.

In the study by Sand et al, the mean serum bilirubin levels in those diagnosed with perforated appendicitis were found to be much higher than those who were diagnosed with uncomplicated appendicitis.<sup>13</sup> The range of direct and indirect bilirubin in patients with acute appendicitis were found to be  $0.93 \pm 0.61$  mg/dl and

0.52±0.25 respectively whereas the range of direct and indirect bilirubin in patients with perforated appendicitis were found to be 1.40±1.25 mg/dl and 0.56±0.18 mg/dl respectively.

Sensitivity, specificity, PPV, NPV and Odds ratio were calculated using a 2×2 table. The sensitivity and specificity of serum bilirubin levels in predicting acute appendicitis and perforated appendicitis was 75.86% and 15.38%. Whereas the PPV and NPV of serum bilirubin in diagnosing acute appendicitis and perforated appendicitis was 85.71% and 8.69%. The Odds ratio was at 0.571. Sensitivity in our present study was higher than documented by Sand et al where, he analysed the sensitivity and specificity of his study of raised serum bilirubin levels in predicting perforated appendicitis was around 70% and 86.0%.<sup>13</sup>

## CONCLUSION

Our study indicates that serum bilirubin levels will be a helpful marker in diagnosing acute appendicitis, but however clinical examination is most important. The levels can definitely help in diagnosing acute appendicitis and its complications which will be handy investigation tool. The patients admitted with signs and symptoms of acute appendicitis with elevated serum bilirubin levels higher than the normal range therefore have a higher probability of perforated appendicitis. Thus, bilirubin levels have been a good diagnostic tool for predicting perforated appendicitis.

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*Ethical approval: The study was approved by the Institutional Ethics Committee*

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