

ORIGINAL RESEARCH

**“ROLE OF RAISED SERUM BILIRUBIN LEVELS IN THE PREDICTION OF APPENDICULAR PERFORATION”**

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**ABSTRACT**

**Background:** Given the foregoing, the aims of the present study were to (1) establish whether hyperbilirubinemia is associated with acute appendicitis; (2) evaluate its validity as a diagnostic marker for acute appendicitis; and (3) establish whether elevated bilirubin levels might predict appendicular perforation. The goal of this study is to determine whether or not preoperative serum bilirubin levels are useful for diagnosing appendicular perforation. The goals of this study were to (1) determine whether serum bilirubin is associated with acute appendicitis, and (2) evaluate its usefulness as a diagnostic marker for this illness. For the purpose of determining whether or not elevated serum bilirubin levels can be used as a predictor of appendicular perforation.

**Results:** Eighty individuals who were diagnosed with acute appendicitis or appendicular perforation and needed immediate appendectomy were included in our analysis. Subjects were given proper resuscitation prior to participation in the study. In order to collect and record patient data, we employed the standard proforma. Patients with complex appendicitis often require a longer recovery time (9.5 days) than those with acute appendicitis (5.5 days). The postoperative diagnosis is statistically significantly related to the length of hospital stay (p0.0001). This highlights the need for a novel diagnostic aid for acute appendicitis. Hyperbilirubinemia has been linked to acute appendicitis, and its significance to the condition has been hypothesised in the medical literature. The hope that serum bilirubin would be useful as a new laboratory marker in the diagnosis of acute appendicitis prompted the current investigation. The purpose of this research was to investigate the association between hyperbilirubinemia and acute appendicitis, to test its validity as a diagnostic marker for this condition, and to determine whether or not elevated bilirubin levels are a reliable predictor of appendicular perforation.

**Conclusion:** Eighty patients hospitalised with a preoperative diagnosis of acute appendicitis who underwent emergency appendectomy between November 2019 and October 2021 will be included in a two-year prospective study conducted by the Department of General Surgery at NRI Medical College, Chinakakani. The total blood bilirubin levels of individuals with perforated and gangrenous appendicitis were substantially greater than those of those with acute appendicitis. When predicting gangrenous or perforated appendicitis, a high total serum bilirubin level has a high negative predictive value but low specificity. Total blood bilirubin is therefore a valuable indicator in patients suspected of perforated or gangrenous appendicitis, and should be used in conjunction with the clinical examination and other laboratory techniques to evaluate patients suspected of appendicitis.

**Keywords:** Appendectomy, serum bilirubin, appendicular perforation, postoperative diagnosis, examination, retrocaecal.

## INTRODUCTION

The most prevalent reason for an urgent surgical abdomen is acute appendicitis.<sup>[1,2]</sup> The most common emergency abdominal operation is an appendectomy, which is frequently the first major procedure done by a surgeon in training.<sup>[1]</sup> Despite advancements in radiographic and laboratory investigations, appendicitis diagnosis remains a conundrum. Around 80% of the time, experienced doctors can diagnose appendicitis using a combination of history, physical examination, and laboratory tests.<sup>[3]</sup> Even while most people with acute appendicitis are easily recognised, the signs and symptoms might be changeable in rare circumstances, making a definitive diagnosis challenging. When the appendix is retrocaecal or retroileal, this is especially true. The percentage of appendectomies when the appendix is later discovered to be normal ranges from 15 to 50%,<sup>[4]</sup> with postoperative problems occurring in up to 50%,<sup>[5]</sup> of these individuals. In certain studies, a delay in diagnosing acute appendicitis leads to perforation and peritonitis, as well as a 50-90 percent increase in mortality.<sup>[6,7]</sup> An appendectomy, as soon as the problem is suspected, appears to be a safe option. The number of needless appendectomies rises with this treatment strategy. Additional laboratory tests such as WBC and CRP,<sup>[8]</sup> scoring systems, ultrasound Imaging,<sup>[9-12]</sup> computed tomography (CT) scan, scintigraphy, MRI, and laparoscopy have all been used to try to arrive at a faster and more accurate diagnosis. None of these techniques are stand-alone; they all complement and supplement an initial clinical evaluation. Elevation in serum bilirubin levels was reported in recent studies. In acute appendicitis and appendicular perforation, however, the impact of an increased total bilirubin level has not been emphasised.<sup>[13]</sup> It is generally known that when microbes infiltrate the body, leukocytes protect it, resulting in an increase in the number of leukocytes. Bacterial invasion in the appendix causes bacteria to transmigrate and proinflammatory cytokines such TNF-alpha, IL6, and cytokines to be released. These substances enter the liver through the superior mesenteric vein (SMV) and affect hepatic blood flow, causing inflammation, abscess, or dysfunction.<sup>[14-20]</sup> This may lead to an increase in serum bilirubin levels. In light of the foregoing, the goal of this study was to determine the association between hyperbilirubinemia and acute appendicitis, assess its validity as a diagnostic marker for acute appendicitis, and determine if raised bilirubin levels might predict appendicular perforation.

## AIM AND OBJECTIVES

### Aim

- To evaluate the diagnostic value of pre-operative serum bilirubin levels in predicting appendicular perforation.

### Objective

- To investigate the link between serum bilirubin and acute appendicitis, as well as to assess its validity as a diagnostic marker for the condition.
- To evaluate if the raised serum bilirubin levels have predictive potential in diagnosing appendicular perforation.

## MATERIALS & METHODS

The study took place from October 2020 to May 2022 in Department of General Surgery at the NRI Medical College, Chinakakani.

**Study Design:** Prospective, non-randomized, observational study.

**Source of date:** Patients admitted in NRI Medical College and Hospital with a pre-operative diagnosis of an acute appendicitis or complicated appendix undergoing emergency appendectomy throughout the research period.

**Study Place:** NRI Medical College and Hospital, Chinakakani.

**Study Period:** October 2020 – May 2022

**Sample Size:** A total of 80 individuals were studied, all of whom had been diagnosed with acute appendicitis or appendicular perforation.

### Inclusion criteria for selection of cases:

1. Patients who are willing to give consent
2. Age > 15 years
3. On admission, all patients who were clinically diagnosed with acute appendicitis and appendicular perforation.
4. Only individuals with a histological report indicating acute appendicitis or perforation of the appendix were included.

### Exclusion criteria for selection of cases:

1. All of the patients that have a documented history of
  - Liver disease or jaundice
  - Chronic alcoholic
  - Hemolytic disease
  - Congenital or Acquired biliary disease.
2. All patients with positive HBsAg, HCV
3. All the patients with hepatobiliary dysfunction

**Procedure:** After formulating the study design, clearance of ethics was obtained from “Ethics Committee” of the institution. Based on the selection criteria, patients with acute appendicitis or appendicular perforation as a clinical diagnosis admitted under the Department of Surgery, NRI Medical College and Hospital, Chinakakani, during the research period are screened for the eligibility. Those patients who are eligible were explained about the nature of the study, and a written/informed consent (Annexure I) was obtained from those

patients who had consented. A detailed history was taken, clinical examination done for all patients, and the findings were noted on a predesigned and pretested proforma (Annexure-II).

**At the time of admission, the following investigations were conducted.**

1. Routine blood tests
2. Blood peripheral smear to rule out hemolytic anemia.
3. Serum Bilirubin levels (Total and Direct bilirubin)
4. Liver Function Tests
5. Seropositivity for Hepatitis B
6. Urine analysis
7. USG Abdomen

The blood bilirubin and LFTs were determined using the hospital's Auto Analyzer equipment, and HbsAg was determined using the ELISA / Spot method using the HEPALISA<sup>®</sup> or HEPACARD<sup>®</sup> kit.

**Table No 1: Reference Range of Serum Bilirubin and Liver Enzymes**

Test	Normal Range
<b>Serum Bilirubin</b>	
Total Bilirubin	0.3-1.0 mg / dl
Direct Bilirubin	0.1-0.3 mg / dl
<b>Liver Enzymes</b>	
SGPT	0-35 U/L
SGOT	0-35 U/L
ALP	30-120 U/L

According to the aforementioned reference values, the findings were classified as 'Normal' or 'Raised' (hyperbilirubinemia). All patients with a clinical picture of an acute appendicitis were operated on, and histopathological investigation was performed after surgery to confirm the diagnosis. The final histological examination was used as gold standard to diagnose and classify individuals with acute appendicitis, acute appendicitis with perforation or gangrene. Patients were classified as positive (acute appendicitis with perforation or gangrene) or negative (acute appendicitis without perforation or gangrene) based on histological examination.

**Statistical Analysis:** The data was collated and statistical analysis was performed using Microsoft Excel spreadsheets and SPSS software version 15. The continuous variables were reported as Mean $\pm$ SD, and categorical variables were presented as absolute numbers and percentages. The normal distribution of the data was checked before analysis. Unpaired t-test and chi-square test were used to analyze normally distributed continuous and categorical variables, respectively. A 2x2 table was used to compute sensitivity, specificity, negative predictive value, positive predictive value and odds ratio. A p value of less than 0.05 was considered significant in all statistical tests.

## RESULTS

In our study on “**Study of Serum Bilirubin Levels in the Prediction of Appendicular Perforation**” conducted from October 2020 up to May 2022 at NRI Medical College, 80 patients with clinically diagnosed acute appendicitis or appendicular perforation who underwent emergency appendicectomy were included in the study. Before being put into the study, patients were appropriately resuscitated. The standard proforma was used to gather and document patient information. The data and values were gathered into a master chart, and the observations that followed were made.

**Table 2: Age Wise Distribution of Patients**

Age group (years)	No of patients	Percentage
16-20	31	38.8%
21-30	28	35%
31-40	12	15
41-50	5	6.2%
51-60	2	2.5%
Above 60	2	2.5%
Total	80	100%

The majority of the patients in this study were people between the ages of 16 and 20. This age group accounts for 38.8% of all cases. The average age of the population was 26.8 years.

**Table 3: Sex Wise Distribution of Patients**

Sex	No. of Patients	Percentage
Male	46	57.5%
Female	34	42.5%

Majority of the patients were males accounting for 57.5% of study population.

**Table 4: Mean Age Distribution among Sex**

Sex	Mean (years)	SD
Male	25.86	9.2
Female	27.56	12.3

The overall mean of study population is 26.8 SD11. The mean of the male population is 27.56 SD12.3 and that of the females is 25.86 SD9.2.

**Table 5: Sex Distribution According To Age Group**

Age group (years)	Male	Female
16-20	17	14
21-30	18	10
31-40	5	7
41-50	3	2

51-60	1	1
Above 60	2	0
Total	46	34

**Table 6: Liver Function Tests**

Parameters	Mean±SD		
	All patients (n=80)	Complicated Appendicitis	Uncomplicated Appendicitis
Total Bilirubin (mg / dl)	1.26±0.98	2.27±1.34	0.96±0.59
Direct Bilirubin (mg / dl)	0.89±0.87	1.76±1.36	0.64±0.42
Indirect Bilirubin (mg / dl)	0.39±0.26	0.64±0.26	0.32±0.21
SGOT (IU/L)	38.2±22.7	55.8±32.1	33±16.2
SGPT (IU/L)	31.2±17.68	49.61±24.54	25.85±10.38
ALP (IU/L)	81.28±44.2	124.11±58.04	68.85±29.89

**Table 7: Distribution of Liver Enzymes**

Liver Enzyme Test	Acute appendicitis	Complicated Appendicitis	Total
<b>SGOT (Normal range 0-35 U/L)</b>			
Normal	48	5	53
Minimally elevated(>1 times - <2times)	14	9	23
Moderately elevated(>2times)	Nil	4	4
Total	62	18	80
<b>SGPT (Normal range 0-35U/L)</b>			
Normal	52	4	56
Minimally elevated(>1 times - <2times)	10	9	19
Moderately elevated(>2times)	Nil	5	5
Total	62	18	80
<b>ALP (Normal range 30-120U/L)</b>			
Normal	58	8	66
Minimally elevated(>1 times - <2times)	4	10	14
Moderately elevated(>2times)	Nil	Nil	Nil
Total	62	18	80

**Table 8: Total Bilirubin Levels**

Total bilirubin (mg / dl)	Number	Percentage
≤1.0	43	53.7%
>1.0	37	46.3%

In this study, 46.3% (n=37) of study participants had raised Serum Bilirubin levels of >1mg/dl and 53.7% (n=43) had serum bilirubin levels in the normal range (≤1 mg/dl).

**Table 9: Serum Bilirubin Levels in Patients with Uncomplicated Acute Appendicitis**

Total bilirubin (mg/dl)	Distribution in population with uncomplicated appendicitis (n=62)	
	Number	Percentage
≤1.0	38	61.3%
>1.0	24	38.7%
Total	62	100%

In our study, 62 patients out of 80 had uncomplicated appendicitis of which 38.7% had serum bilirubin of >1 mg/dl.

**Table 10: Serum Bilirubin Levels in the Patients with Complicated Acute Appendicitis**

Total bilirubin (mg/dl)	Distribution in population with complicated appendicitis (n=18)	
	Number	Percentage
≤1.0	5	27.8%
>1.0	13	72.2%
Total	18	100%

Of the 80 patients in our study, 18 patients had complicated appendicitis and elevated serum bilirubin levels were observed in thirteen of them (72.2%).

**Table 11: Total Leucocyte Count**

TLC count (/mm <sup>3</sup> )	Distribution (n= 80)	
	Number	Percentage
<11,000	32	40%
>11,000	48	60%

It was observed that 60% of patients diagnosed with an appendicitis had raised total leucocyte counts of >11000/mm<sup>3</sup>.

**Table 12: Differential Leucocyte Count (DLC)**

Parameter		Mean	SD
Total count (/mm <sup>3</sup> )		12493.75	4690.12
Differential count	Neutrophils	68.08	11.83
	Lymphocytes	25.68	11.71
	Eosinophils	2.58	2.01
	Monocytes	3.38	2.37

In this study, the mean of the TLC count of all the cases was  $12493.75 \pm 4690.12/\text{mm}^3$ , in which majority of the cells are neutrophils  $68.08 \pm 11.83\%$  followed by lymphocytes  $25.68 \pm 11.71\%$ .

**Table 13: Pre-Operative Diagnosis**

Pre-operative diagnosis	Distribution (n=80)	
	Number	Percentage
Acute appendicitis	65	81.2%
Perforated/ Gangrenous appendicitis	15	18.8%

In the current study population of 80 patients, 65 of them were diagnosed with an acute appendicitis, whereas 15 were suspected of having perforated /gangrenous appendicitis pre operatively.

**Table 14: Ultrasonogram Finding**

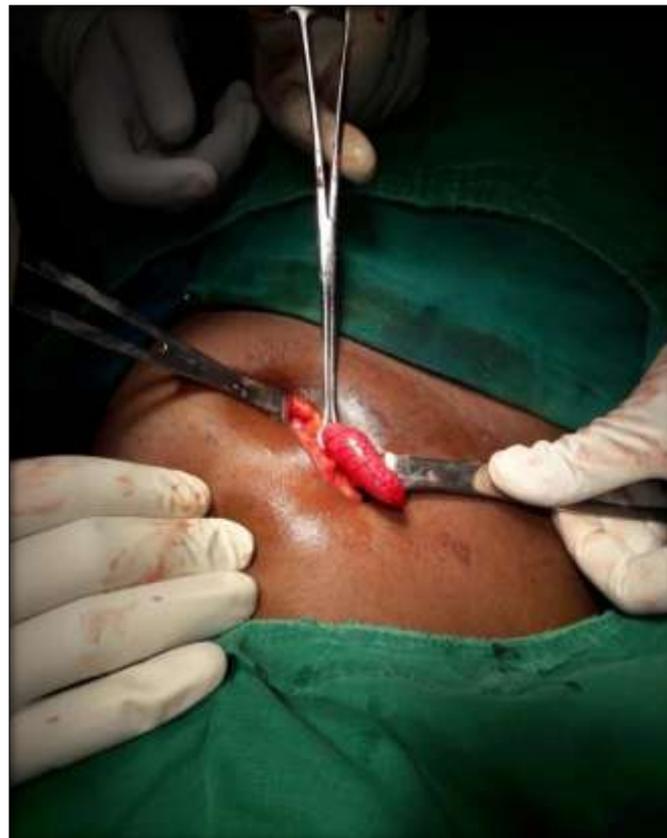
Ultrasonographic Findings	Distribution (n=80)	
	Number	Percentage
Acute appendicitis	65	81.2%
Perforated/ Gangrenous appendicitis	15	18.8%

On Ultrasonographic examination, 65 out of 80 patients had acute appendicitis, and 15 of them were diagnosed with perforated/gangrenous appendicitis.

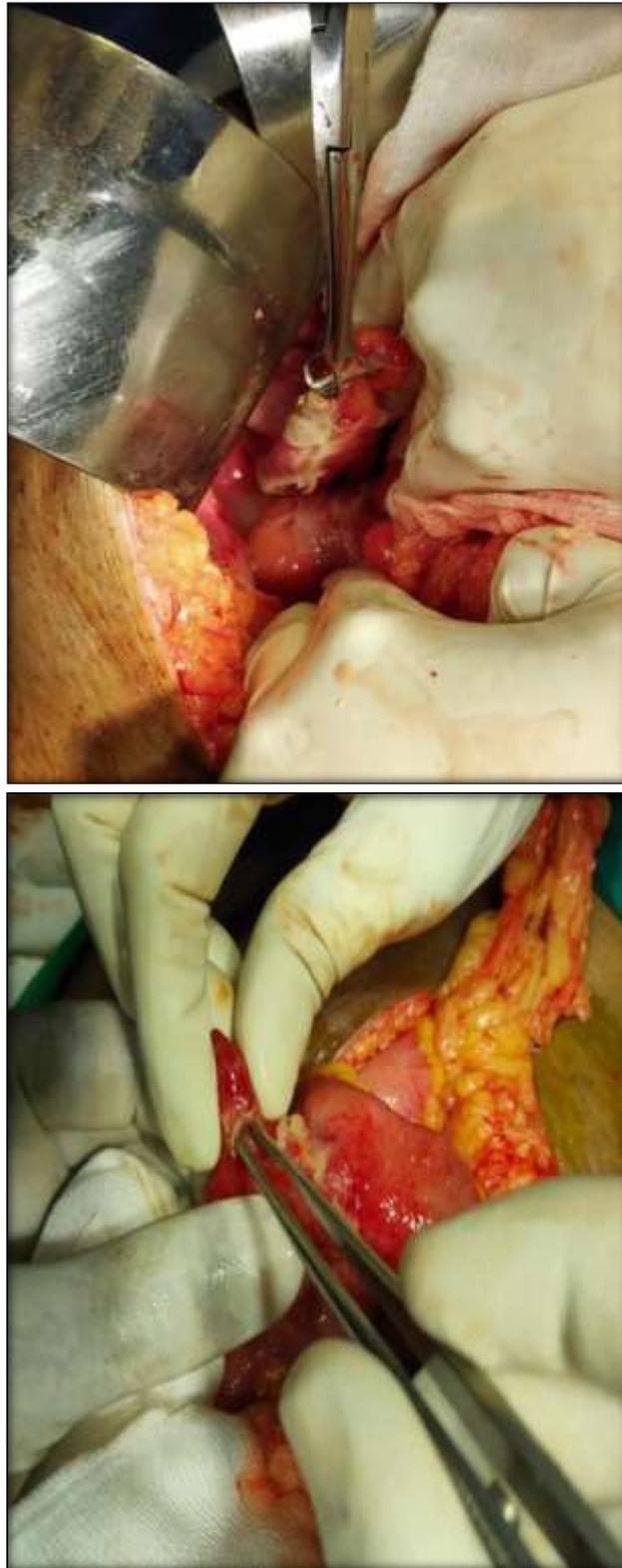
**Table 15: Per Operative Diagnosis**

Per-operative diagnosis	Distribution (n=80)	
	Number	Percentage
Acute appendicitis	63	78.75%
Perforated appendicitis	13	16.25%
Gangrenous appendicitis	4	5%

Intraoperatively, of the 80 patients, 63 patients had features of acute appendicitis and 13 had perforated appendicitis and 4 patients had features suggestive of gangrenous appendicitis.



**Figure 1: Intra operative images of Acute Appendicitis**



**Figure 2: Intra operative images of Perforated Appendix**



**Figure 3: Intra operative Image of Gangrenous Appendix**



**Figure 4: Specimen of Gangrenous Appendix**

**Table 16: Histopathological Diagnosis**

HPE diagnosis	Distribution (n=80)	
	Number	Percentage
Acute appendicitis	62	77.5%
Perforated appendicitis	14	17.5%
Gangrenous appendicitis	4	5%

On histopathological examination, 62 patients were confirmed to have acute appendicitis and 14 patients had perforated appendicitis and 4 cases were diagnosed with gangrenous appendicitis.

**Table 17: Comparison of Serum Bilirubin Levels in Patients with Acute Appendicitis and Complicated Appendicitis**

Bilirubin levels(mg/dL)			Diagnosis			
	Acute appendicitis		Complicated appendicitis		Total	
	Mean	SD	Mean	SD	Mean	SD
Total bilirubin	0.96	0.59	2.27	1.34	1.26	0.98
Direct bilirubin	0.64	0.42	1.76	1.36	1.89	0.87
Indirect bilirubin	0.32	0.21	0.64	0.26	0.39	0.26

The mean of serum total bilirubin levels in the patients diagnosed with acute appendicitis was  $0.96 \pm 0.59$ , and in the cases with perforated/ gangrenous appendicitis was  $2.27 \pm 0.134$ . The mean of total bilirubin of this study population is  $1.26 \pm 0.98$ . The direct and indirect bilirubin levels in the patients with acute appendicitis were  $0.64 \pm 0.42$  and  $0.32 \pm 0.21$  respectively. The direct and indirect serum bilirubin levels in the people with complicated appendicitis were  $1.76 \pm 1.36$  and  $0.64 \pm 0.26$  respectively.

**Table 18: Correlation of Acute Appendicitis and Appendicular Perforation with Total Serum Bilirubin Levels**

Serum bilirubin (mg/dL)	Final diagnosis (n=80)			
	Acute appendicitis(n=62)		Perforated / gangrenous appendix (n=18)	
	Number	Percentage	Number	Percentage
>1.0	24	38.7%	13	72.2%
≤1.0	38	61.3%	5	27.8%
Total	62	100%	18	100%

There was a statistically significant relationship between the serum bilirubin levels and complicated appendicitis with p value of 0.012.

**Table 19: The accuracy of serum bilirubin as a predictor of appendicular perforation**

From the above table, the following values were calculated:

Parameters	Accuracy
Sensitivity	72.22%
Specificity	61.3%
Positive predictive value	35.14%
Negative predictive value	88.37%
Odds ratio	4.12

Serum bilirubin's sensitivity and specificity in predicting perforated or gangrenous appendicitis were 72.22 percent and 61.3 percent, respectively. Similarly, the test has a

negative predictive value of 88.37 percent and a positive predictive value of 35.14 percent. The test's odds ratio was determined to be 4.12. The mean post-operative duration of stay is 9.5 days and 5.5 days for patients with complicated appendicitis and acute appendicitis, respectively. There is a statistical significant relation between the post-operative duration of stay and the postoperative diagnosis with a p value of <0.00001.

## DISCUSSION

Acute Appendicitis is the most prevalent cause of acute surgical conditions of the abdomen, and it is also the most usually misdiagnosed ailment. Emergency appendectomy is the most commonly done procedure for acute appendicitis worldwide. The lifetime risk is 8% for western population to develop acute appendicitis.<sup>[3]</sup>

Acute appendicitis is more common in people in their second and third decades of life. It is uncommon in infancy and old age, but more prevalent in youth and early adulthood. Prior to puberty, it affects both boys and girls equally. By the age of 25, the male-to-female ratio among young adults had risen to 3:2.<sup>[1]</sup> Males have a 12 percent lifetime chance of having an appendectomy, while females have a 25 percent lifetime risk, and around 7% of the population have an appendectomy for acute appendicitis.<sup>[22,23]</sup>

Appendicitis is thought to be caused by blockage of the appendicular lumen in the majority of cases.<sup>[3]</sup> These luminal obstructions are usually caused by faecolith. Less common causes are lymphoid tissue hypertrophy, intestinal parasites, and tumours.<sup>[21]</sup> The bacterial ecology of the appendix is typically comparable to that found in the large intestine.

The most prevalent bacteria found in normal appendix, acute appendicitis, perforated appendix, and gangrenous appendix are *Escherichia coli* and *Bacteroides fragilis*. However, a wide range of facultative and anaerobic microorganisms may be present.<sup>[21]</sup>

Acute appendicitis is diagnosed mostly by clinical examination. It might be difficult to make a good diagnosis since not all patients have the usual signs and symptoms of acute appendicitis. The diagnosis of an acute appendicitis is frequently misdiagnosed due to a variety of presenting symptoms and clinical indications, particularly in women. In 15 to 50 percent of instances, operating only on clinical suspicion might result in the removal of a healthy appendix.<sup>[4]</sup> Additional testing, expectant care, or both can help with the correct diagnosis of appendicitis.

The above-mentioned delay in diagnosis might result in appendiceal perforation or gangrene, increasing morbidity. An appendectomy should be performed as soon as the problem is detected; nevertheless, this technique results in an unneeded appendectomy. The notion that removing a normal appendix is preferable than delaying diagnosis does not hold up, especially in the elderly, as such surgeries are linked with complications in 50% of instances.<sup>[1,5]</sup> As a result, despite breakthroughs in numerous laboratory and radiographic examinations, diagnosing appendicitis remains a challenge.

The best way to treat acute appendicitis is still up for dispute, with numerous studies suggesting that conservative, nonoperative treatment may be possible. Many other tests, scoring systems, ultrasound imaging, CT, MRI, and laparoscopy can be used to diagnose acute appendicitis accurately and quickly. None of the aforementioned tests can detect acute appendicitis on their own, and they are always inferior to a clinical examination and signs unless they are used together.

As a result, a new tool to aid in the diagnosis of acute appendicitis would be helpful. The relevance of hyperbilirubinemia and its link to acute appendicitis has been suggested in the literature, and it has been speculated that there is a link between the two.<sup>[27]</sup>

Hyperbilirubinemia is defined as increased bilirubin content in blood which can be either due to increased bilirubin production or defect in bilirubin metabolism and clearance. Numerous types of bacterial infection have been proved to accompany hepatic dysfunction in bile acid formation and its flow. The inflammatory mediators will cause cholestasis by impairing hepato-cellular and the bile duct function.<sup>[25]</sup>

In cases of perforated and gangrenous appendicitis, there will be translocation or transmigration of bacteria/ toxins/ cytokines, which causes in bacteraemia, resulting in invasion of bacteria into the liver parenchyma and interference with bile excretion. This, in the end, will produce hyperbilirubinemia, a well-known side effect in severe microbial infection, mainly in septic patients.<sup>[24]</sup> Elevated serum bilirubin levels will aid in the accurate clinical diagnosis of acute appendicitis and, more significantly, will aid in the foreseeing and prevention of acute appendicitis sequelae.

This study was motivated by the question of whether serum bilirubin may be used as a novel laboratory marker to help in the identification of acute appendicitis. Is it credible enough to assist us predict an imminent event complication of acute appendicitis, if so?

The goal of this study was to look at the link between hyperbilirubinemia and acute appendicitis, examine its reliability as a diagnostic marker for acute appendicitis, and see if increased bilirubin levels might predict appendicular perforation.

The current study is a two-year prospective study undertaken at the Department of General Surgery, NRI Medical College, Chinakakani, on 80 patients hospitalised with a preoperative diagnosis of acute appendicitis who underwent an emergency appendectomy between November 2019 and October 2021.

In our 80-patient research, 46 patients (57.5%) were men, whereas the remaining 34 patients (42.5%) were women. This remark was similar to other studies, such as by Jamaluddin M et al.,<sup>[28]</sup> who observed that of the 71 cases, 37(52.10%) were males and 34(47.90%) were females. Poras Chaudhary et al. stated in their study that out of 50 patients, 40 cases were males, and ten were female.<sup>[29]</sup> A similar result was also declared in a survey by Atahan et al.,<sup>[30]</sup> whereas Sand M et al stated that females had more preponderance than males.

**Table 20: Comparison of Sex in Various Studies**

<b>Studies</b>	<b>Males (%)</b>	<b>Females (%)</b>
Sand M et al	43.1	56.9
Khan S	64.5	35.5
Poras et al	80	20
Jamaluddin M et al	52.1	47.9
Lal A et al, <sup>[31]</sup>	57	43
Present Study	57.5	42.5

The majority of the patients in our research were young people between the ages of 16 and 20. This age group accounts for 38.8% of the cases. The average age of acute appendicitis

presentation was 26.8 years. Males had a mean and standard deviation of 25.86 and 9.2, respectively. Females had a mean and standard deviation of 27.56 and 12.3, respectively. The current study's population's mean age of distribution matches those of other studies. According to Poras Chaudhary et al., the average age was 27.1 years, with a mean age of  $26.93 \pm 9.33$ .<sup>[29]</sup> According to Khurshid Anwar et al., the average age of 964 patients included in study was 28.7 years.<sup>[32]</sup>

**Table 21: Comparison of Age in Various Studies**

Studies	Age(Mean in years)
Sand M et al	35.6
Khan S	29.5
Poras et al	26.9
Estrada JJ et al	31
Emmanuel et al	27
Khurshid Anwar et al	28.7
Present Study	$26.8 \pm 11$

Acute appendicitis was shown to be more prevalent in younger boys in our study. In the 16-to-30-year-old group, the male-to-female ratio is 1.45:1. Female patients ranging in age from 16 to 20 were the majority. Females have an equal or larger incidence of decreasing the ratio after 30 years. 'The condition is somewhat more prevalent in men, with a male: female ratio of 1.4:1 in teens and early adults, the male-female ratio climbs to 3:2 by age 25; after that, the larger prevalence in males reduces,' according to Addiss DG et al. in a journal.<sup>[22]</sup>

Pre-operatively, 65 patients (81.2%) were diagnosed with an acute appendicitis, and 15 patients (18.8%) were suspected with complicated appendicitis in the study group of 80 patients. The same was confirmed intraoperatively and later postoperatively by histopathological examination. Per operatively, 63 people were found to have acute appendicitis features, 13 had perforated appendicitis, and four of them had features suggestive of gangrenous appendicitis. On histopathological examination, 62 patients were confirmed to have acute appendicitis, and 14 patients had perforated appendicitis, and four cases were diagnosed as gangrenous appendicitis. Based on the final histological examination report, the study population was categorized into acute appendicitis without perforation and complicated appendicitis (appendicular perforation/gangrene).

Out of 80 individuals in this research, 43 had a normal total bilirubin value of less than 1.0 mg/dL (53.7%), while 37 had hyperbilirubinemia (46.3 percent). This is in line with the findings of Jamaluddin M et al., who found that "Of the 71 patients, total serum bilirubin was elevated in 41 (57.70 percent) of them,"<sup>[28]</sup> and Poras Chaudhary et al., who found that "Total SB (TSB) was raised in 38 (76 percent) cases, whereas 12 (24 percent) cases had normal TSB level."<sup>29</sup> In a study of 157 individuals with acute appendicitis, Estrada et al. discovered hyperbilirubinemia in 59 (38%) of the patients.<sup>[27]</sup> 87.7% of patients with acute appendicitis had elevated serum bilirubin levels in a study conducted by Khan et al. Other studies that had reported similar results were Agarwal et al, Wasnik et al, Emmanuel et al, Lal A et al, etc.

**Table 22: Comparison of Hyperbilirubinemia in Various Studies**

Studies	Tot. No. of patients with Hyperbilirubinemia			
	In the study population	%	In patients with Complicated Appendicitis	%
Sand M et al	134/538	24.9	73/113	64.6
Emmanuel et al	140/472	29.6	27/45	60
Estrada	59/157	37.5	23/41	56
Poras et al	38/50	76	8/8	100
Shaik KhaderBasha et al, <sup>[34]</sup>	45/100	45	19/25	76
Lal A et al	62/100	62	35/44	79.5
Lalrammuana	159/215	74	36/51	70.6
Present study	37/80	46.3	13/18	72.22

All the 80 patients had a mean total serum bilirubin of  $1.26 \pm 0.98$  mg/dL, which is somewhat higher than the usual range (1.0 mg/dL). The study population's mean direct and indirect bilirubin was  $0.89 \pm 0.87$  and  $0.39 \pm 0.26$ , respectively. In cases of simple appendicitis, the average was  $0.96 \pm 0.59$ . The mean bilirubin level in perforated or gangrenous appendicitis was  $2.27 \pm 1.34$ , which is significantly higher than the normal range, indicating hyperbilirubinemia. Direct and indirect bilirubin levels were  $0.64 \pm 0.42$  mg/dL and  $0.32 \pm 0.21$ , respectively, in individuals with acute appendicitis. In patients with appendicular perforation, direct and indirect bilirubin levels were  $1.76 \pm 0.36$  mg/dL and  $0.64 \pm 0.26$  mg/dL, respectively. In perforated or gangrenous appendix, total serum bilirubin was substantially higher ( $P < 0.05$ ) than in acute appendicitis. This was supported by Khan S et al findings' which indicated an average blood bilirubin level of 2.38 mg/dL in his research cohort.<sup>15</sup> In his research population with complex appendicitis, Poras Chaudhary et al. discovered a mean of 3.62 mg/dL.<sup>[29]</sup> In the current study, there was a statistically significant result between the serum bilirubin levels and complicated appendicitis with p value 0.012. Such similar results were also observed by Sand et al, Poras et al, Estrada et al, and Shaik KhaderBasha et al in their studies. Emmanuel et al in his study observed there was a high significance between serum bilirubin and complicated appendicitis with p value  $< 0.001$ . But Lalrammuana reported there is no statistical significance between the two variables with p value  $> 0.05$ . In their study, Sand et al. discovered that individuals with appendicular perforation had considerably higher mean bilirubin levels than those with nonperforated appendicitis.<sup>26</sup> As a result, we deduce that individuals with appendicitis-like symptoms and higher bilirubin levels are more likely to have perforated appendix than those with normal or slightly raised total blood bilirubin.

**Table 23: Comparison of Total Bilirubin Levels in Various Studies**

Studies	Mean total bilirubin			P value
	Overall	In Acute Appendicitis	In Complicated Appendicitis	
Sand M et al	0.9±0.6	0.8±0.5	1.5±0.9	<0.05
Emmanuel et al	1.22	1.09	1.35	<0.001
Poras et al	2.57±0.64	1.52±0.59	3.62±0.70	<0.001
Shaik Khader Basha et al, <sup>[34]</sup>	1.49±1.03	1.08±0.48	2.74±1.24	<0.001
Lalrammuana	1.54±0.7	1.46±0.6	1.56±0.8	>0.05
Present study	1.26±0.98	0.96±0.59	2.27±1.34	0.012

The liver enzyme SGOT was normal in 66.25% of patients, minimally elevated (<2 times) in 28.7%, and moderately high (>2 times) in 5% of all the cases. SGPT was normal in 70%, minimally elevated (<2 times) in 23.7%, and moderately elevated (>2 times) in 6.2% of the total patients. ALP was within the standard limit in 82.5% and minimally elevated in 17.5% of the patients. Within the study population, the mean of SGOT, SGPT, and ALP were 38.2±22.7, 31.2±17.68, and 81.28±44.2, respectively. It was also observed that, liver enzymes are elevated in cases of complicated appendicitis compared to acute appendicitis. The total leucocyte count was raised in 60% of all patients diagnosed with appendicitis, according to the findings of this investigation. The mean TLC count for all patients was 12493.75 ±4690.12/mm<sup>3</sup>, with neutrophils accounting for 68.29 ±11.83 percent of cells and lymphocytes accounting for 25.68 ±11.7 percent. These findings were in line with those of another research, Jamaluddin M et al.,<sup>[28]</sup> who claimed in their survey that "total leukocyte count was raised in 33 (46.5%) of the 71 patients." 'Mean WBC was 16.4 10<sup>3</sup>/L (SD, 5.2; 3.1 to 32.0 10<sup>3</sup>/L) for all the patients,' Hany Noh et al. noted.<sup>[33]</sup> The mean WBCs in the basic and difficult groups were both raised, with the complicated group having considerably higher levels.' Fifteen out of 18 patients with complicated appendicitis had total leucocyte count >11000 cells/mm<sup>3</sup>, and 33 of 62 patients with acute appendicitis had total leucocyte count >11000 cells/mm<sup>3</sup>. It was observed that there was a statistically significant relationship between the total leucocyte count and complicated appendicitis with p value 0.02.

The mean total leucocyte count of the study population is 12493.75±4690.12/mm<sup>3</sup>. The mean total leucocyte count of the patients with acute appendicitis and complicated appendicitis were 11583.87±3730.5 cells/mm<sup>3</sup> and 15627.78±6234.3 cells/mm<sup>3</sup> respectively.

**Table 24: Comparison of Total Leucocyte Count in Various Studies**

Studies	Total Leucocyte Count (Mean)	
	Overall	In Complicated Appendicitis
Sand M et al	11600±4600	14400±4600
Poras et al	11926±4378	12162±4624
Present Study	12493±4690	15627±6234

In this study, all patients underwent ultrasonography imaging, and acute appendicitis was diagnosed in 65 (81.2%) patients, and 15 (18.8%) patients were diagnosed with perforated or gangrenous appendix. Ultrasound was highly sensitivity for detecting complicated appendicitis, and so ultrasonography is a useful tool to diagnose acute appendicitis or appendicular perforation. The total blood bilirubin levels of 38 patients (61.3%) with uncomplicated acute appendicitis (n=62) were normal (1.0 mg/dL), whereas 24 patients (38.7%) had high total serum bilirubin levels (>1 mg/dl). Only 5 (27.8%) patients with perforated or gangrenous appendicitis (n=18) had total serum bilirubin levels within acceptable limits, whereas the remaining 13 (72.2%) had increased total serum bilirubin levels. As a result, hyperbilirubinemia was common in individuals with perforated or gangrenous appendicitis (72.2%). A 2x2 table was used to assess the sensitivity, specificity, positive predictive value, negative predictive value, and odds ratio for total serum bilirubin as a test for predicting gangrene or perforation of the appendix. Serum bilirubin had a sensitivity and specificity of 72.22 percent and 61.3 percent, respectively, in predicting perforated or gangrenous appendicitis. Likewise, the test's negative and positive predictive values are 88.37% and 35.14%, respectively. The odds ratio of the test was calculated to be 4.12.

**Table 25: Comparison of Accuracy in Various Studies**

Studies	Sensitivity	Specificity	PPV	NPV
Sand M et al	70%	86%	51%	93%
Khan S	82%	100%	100%	17.3%
Emmanuel et al	60%	70%	21%	92%
Poras et al	100%	92.9%	72.7%	100%
Shaik KhaderBasha et al, <sup>[34]</sup>	76%	65.33%	42.22%	89%
Lal A et al	69.2%	94.6%	-	-
Present Study	72.22%	61.3%	35.14%	88.37%

A single rise in total blood bilirubin without a substantial increase in liver enzymes was discovered in our study, which is a strong predictor of a ruptured or gangrenous appendix. Total serum bilirubin had a less specificity of 61.3 percent and a high sensitivity of 72.22 percent in our research. Higher sensitivity than the specificity which was observed in our study is consistent with those results by Poras et al and Shaik KhaderBasha et al. Whereas high specificity than sensitivity of the test is observed in the studies done by Sand M et al, Khan S, Emmanuel et al and Lal A et al. Hyperbilirubinemia exhibited an 86 percent specificity for appendiceal perforation or gangrene, according to Sand et al.<sup>[26]</sup> Poras et al and Emmanuel et al observed the specificity to be 92.9% and 70% respectively. Total Serum Bilirubin as an investigation in predicting perforated or gangrenous appendicitis has high negative predictive value than the positive predictive value. The negative predictive value was 88.37%, comparable to a study done by Poras Chaudhary et al., which showed 100%.<sup>[29]</sup> Similarly, 93% NPV was observed by Sand M et al, and 92% by Emmanuel et al. Estrada et al., found that in individuals with hyperbilirubinemia (>1.0 mg/dL), the probability of having a ruptured or gangrenous appendix was three times higher.<sup>[27]</sup>

The mean post-operative duration of stay is 9.5 days and 5.5 days for patients with complicated appendicitis and acute appendicitis, respectively. This indicates that the patients with complicated appendicitis had more duration of post-operative stay, which is consistent with the other studies. The limitations of the study are this is single centre study. The population size is less to be extrapolated to the general population. There is a chance of observer dependent variations during the ultrasonographical examination of appendix which may alter the preoperative diagnosis. In the past, only a few research studies have assessed the relation between serum bilirubin levels and appendicitis. Our study has limitations as to the limited sample size and the fact that it was conducted in only one location and so it can be recommended that further larger studies can be done in this area and this study can act as a guide for future studies. As a result, elevated serum bilirubin can be utilised as a test to identify and treat perforated or gangrenous appendicitis in individuals who are suspected of perforation or gangrene.

## CONCLUSION

Our study concludes that,

- Total blood bilirubin levels were significantly higher in perforated and gangrenous appendicitis patients than in acute appendicitis patients.
- The total serum bilirubin level is a very sensitive, but less specific, predictor of gangrenous or perforated appendicitis, with a strong negative predictive value.
- As a result, total serum bilirubin is a useful indicator in patients suspected of having perforated or gangrenous appendicitis, and it should be used in conjunction with the clinical examination and other laboratory procedures to evaluate patients suspected of appendicitis.

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