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A Comparative Study of Diagnostic Value of Hyperbilirubinemia in Predicting Appendicitis and Its Complications

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I. Introduction

The most common cause of acute abdomen is Appendicitis. The diagnosis of acute appendicitis is based on clinical history and physical examination. It is difficult to diagnose in cases of retrocaecal or retro ileal appendix. Appendicectomy is the most commonly performed abdominal surgery. 15-30% of appendicectomy specimen found to be normal.In order to decrease the number of unnecessary appendicectomy, significance of labarotory investigations like White Blood Cells,,CReactive Protein, etc have been emphasised.Ultrasonagram abdomen has been widely accepted as the diagnostic tool for appendicitis.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. 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 siginificance of which is not stressed.On bacterial invasion of the appendix, there is transmigration of bacteria and release of proinflammatory cytokines like TNF α,.IL6 . The cytokines reach the liver through the superior mesentric vein and may lead to inflammation, abscess and liver dysfunction. In view of the above context, the present study was undertaken to assess the 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.

II. 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.

III. Materials And Methods

The study was conducted in the Department of General Surgery, Govt.Rajaji Hospital and Medical College, Madurai during the period of August 2017 to August 2018.

Study design
A prospective non randomised study.

Source
The present study was conducted in the Department of Surgery, Govt.Rajaji Hospital and Medical College, Madurai

Source of data
Patients admitted with clinical diagnosis of acute appendicitis or appendicular perforation under the Department of Surgery, Govt.Rajaji Hospital and Medical College, Madurai 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 =
Where,
Z2 x p x
q d2
n = Sample size
Z = 1.96 ≈ 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 clinicallyon 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 ofo
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.

IV. Results

A total of 100 patients with clinical diagnosis of acute appendicitis or appendicular perforation admitted in the Department of General surgery, Govt.Rajaji Hospital and medical college,Madurai were studied. 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.

Table 3: Distribution of patients by age

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

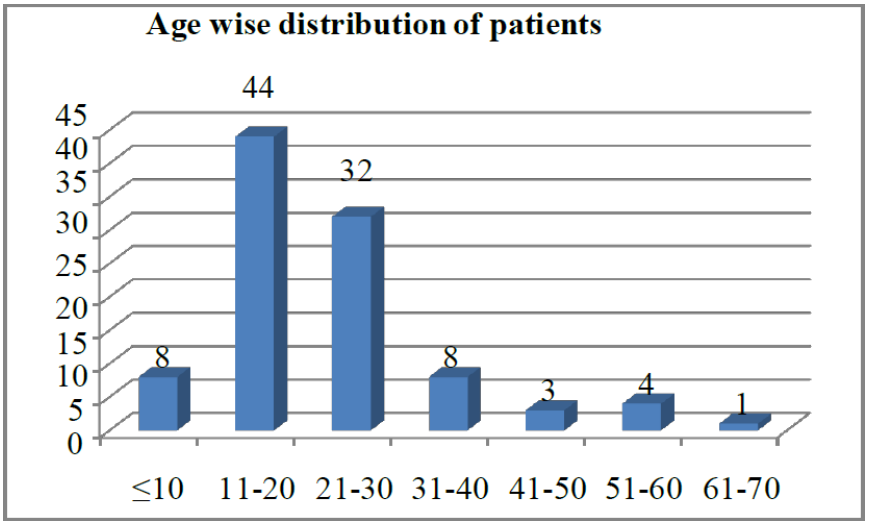


Table 4: Liver Function Tests

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

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

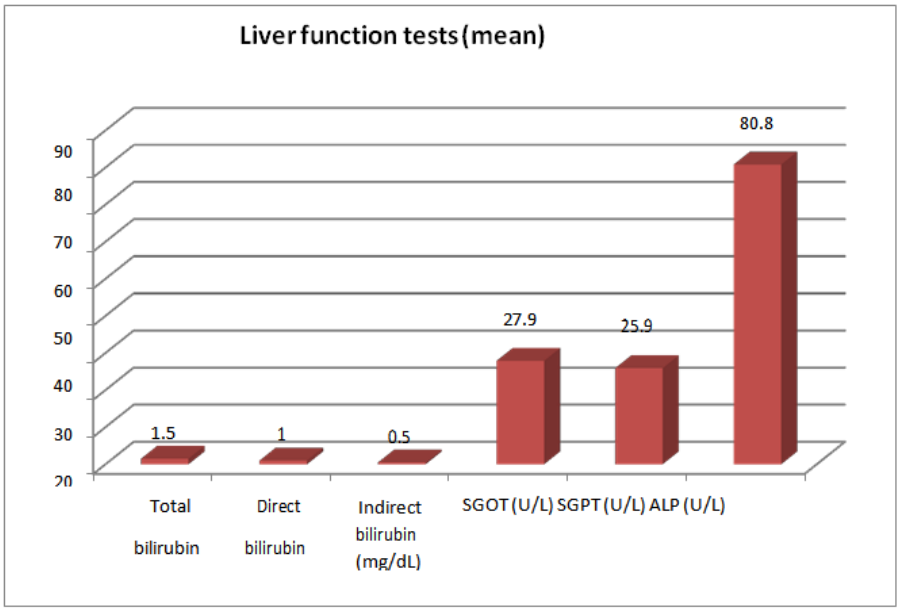


Table 5: Total bilirubin levels

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

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

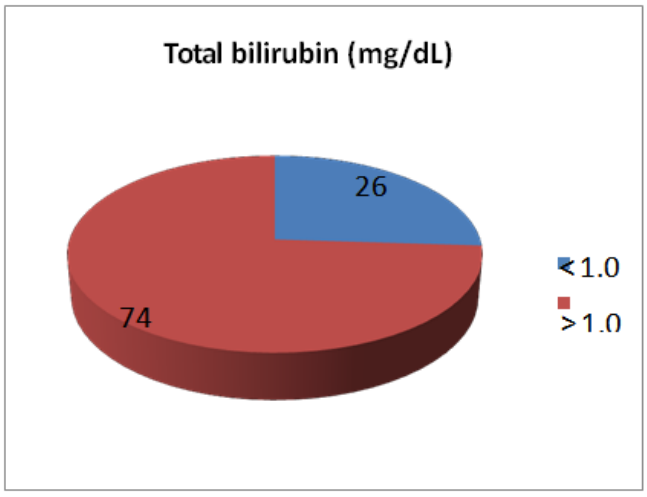


Table 6: Bilirubin levels in patients with uncomplicated acute appendicitis as diagnosis

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

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

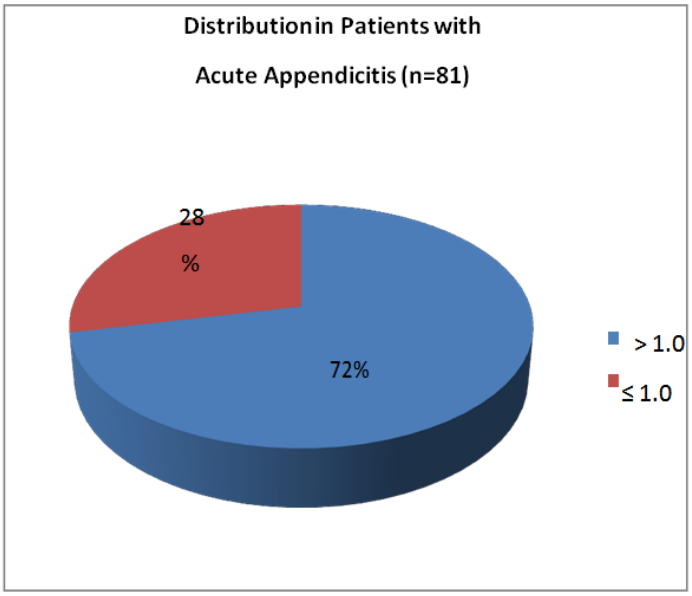


Table 7. Bilirubin levels in patients with Appendicular perforation diagnosis

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

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

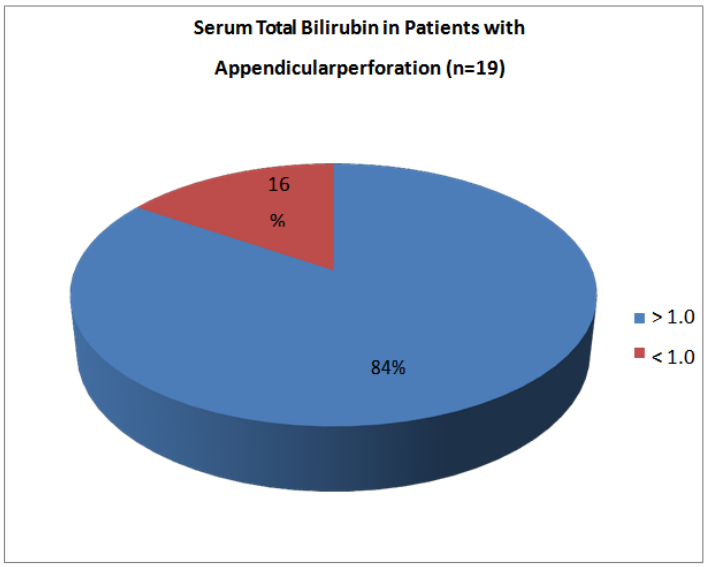


Table 8. Histopathological diagnosis

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

Histopathologically, 81 patients (81%) were confirmed as Acute appendicitis while 19 patients (19%) were diagnosed with Appendicular perforation.

Histopathologicaldiagnosis

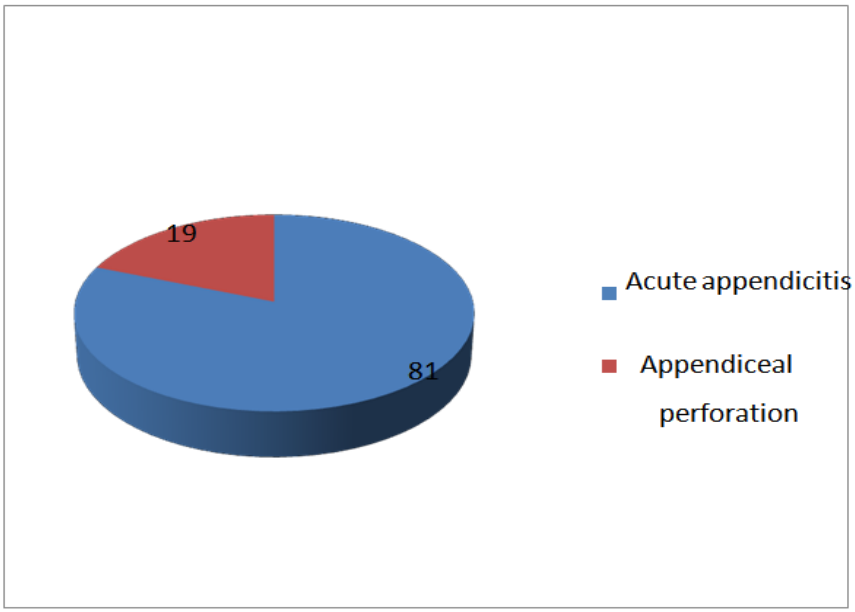


Table 9. Comparison of mean serum bilirubin levels in patients with acute appendicitis and Appendicular perforation

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

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.

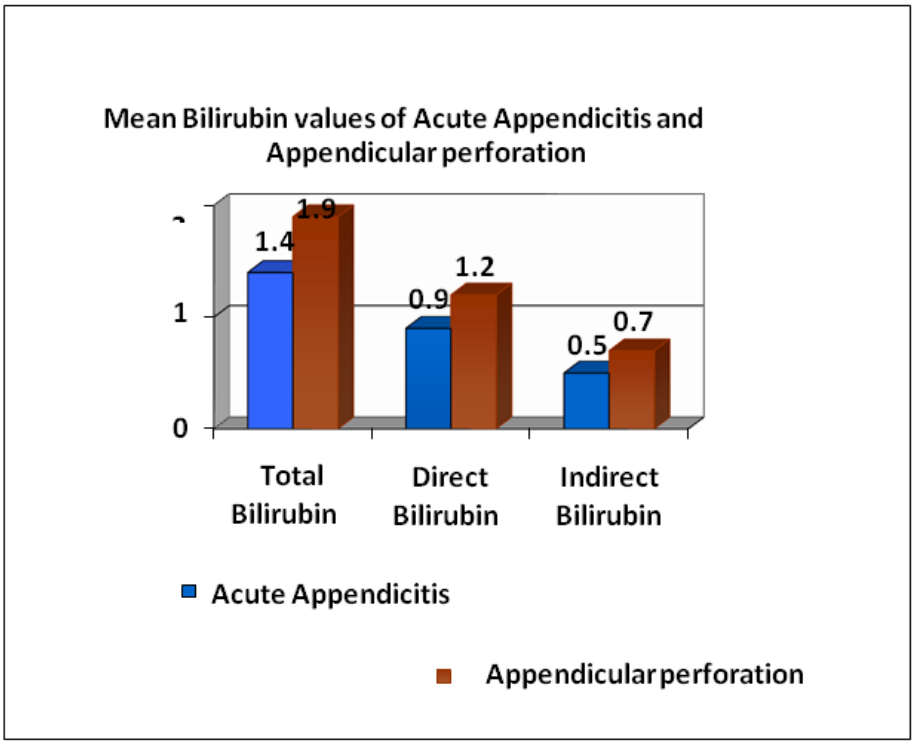
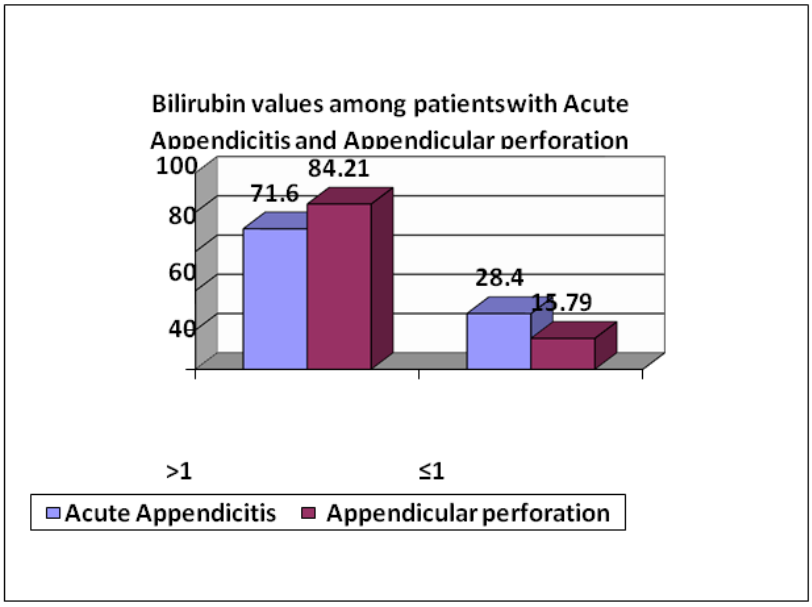


Table 10. Correlation of acute appendicitis and Appendicular perforation with total serum bilirubin levels

Serum bilirubin (mg/dL)	Final diagnosis (n=100)			
	Acute appendicitis (n=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**

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



From Table, following values were calculated as -

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:

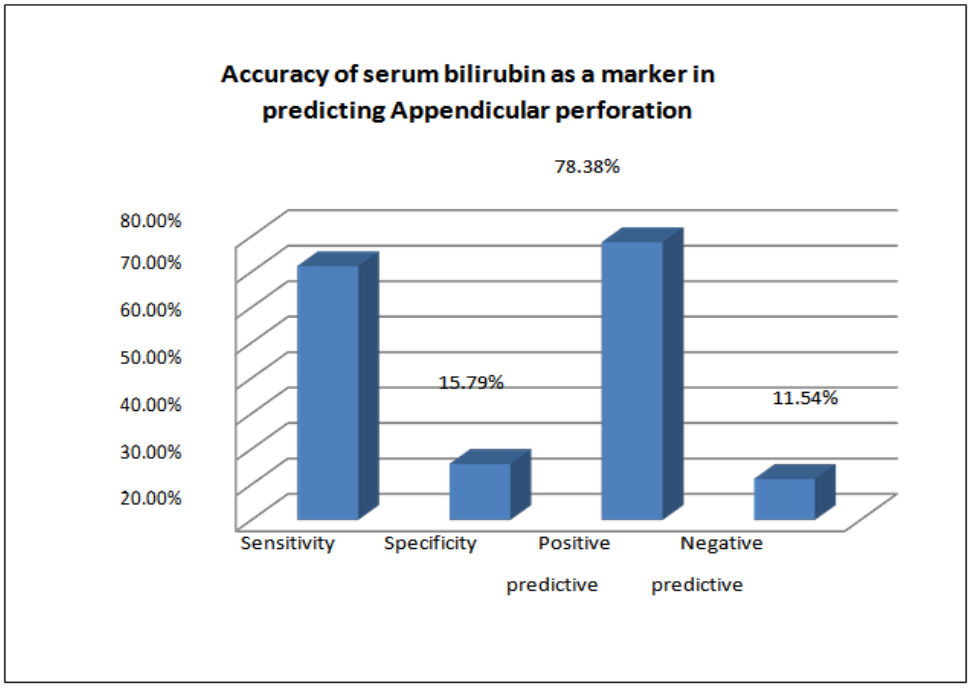
$$= \frac{ad}{bc} = \frac{58 \times 3}{23 \times 16} = 0.472$$

Therefore, Odds ratio is 0.472.

Table 11. Accuracy of serum bilirubin as a marker in predicting Appendicular perforation

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

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 r atio was calculated to be 0.472.



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.[33,34] 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 (> 1.0 mg/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 (≤ 1.0 mg/dL).

Estrada et al[54] had found hyperbilirubinemia in 59 (38%) of 157 patients studied with acute appendicitis.

The mean total serum bilirubin of all 100 patients was 1.5 ± 0.8 mg/dL (range, 0.7 – 2.3 mg/dL), which was above the normal range (≤

1.0 mg/dL) considered for the study, hence indicating the occurrence

of hyperbilirubinemia. The mean of Direct bilirubin was 1.0 ± 0.7 mg/dL (range, 0.3-1.7 mg/dL) while that of Indirect bilirubin was 0.5±0.2 mg/dL (range, 0.3 – 0.7 mg/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 2.38 mg/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 (>1.0 mg/dL) while only 23 patients (28.4%) had normal bilirubin levels (≤1.0 mg/dL). In patients diagnosed with Appendicular perforation (n=19), 16 patients (84.21%) had bilirubin elevated (>1.0 mg/dL), while only 3 patients (15.79%) had normal levels (>1.0 mg/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% byLymphocytes.

On Ultrasonography, 69 patients (69%) were diagnosed as Acute appendicitis, 13 pateints (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 ±0.65 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). 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[68] 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±0.57 mg/dL and 0.5±0.21 respectively. Similarly, 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.

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 predicative 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 al[68] in which, he found the sensitivity and specificity in his study of hyperbilirubinemia for predicting Appendicular perforation to be 70% and 86.0% respectively.

V. 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.

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