

EVALUATION OF HYPERBILIRUBINEMIA AS A NEW DIAGNOSTIC MARKER FOR ACUTE APPENDICITIS AND ITS ROLE IN THE PREDICTION OF APPENDICULAR PERFORATION

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ABSTRACT: BACKGROUND AND OBJECTIVES: 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 and if so, does it have the predictive capacity to warn us about appendicular perforation.

MATERIALS & METHODS: This one year cross sectional study was conducted in the Department of Surgery, HKE's Basaveshwar Teaching and General Hospital, Gulbarga attached to Mahadevappa Rampure Medical College, Gulbarga during the period of December 2010 to November 2011. A total of 100 patients with clinical diagnosis of acute appendicitis or appendicular perforation were studied. The serum bilirubin and liver function tests were carried out in all the patients. **RESULTS:** In this study, males (56%) outnumbered females (44%) and overall mean age was 23.1±11.99 years. Of the 100 patients, 81% were confirmed as acute appendicitis while 19% were diagnosed with appendicular perforation. Of 81 patients with acute appendicitis, 71.6% had raised bilirubin levels, while 28.4% had normal levels. 19 patients were diagnosed as appendicular perforation, 16 patients (84.21%) had raised bilirubin levels, while the remaining 03 patients (15.79%) had normal levels. The Sensitivity and Specificity of serum bilirubin as a marker in predicting acute appendicitis and appendicular perforation was 71.6% and 15.79% respectively. Similarly the Positive predicative value and Negative predicative value for the same was 78.38% and 11.54% respectively with odds ratio 0.472.

CONCLUSION: Serum bilirubin levels appear to be a promising new laboratory marker for diagnosing acute appendicitis and also promises to have a predictive potential for the diagnosis of appendicular perforation. Patients with clinical signs and symptoms of appendicitis and with hyperbilirubinemia double the normal range (Raise in Direct Bilirubin being still higher) should be identified as having a higher probability of Appendicular perforation suggesting, serum bilirubin levels have a predictive potential for the diagnosis of Appendicular perforation.

KEYWORDS: Acute Appendicitis; Appendicular Perforation; Hyperbilirubinemia; Serum Bilirubin.

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INTRODUCTION: Acute appendicitis is the commonest cause of "Acute Surgical abdomen"¹. Appendectomy is the most frequently performed urgent abdominal operation and is often the first major procedure performed by a surgeon in training.^{1,2} 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.³

LIST OF ABBREVIATIONS USED: ALP - Alkaline phosphatase, ALT - Alanine transaminase, AST - Aspartate transaminase, ATP - Adenosine triphosphate, cm - Centimeter(s), CRP-C-reactive protein, CT - Computed tomography, dL - Deciliter(s),

DLC - Differential leukocyte count, E. Coli - Escherichia coli, ELISA - Enzyme linked immunosorbent assay, g - Gram(s), HbsAg - Hepatitis B surface antigen, IL-6 - Interleukin-6, LFT - Liver function tests, mg - Milligram(s), mL - Milliliter(s), mm - Millimeter(s), n - Total number, NPV - Negative predictive value, OR - Odds ratio, PPV - Positive predictive value, SB - Serum bilirubin, SGOT - Serum glutamic oxaloacetic transaminase, SGPT - Serum glutamic pyruvic transaminase, SMV - Superior mesenteric vein, Sr. - Serum, TLC - Total leukocyte count, TNF - Tumor necrosis factor, TSB - Total serum bilirubin, USG - Ultrasonography, WBC - White blood cells.

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%.⁴ and postoperative complications can occur in up to 50%.⁵ of these patients. Delay in diagnosis of Acute Appendicitis leads to perforation and peritonitis and increased mortality. Perforation ranges 50-90% in various series.^{6,7}

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To supplement the clinical diagnosis 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.⁸ The use of Ultrasonography (USG) as a diagnostic tool for appendicitis has been widely known and studied.^{9,10,11,12} 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,¹³ and the Modified Alvarado score.¹⁴

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.¹⁵ 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.^{16,17,18,19,20, 21,22}

In view of the above context, the present study was undertaken to assess relationship between hyperbilirubinemia and acute appendicitis and to evaluate its credibility as a diagnostic marker for acute appendicitis and also, to see whether elevated bilirubin levels have a predictive potential for the diagnosis of appendicular perforation.

OBJECTIVES:

The objectives of the study were;

1. To study the relationship between hyperbilirubinemia and acute appendicitis; and to evaluate its credibility as a diagnostic marker for acute appendicitis.
2. To evaluate whether elevated bilirubin levels have a predictive potential for the diagnosis of appendicular perforation.

MATERIALS AND METHODS: The study was conducted in the Department of General Surgery, HKE's Basaveshwar Teaching and General Hospital, Gulbarga attached to Mahadevappa Rampure Medical College, Gulbarga during the period of December 2010 to November 2011.

Study Design: A one year cross sectional study.

Source: The present study was conducted in the Department of Surgery, HKE's Basaveshwar Teaching and General Hospital, Gulbarga attached to Mahadevappa Rampure Medical College, Gulbarga.

Study Period: One year from December 2010 to November 2011.

Source of Data: Patients admitted with clinical diagnosis of acute appendicitis or appendicular perforation under the Department of Surgery, HKE's Basaveshwar Teaching and General Hospital, Gulbarga during the study period.

Sample Size: A total of 100 patients with clinical diagnosis of acute appendicitis or appendicular perforation were studied.

Sampling Method: The sample size was calculated based on the following formula.

$$n = \frac{Z^2 \times p \times q}{d^2}$$

Where,

n = Sample size

Z = 1.96 \approx 2 (considering confidence as 95%)

p = prevalence (prevalence is taken as 50% as exact prevalence is not known)

q = 100 - p that is, 50%

d = Absolute error which was 10%

Selection Criteria:

Inclusion:

- All patients diagnosed as acute appendicitis clinically on admission.
- All patients diagnosed as appendicular perforation clinically on admission.
- For both these groups, only patients with histopathological report suggestive of acute appendicitis or appendicular perforation were included.

Exclusion:

- All patients documented to have a past history of-
 - Jaundice or Liver disease.
 - Chronic alcoholism (That is intake of alcohol of > 40 g/day for Men and > 20 g/day in Women for 10 years).
 - Hemolytic disease.
 - Acquired or congenital biliary disease.
- All patients with positive HBsAg.
- All patients with cholelithiasis.
- All patients with cancer of hepato-biliary system.

Procedure: Ethical clearance has been obtained from "Ethical Clearance Committee" of the institution for the study. It is in the form of signature from Head of Dept. Surgery and Dean of M R Medical College, Gulbarga. Based on the selection criteria patients admitted with clinical diagnosis of acute appendicitis or appendicular perforation under Department of Surgery, HKE's Basaveshwar Teaching and General Hospital, Gulbarga during the study period were screened for eligibility. The eligible patients were briefed about the nature of the study and a written informed consent (Annexure I) was obtained from the consented patients. Thorough history was taken and clinical examination was done for all patients and findings were recorded on predesigned and pretested proforma (Annexure II).

The following Tests were Carried Out on Admission;

- Routine blood investigations (Complete blood count, platelet count, reticulocyte count).
- Peripheral smear to rule out hemolytic anemia.
- Serum haptoglobin if peripheral smear and blood tests indicate features of 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).

The serum bilirubin and LFTs were carried out using the Auto Analyser (cobas c 111) machine available in the hospital and HbsAg was tested by ELISA / Spot technique using HEPALISA® or HEPACARD® kit.

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

Reference Range of Serum Bilirubin and Liver Enzymes.²³

The results were grouped as 'Normal' or 'Raised' (hyperbilirubinemia) as per the above reference values.

Statistical Analysis: The data obtained was tabulated on Microsoft excel spreadsheet and analysed as below.

- Patients with clinical diagnosis of acute appendicitis having hyperbilirubinemia were expressed in percentage as;

$$\text{Patients with clinical diagnosis of acute appendicitis with elevated Serum bilirubin level} = \frac{\text{Number of patients with raised bilirubin}}{\text{Total number of patients with acute appendicitis}} \times 100$$

All Patients with Clinical Diagnosis of Acute Appendicitis:

- Mean of the level of elevation of Serum bilirubin was calculated for patients with clinical diagnosis of acute appendicitis.
- Patients with clinical diagnosis of appendicular perforation having hyperbilirubinemia were expressed in percentage as;

$$\text{Patients with clinical diagnosis of a ppendicular perforation with elevated Serum bilirubin} = \frac{\text{Number of patients with raised bilirubin}}{\text{Total number of patients with appendicular perforation}} \times 100$$

All Patients with Clinical Diagnosis of Appendicular Perforation:

- Mean of the level of elevation of serum bilirubin were calculated for patients with clinical diagnosis of appendicular perforation.
- A hypothesis was made based on the observation of the level of the two means.
- Also, sensitivity, specificity, positive predictive value, negative predictive value and Odds ratio was determined by 2 x 2 table as below.

	Acute appendicitis	Appendicular perforation
Raised Sr. Bilirubin	A	B
Normal Sr. Bilirubin	C	D
	a + c	b + d

$$\text{Sensitivity: } \frac{a}{a + c} \times 100$$

$$\text{Specificity: } \frac{d}{b + d} \times 100$$

$$\text{Positive predictive value : } \frac{a}{a + b} \times 100$$

$$\text{Negative predictive value : } \frac{d}{c + d} \times 100$$

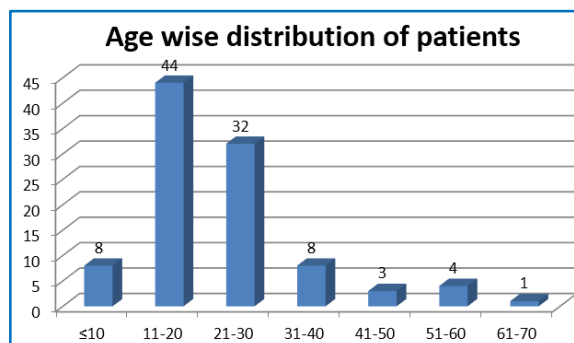
$$\text{Odds ratio: } \frac{ad}{Bc}$$

RESULTS: A total of 100 patients with clinical diagnosis of acute appendicitis or appendicular perforation admitted in the Department of General surgery, HKE's Basaveshwar Teaching & General Hospital, Gulbarga attached to Mahadevappa Rampure Medical College, Gulbarga were studied.

Age Group (years)						
≤10	11-20	21-30	31-40	41-50	51-60	61-70
8	44	32	8	3	4	1

Table 3: Distribution of patients by age

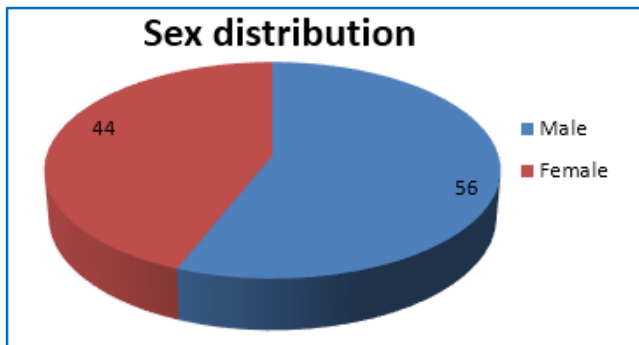
As per the study, the age group 11-20years is most commonly affected (44%) followed by age group 21-30 (32%). The youngest patients of this study were of 8 years old while the oldest patient was a 70 year lady.



Sex	Number	Percentage
Male	56	56
Female	44	44
Total	100	100.00

Table 4: Sex Distribution

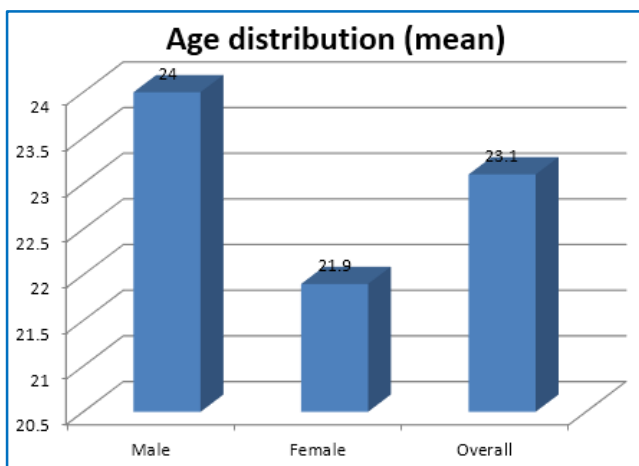
Out of 100 patients enrolled for the study, 56 patients (56%) were males while the remaining 44 patients (44%) were females.



Sex	Age (yrs)	SD
Male	24	11.93
Female	21.9	11.93
Overall	23.1	11.99

Table 5: Mean Age distribution among sex

The overall mean age of all 100 patients was 23.1±11.99 years (Range, 11.11-35.09 years). The average age in males and females was 24±11.93 years (Ange, 12.07-35.93 years) and 23.1±11.93 years (Range, 11.17-35.03 years) respectively.

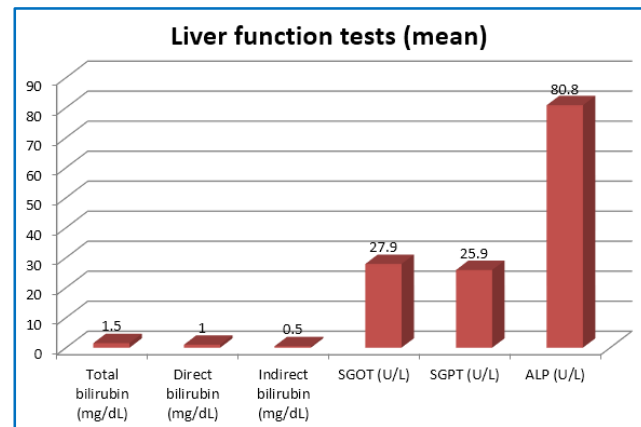


Parameters	Mean	SD
Total bilirubin (mg/dL)	1.5	0.8
Direct bilirubin (mg/dL)	1.0	0.7
Indirect bilirubin (mg/dL)	0.5	0.2
SGOT (U/L)	27.9	12.2
SGPT (U/L)	25.9	11.0
ALP (U/L)	80.8	21.6

Table 6: Liver Function Tests

The mean Total bilirubin of all 100 patients was 1.5±0.8mg/dL (Range, 0.7-2.3mg/dL) while the Direct bilirubin was 1.0±0.7mg/dL (Range, 0.3-1.7mg/dL). The

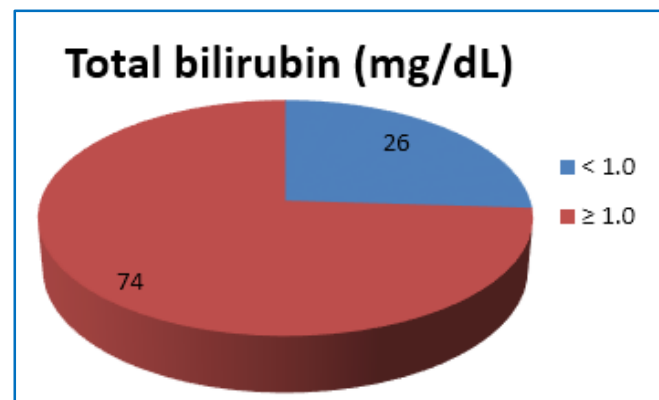
mean SGOT and SGPT were 27.9±12.2 U/L (Range, 15.7-40.1 U/L) and 25.9±11.0 U/L (Range, 14.9-35.9U/L). The mean ALP values were 80.8±21.6 U/L (Range, 59.2 -102.4 U/L).



Total bilirubin (mg/dL)	Number	Percentage
< 1.0	26	26.0
≥ 1.0	74	74.0
Total	100	100.00

Table 7: Total bilirubin levels

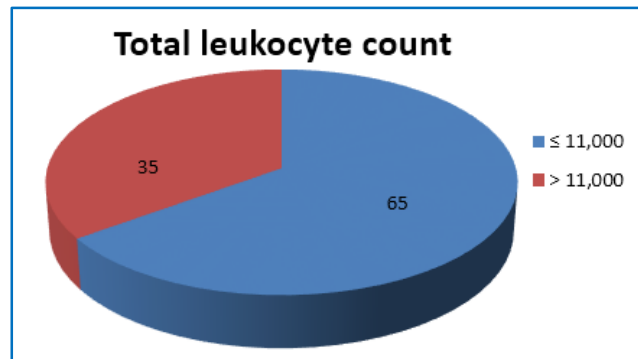
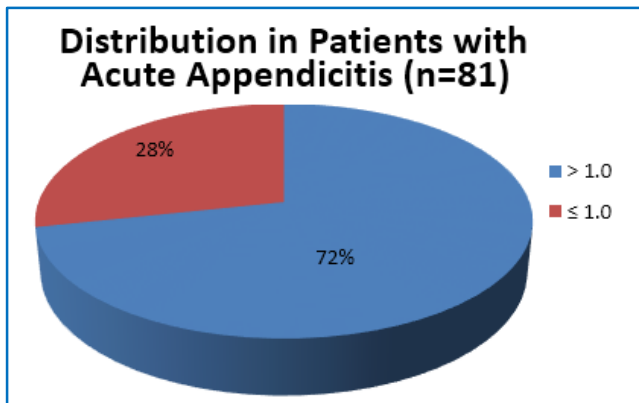
26 patients (26%) of all 100 patients were found to have normal bilirubin levels (≤1.0mg/dL), while 74 patients (74%) had raised bilirubin levels (>1.0mg/dL).



Total bilirubin (mg/dL)	Distribution in Patients with uncomplicated Acute Appendicitis (n=81)	
	Number	Percentage
> 1.0	58	71.60
≤ 1.0	23	28.40
Total	81	100.00

Table 8: Bilirubin levels in patients with uncomplicated acute appendicitis as diagnosis

Of 81 patients diagnosed as uncomplicated acute appendicitis, 58 patients (71.6%) had raised bilirubin levels (> 1.0mg/dL), while the remaining 23 patients (28.4%) had normal levels (≤ 1.0mg/dL).



Total bilirubin (mg/dL)	Distribution in Patients with Appendicular perforation (n=19)	
	Number	Percentage
> 1.0	16	84.21
< 1.0	03	15.79
Total	19	100.00

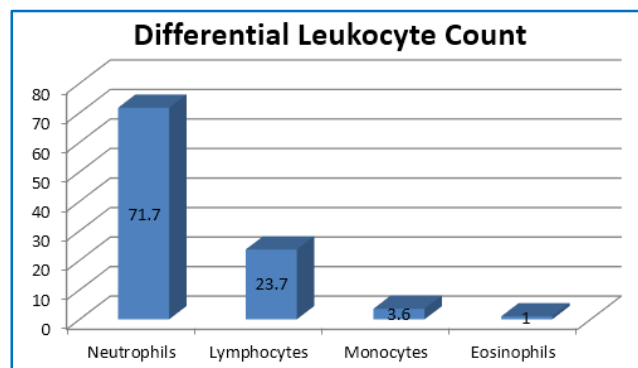
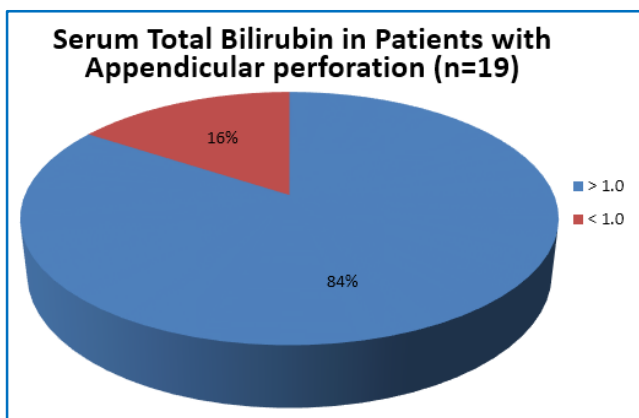
Table 9: Bilirubin levels in patients with Appendicular perforation diagnosis

Differential Leukocyte Count (DLC)	Mean value		
	Mean	SD	
Total count (/mm ³)	10030	3712	
Differential count	Neutrophils	71.7	11.5
	Lymphocytes	23.7	10.7
	Monocytes	3.6	2.6
	Eosinophils	1.0	1.4

Table 11: Differential Leukocyte Count (DLC)

19 patients diagnosed as appendicular perforation, 16 patients (84.21%) had raised bilirubin levels (>1.0mg/dL), while the remaining 03 patients (15.79%) had normal levels (≤1.0mg/dL).

The mean of TLC count in all patients was 10030±3712/mm³ (Range, 6318 - 13742/mm³), in which the highest percentage constituted neutrophils with 71.7% followed by 23.7% by Lymphocytes.



TLC count (/mm ³)	Distribution (n=100)	
	Number	Percentage
≤ 11,000	65	65
> 11,000	35	35
Total	100	100.00

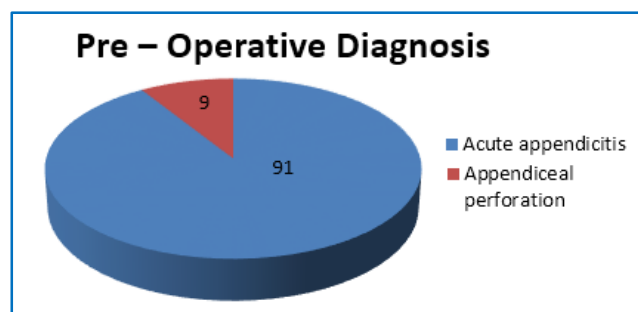
Table 10: Total leukocyte count (TLC)

Pre - Operative Diagnosis	Distribution (n=100)	
	Number	Percentage
Acute appendicitis	91	91
Appendicular perforation	09	09
Total	100	100

Table 12: Pre-Operative Diagnosis

65 patients (65%) had Total Leukocyte count less than 11,000/mm³ while 35 patients (35%) counts above 11,000/mm³.

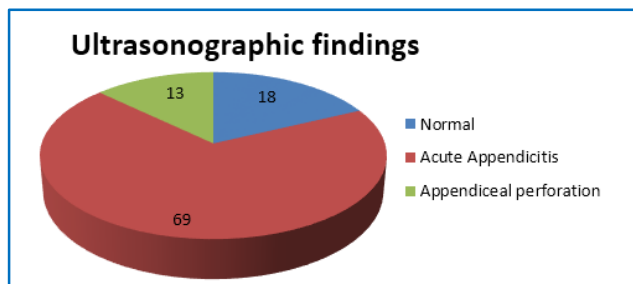
In the study population of 100 patients, 91 patients (91%) were diagnosed as acute appendicitis while 9 patients (9%) were diagnosed with appendicular perforation.



Findings	Distribution (n=100)	
	Number	Percentage
Normal	18	18
Acute Appendicitis	69	69
Appendicular perforation	13	13
Total	100	100

Table 13: Ultrasonographic Findings

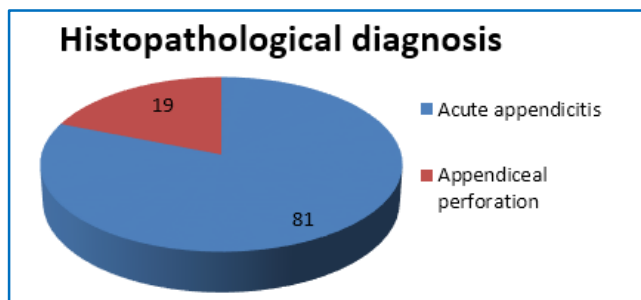
On Ultrasonography, 69 patients (69%) were diagnosed as acute appendicitis, 13 patients (13%) as appendicular perforation and 18 patients (18%) were reported as normal ultrasonographic findings.



Diagnosis	Distribution (n=100)	
	Number	Percentage
Acute appendicitis	81	81
Appendicular perforation	19	19
Total	100	100

Table 14: Histopathological Diagnosis

Histopathological, 81 patients (81%) were confirmed as acute appendicitis while 19 patients (19%) were diagnosed with appendicular perforation.

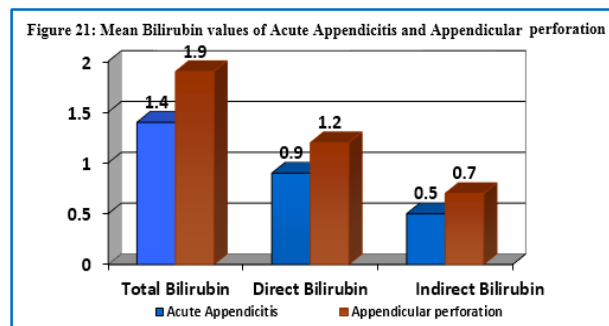


Bilirubin levels (mg/dL)	Diagnosis			
	Acute appendicitis		Appendicular perforation	
	Mean	SD	Mean	SD
Total bilirubin	1.4	0.65	1.9	1.16
Direct bilirubin	0.9	0.57	1.2	1.06
Indirect bilirubin	0.5	0.21	0.70	0.33

Table 15: Comparison of mean serum bilirubin levels in patients with acute appendicitis and Appendicular perforation

The mean bilirubin levels in patients diagnosed with Acute appendicitis was 1.4 ± 0.65 mg/dL (range, 0.75 - 2.05 mg/dL) while in patients diagnosed with Appendicular perforation was 1.9 ± 1.16 mg/dL (range, 0.74 - 3.06 mg/dL). The Direct bilirubin and Indirect bilirubin in patients diagnosed with Acute appendicitis were 0.9 ± 0.57 mg/dL and

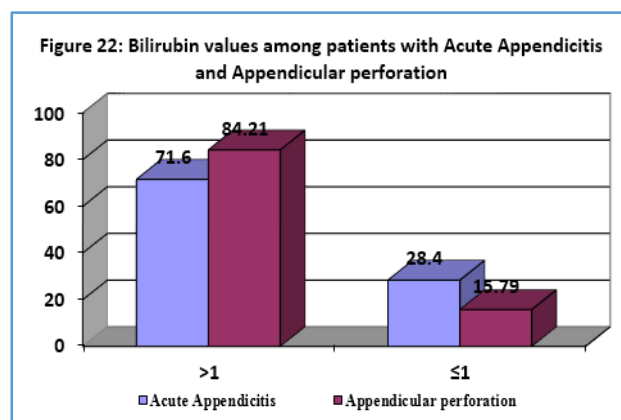
0.5 ± 0.21 respectively. The Direct bilirubin and Indirect bilirubin in patients diagnosed with Appendicular perforation were 1.2 ± 1.06 mg/dL and 0.70 ± 0.33 mg/dL respectively.



Serum bilirubin (mg/dL)	Final diagnosis (n=100)			
	Acute appendicitis (n=81)		Appendicular perforation (n=19)	
	Number	%	Number	%
> 1.0	58	71.6	16	84.21
≤ 1.0	23	28.4	03	15.79
Total	81	100.00	19	100.00

Table 16: Correlation of acute appendicitis and Appendicular perforation with total serum bilirubin levels

58 patients (71.6%) of the total patients diagnosed with Acute appendicitis (n=81) were found to have elevated bilirubin levels (>1.0mg/dL) while 23 patients (28.4%) had normal bilirubin levels (≤1.0mg/dL). Similarly, 16 patients (84.21%) of the total patients diagnosed with Appendicular perforation (n=19) were found to have elevated bilirubin levels (>1.0mg/dL) while 03 patients (15.79%) had normal bilirubin levels (≤1.0mg/dL).



Sensitivity

$$= \frac{a}{a+c} = \frac{58}{58+16} = 71.6\%$$

Therefore, sensitivity of bilirubin in predicting acute appendicitis and appendicular perforation diagnosis was 71.6%.

Specificity

$$= \frac{d}{b+d} = \frac{3}{16+3} = 15.79\%$$

Therefore, specificity of bilirubin in predicting acute appendicitis and appendicular perforation diagnosis was 15.79%.

Positive predictive value

$$= \frac{a}{a + b} = \frac{58}{58 + 16} = 78.38\%$$

Therefore, Positive predictive value of bilirubin in predicting acute appendicitis and appendicular perforation diagnosis was 78.38%.

Negative predictive value

$$= \frac{d}{c + d} = \frac{3}{23 + 3} = 11.54\%$$

Therefore, Negative predictive value of bilirubin in predicting acute appendicitis and appendicular perforation diagnosis was 11.54%.

Odds ratio:

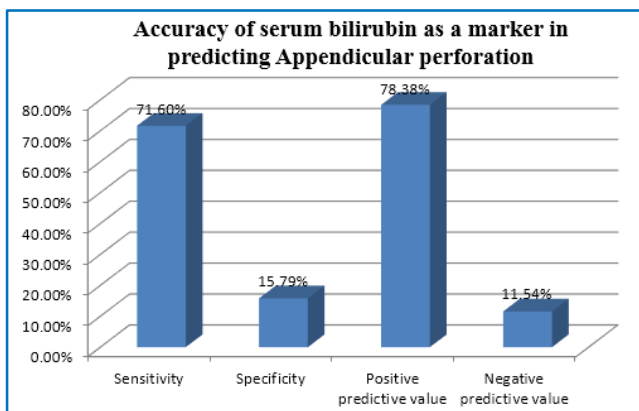
$$= \frac{ad}{bc} = \frac{58 \times 3}{23 \times 16} = 0.472$$

Therefore, Odds ratio is 0.472.

	Accuracy
Sensitivity	71.6%
Specificity	15.79%
Positive predictive value	78.38%
Negative predictive value	11.54%
Odds ratio	0.472

Table 17: Serum bilirubin as a marker in predicting appendicular perforation

The Sensitivity and Specificity of serum bilirubin as a marker in predicting acute appendicitis and appendicular perforation was 71.6% and 15.79% respectively. Similarly the Positive predicative value and Negative predicative value for the same is 78.38% and 11.54% respectively. The Odds ratio was calculated to be 0.472.



DISCUSSION: Acute appendicitis is the most common cause of ‘acute abdomen’ in young adults. Appendectomy is the most frequently performed urgent abdominal operation and is often the first major procedure performed by a surgeon in training.¹ About 8% of people in Western countries have appendicitis at some time in their lifetime. The peak incidence of acute appendicitis is in the second and third decade of life.

It is relatively rare in infants, and becomes increasingly common in childhood and early adult life. The incidence of appendicitis is equal in males and females before puberty. In teenagers and young adults, the male – female ratio increases to 3: 2 at age 25.¹The lifetime rate of appendicectomy is 12% for men and 25% for women, with approximately 7% of all people undergoing appendectomy for acute appendicitis during their lifetime.

Obstruction of the lumen is believed to be the major cause of acute appendicitis. Faecoliths are the usual cause of obstruction. Less- common causes are hypertrophy of lymphoid tissue, tumors, intestinal parasites.The bacteriology

of normal appendix is similar to that of normal colon. The principal organism seen in normal appendix, in acute appendicitis, and in perforated appendicitis are Escherichia Coli and Bacteroids fragilis. However a wide variety of both facultative and anaerobic bacteria may be present.

The diagnosis of acute appendicitis is essentially clinical; however, a decision to operate based on clinical suspicion alone can lead to the removal of a normal appendix in 15 to 50% of cases.⁴ The premise that it is better to remove a normal appendix than to delay diagnosis does not stand up to close scrutiny, particularly in the elderly¹ as such procedures are associated with complications in 50% cases.⁵ Hence, the diagnosis of Appendicitis still remains a dilemma in spite of the advances in various laboratory and radiological investigations.

A new tool to help in the diagnosis of acute appendicitis would thus be welcome. Serum Bilirubin level elevation will help in the accuracy of clinical diagnosis of acute appendicitis and more importantly help in foreseeing and preventing impeding complications of acute appendicitis. This study was taken up with this thought – that is it possible to add serum bilirubin as a new laboratory marker to aid in the diagnosis of acute appendicitis and if so, does it have the credibility to help us foresee an impending complication of acute appendicitis?

Importance of hyperbilirubinemia and its association in acute appendicitis has been postulated recently. There are only a few case reports in the available literature that describe the finding of hyperbilirubinemia in patients of acute appendicitis.²³ It is hypothesized that an association exists between hyperbilirubinemia and acute appendicitis and its complications.²³ The present study was undertaken to study the relationship between hyperbilirubinemia and acute appendicitis and to evaluate its credibility as a diagnostic marker for acute appendicitis and also, to evaluate whether elevated bilirubin levels have a predictive potential for the diagnosis of appendicular perforation.

This study was conducted in the Department of General Surgery, HKE’s Basaveshwar Teaching and General Hospital, Gulbarga over a period of one year from December 2010 to November 2011 on 100 patients with clinical diagnosis of acute appendicitis and appendicular perforation. In the present study of the 100 patients enrolled for the study, 56 patients (56%) were males while the remaining 44 patients (44%) were females.The mean age in our study population (100 patients) was 23.1±11.99 years (Range, 11.11–35.09 years).

This is consistent with the quoted incidence of Appendicitis in the literature where it is most frequently seen in patients in their second through fourth decades of life. The average age group in males 24±11.93 years (range, 12.07 – 35.93 years) was slightly higher than females 23.1±11.93 years (range, 11.17 –35.03 years). Hyperbilirubinemia (> 1.0mg/dL) in our study was found in 74 patients (74%) of all the 100 patients (n=100) enrolled in the study, while 26 patients (26%) had normal bilirubin levels (≤ 1.0mg/dL). Estrada et al,²³had found hyperbilirubinemia in 59 (38%) of 157 patients studied with acute appendicitis.

The mean total serum bilirubin of all 100 patients was 1.5±0.8mg/dL (Range, 0.7–2.3mg/dL), which was above the normal range (≤1.0mg/dL) considered for the study, hence indicating the occurrence of hyperbilirubinemia. The mean of Direct bilirubin was 1.0±0.7mg/dL (Range,0.3-1.7mg/dL) while that of Indirect bilirubin was 0.5±0.2mg/dL

(range, 0.3 – 0.7mg/dL). Our finding was consistent with hyperbilirubinemia found in a study conducted by Khan S,¹⁵ who found average level of serum bilirubin in his study population to be 2.38mg/dL.

All patients were found to have SGOT and SGPT within the normal range, thus excluding any associated liver pathology (Exclusion criteria). The mean SGOT and SGPT were 27.9±12.2 U/L (Range, 15.7-40.1 U/L) and 25.9±11.0 U/L (range, 14.9 – 35.9 U/L). The mean ALP values were 80.8±21.6 U/L (Range, 59.2 -102.4 U/L). In our study population of 100 patients, 91 patients (91%) were diagnosed as acute appendicitis pre-operatively while 09 patients (9%) were diagnosed with appendicular perforation. The diagnosis was confirmed post-operatively by histopathological reports (HPR) and those differing from the pre-operative diagnosis were excluded from the study.

Amongst the patients diagnosed with Acute appendicitis without perforation (n=81), 58 patients (71.6%) were found to have elevated bilirubin (>1.0mg/dL) while only 23 patients (28.4%) had normal bilirubin levels (≤1.0mg/dL). In patients diagnosed with Appendicular perforation (n=19), 16 patients (84.21%) had bilirubin elevated (>1.0mg/dL), while only 3 patients (15.79%) had normal levels (≤1.0mg/dL). Thus, Hyperbilirubinemia was found in most of the patients diagnosed with acute appendicitis (71.6%) or appendicular perforation (84.21%).

The total leukocyte count was found elevated in just 35 patients (35%) of the total 100 patients. The mean of TLC count in all patients was 10030±3712/mm³ (range, 6318 - 13742/mm³), in which the highest percentage constituted Neutrophils with 71.7% followed by 23.7% by Lymphocytes. On Ultrasonography, 69 patients (69%) were diagnosed as acute appendicitis, 13 patients (13%) as appendicular perforation and 18 patients (18%) were reported as normal ultrasonographic findings. Ultrasonography per-se was 82% sensitive for appendicitis and/or appendicular perforation, hence Ultrasonography is a helpful tool in diagnosing appendicitis or perforation.

The mean bilirubin levels in patients diagnosed with Acute appendicitis was 1.4±0.65mg/dL (Range, 0.75–2.05mg/dL) while in patients diagnosed with Appendicular perforation was 1.9±1.16mg/dL (Range, 0.74–3.06mg/dL). Hence, we see that patients with appendicular perforation had higher levels of bilirubin as compared to that of acute appendicitis. So we infer that, patients with features suggestive of appendicitis with higher values of bilirubin, are more susceptible of having appendicular perforation than those with normal or slightly elevated total serum bilirubin.

Sand et al,²⁴ in his study found the mean bilirubin levels in patients with Appendicular perforation to be significantly higher than those with a non-perforated appendicitis. The Direct bilirubin and indirect bilirubin in patients diagnosed with acute appendicitis were 0.9±0.57mg/dL and 0.5±0.21 respectively. Similarly, direct bilirubin and indirect bilirubin in patients diagnosed with appendicular perforation were 1.2±1.06mg/dL and 0.70±0.33mg/dL respectively. The Sensitivity, Specificity, Positive predictive value, Negative predictive value and Odds ratio was calculated from a 2x2 table. Sensitivity and Specificity of bilirubin in predicting acute appendicitis and appendicular perforation diagnosis was 71.6% and 15.79% respectively.

Similarly Positive predictive value and Negative predictive value of bilirubin in predicting acute appendicitis and appendicular perforation diagnosis was 78.38% and

11.54% respectively. The Odd's ratio was calculated to be 0.472. The sensitivity in our study was more than that by Sand et al²⁴ in which, he found the sensitivity and specificity in his study of hyperbilirubinemia for predicting Appendicular perforation to be 70% and 86.0% respectively.

CONCLUSION: The present study suggests;

- Serum bilirubin levels appears to be a promising new laboratory marker for diagnosing acute appendicitis, however diagnosis of appendicitis remains essentially still - clinical. Its level come out to be a credible aid in diagnosis of acute appendicitis and would be helpful investigation in decision making.
- 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 suggesting, serum bilirubin levels have a predictive potential for the diagnosis of Appendicular perforation.

SUMMARY: Acute appendicitis is the most common cause of 'acute abdomen' in young adults. Diagnosis of Appendicitis still remains a dilemma in spite of the advances in various laboratory and radiological investigations. Importance of hyperbilirubinemia or elevated Serum Bilirubin and its association in acute appendicitis has been postulated recently. It is hypothesized that an association exists between hyperbilirubinemia and acute appendicitis and its complications.

The present study was undertaken to assess relationship between hyperbilirubinemia and acute appendicitis and to evaluate its credibility as a diagnostic marker for acute appendicitis and also, to see whether elevated bilirubin levels have a predictive potential for the diagnosis of appendicular perforation. The present study was conducted in the Department of Surgery, HKE's Basaveshwar Teaching and General Hospital, Gulbarga during the period of December 2010 to November 2011. A total of 100 patients with clinical diagnosis of acute appendicitis or appendicular perforation were studied. The serum bilirubin and LFTs were carried out in all the patients.

In this study, males (56%) outnumbered females (44%) and overall the mean age was 23.1±11.99 years. Mean total bilirubin was noted as 1.5±0.8mg/dL (range, 0.7 – 2.3mg/dL) while direct bilirubin was 1.0±0.7mg/dL (0.2-1.7mg/dL). The mean SGOT and SGPT were 27.9±12.2 U/L (range, 15.7-40.1 U/L) and 25.9±11.0 U/L (range, 14.9 – 35.9 U/L). The mean ALP values were 80.8±21.6 U/L (range, 59.2 -102.4 U/L). Normal bilirubin values were seen in 26% patients while, 74% had raised bilirubin levels (Hyperbilirubinemia). Of 81 patients with acute appendicitis, 71.6% had raised bilirubin levels, while 28.4% had normal levels.

19 patients were diagnosed as appendicular perforation, 16 patients (84.21%) had raised bilirubin levels, while the remaining 03 patients (15.79%) had normal levels. The total leukocyte count was less than 11,000/mm³ in 65% patients while, 35% patients had counts above 11,000/mm³. Of the 100 patients, 91% were diagnosed as acute appendicitis clinically while 9% were diagnosed with appendicular perforation. On Ultrasonography, 82% patients were diagnosed with acute appendicitis or appendicular perforation while 18% had normal findings. Post-operatively 81% were confirmed as acute appendicitis while 19% were diagnosed with appendicular perforation.

The mean bilirubin levels in patients diagnosed with acute appendicitis was 1.4 ± 0.65 mg/dL (range, 0.75–2.05 mg/dL) while in patients diagnosed with Appendicular perforation was 1.9 ± 1.16 mg/dL (range, 0.74–3.06 mg/dL). The Direct bilirubin and indirect bilirubin in patients diagnosed with acute appendicitis was 0.9 ± 0.57 mg/dL and 0.5 ± 0.21 respectively. The Direct bilirubin and indirect bilirubin in patients diagnosed with appendicular perforation was 1.2 ± 1.06 mg/dL and 0.70 ± 0.33 mg/dL respectively.

58 patients (71.6%) of the total patients diagnosed with acute appendicitis (n=81) were found to have elevated bilirubin levels while 23 patients (28.4%) had normal bilirubin levels. Similarly, 16 patients (84.21%) of the total patients diagnosed with Appendicular perforation (n=19) were found to have elevated bilirubin levels while 03 patients (15.79%) had normal bilirubin levels. The Sensitivity and Specificity of serum bilirubin as a marker in predicting acute appendicitis and appendicular perforation was 71.6% and 15.79% respectively. Similarly the Positive predicative value and Negative predicative value for the same was 78.38% and 11.54% respectively with odds ratio 0.472.

Serum bilirubin levels appears to be a promising new laboratory marker for diagnosing acute appendicitis, however diagnosis of appendicitis is essentially still - clinical. Patients with clinical signs and symptoms of appendicitis and with hyperbilirubinemia double the normal range (Raise in Direct Bilirubin being still higher) should be identified as having a higher probability of Appendicular perforation suggesting, serum bilirubin levels have a predictive potential for the diagnosis of Appendicular perforation.

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