## **Original Research Article**

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# Hyperbilirubinemia as a diagnostic marker for acute appendicitis

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#### **ABSTRACT**

**Background:** Appendicitis is one of the commonest cause of abdominal pain requiring emergency surgery. Different clinical signs and symptoms always mimic the diagnosis of acute appendicitis with number of causes leading to pain in right iliac fossa, especially in females. Accurate diagnosis can be aided by additional tests. A delay in diagnosis can lead to appendiceal perforation with increased morbidity, and an appendectomy as soon as the condition is suspected, may increase the number of unnecessary appendicectomies. Objective of present study was to evaluate the role of hyperbilirubinemia as a diagnostic marker for Acute Appendicitis.

Methods: This is a prospective study of 100 patients carried out at Dr. D.Y. Patil Medical College, Hospital and Research Centre, Pimpri, Pune from May 2015 to September 2017. Patients presenting to surgical OPD with pain in Right iliac fossa will be evaluated. Those with a clinical diagnosis of acute appendicitis will be included in the study. Results: Acute appendicitis is one of the most common emergencies and appendicectomy is one of the most frequently done abdominal operations. Clinical diagnosis using time tested clinical signs is effective in diagnosing appendicitis. However, bilirubin supports diagnosis and hence avoids chances of error in diagnosis. The investigation Bilirubin alone is not sufficient to accurately diagnose acute appendicitis, however the clinical findings, ALVARADO SCORE when combined can predict appendicitis. There is significant difference in total bilirubin in acute and probable cases of appendicitis but it can be used to differentiate both of them. In present study Mean bilirubin for acute appendicitis was 1.23mg/dl and probable cases of appendicitis was 0.84mg/dl, with SD for acute appendicitis was 0.598 and probable cases of appendicitis was 0.486. In our study bilirubin provide the highest diagnostic accuracy for acute appendicitis case. Normal inflammatory markers cannot exclude appendicitis, which remains a clinical diagnosis. The presence of history of pain and or signs of peritoneal inflammation which help you in diagnosing acute appendicitis.

Conclusions: Hyperbilirubinemia can be a diagnostic marker for acute appendicitis.

**Keywords:** Acute appendicitis, Hyperbilirubinemia, TLC

### INTRODUCTION

Appendicitis is one of the commonest cause of abdominal pain requiring emergency surgery. Different clinical signs and symptoms always mimic the diagnosis of acute appendicitis with number of causes leading to pain in right iliac fossa, especially in females<sup>1</sup>. Accurate diagnosis can be aided by additional tests. A delay in

diagnosis can lead to appendiceal perforation with increased morbidity, and an appendectomy as soon as the condition is suspected, may increase the number of unnecessary appendicectomies.<sup>2,3</sup> Timely accurate diagnosis has been attempted with the use of various scoring systems, additional laboratory tests, ultrasonography etc. None of the methods stand alone, as they all come in support of, and are secondary to a primary assessment.

The bacteria present in the portal blood are usually cleared by detoxification and immunological action of reticuloendothelial system of liver that act as first line defence in clearing toxic substances, bacteria and their products. But when bacterial load overwhelms the Kupffer Cell function, the damage to hepatocytes is reflected in serum bilirubin levels alone or in combination with liver enzymes depending upon the type, severity and site of lesion.4 Jaundice has been associated appendicitis with and studies have hyperbilirubinemia as a predictor of appendiceal perforation.<sup>5,6</sup> However, these studies have not focused on the value of bilirubin as a specific marker for acute appendicitis.<sup>7</sup>

The present study will evaluate the relationship between hyperbilirubinemia and appendicitis and its predictive potential for the diagnosis of complicated appendicitis. This can prove to be a credible aid in diagnosis of acute appendicitis with prompt decision making.

Aims of present study was to evaluate the role of hyperbilirubinemia as a diagnostic marker for Acute Appendicitis.

Objective was to study the incidence of hyperbilirubinemia in acute appendicitis, to determine the role of hyperbilirubinemia in predicting the severity of acute appendicitis and to compare the efficacy of bilirubin levels versus Alvarado score in diagnosing severity Acute Appendicitis.

## **METHODS**

This is a prospective study of 100 patients carried out at Dr. D.Y. Patil Medical College, Hospital and Research Centre, Pimpri, Pune from May 2015 to September 2017.

Sample size calculation:

 $n=Z^2pq/L^2$ 

Z=1.96 Standard normal variation; L=Allowable Error; P=number of positive case/total number of case in study; Q=1-p

Patients presenting to surgical OPD with pain in Right iliac fossa will be evaluated. Those with a clinical diagnosis of acute appendicitis will be included in the study.

#### Exclusion criteria

- H/O alcoholic liver disease
- Hemolytic or liver disease associated with hyperbilirubinemia
- H/O gastrointestinal/hepatopancreaticobiliary malignancy in past
- Patients with appendicular lump

Investigations will be done to support the diagnosis:

- Total leucocyte count
- C- Reactive Protein.
- C- Reactive Protein

Serum bilirubin levels will be estimated. Hyperbilirubinemia will be defined as a serum bilirubin level greater than 1 mg/ dl. Alvarado scoring will be done for all patients.

Patients will be subjected to open / laparoscopic appendectomy after written and informed consent (Appendix A2) and specimens will be sent for histopathological examination.

The Histopathological report will be considered as the gold standard for categorizing the patients as having normal appendix, acute appendicitis and chronic appendicitis. All the findings clinical examination, investigations, Alvarado score, intra-operative details and HPE report will be recorded in the study proforma (Appendix B).

#### Evaluation

Serum bilirubin levels in cases with a clinical diagnosis of Acute Appendicitis. Comparison of serum bilirubin levels and Alvarado score. Comparison of serum bilirubin levels and HPE report.

#### Statistical analysis

Data analysis was done using the SPSS (Statistical Package for the Social Science) Version 17 for window. demographic variable, Incidence hyperbilirubinemia, Severity of Acute Appendicitis, HPE finding were calculated with no and percentage. The Mann Whiteny test was used to find significance difference of Alvarado score according to incidence of hyperbilirubinemia. ANOVA test was use to find the significance difference of Sr. Bilirubin level, CRP level, TLC level according to Severity of Acute Appendicitis and HPE finding. Chi-square test was used to find the significance association between Incidence of hyperbilirubinemia and HPE finding. A probability value of 0.05 was accepted as the level of statistical significance.

## **RESULTS**

Age group 21-30 were common in the study group.

Table 1: Age distribution of cases in study group.

Age (Yrs.)	No of cases	Percentage
11-20	31	31
21-30	54	54
>30	15	15
Total	100	100

Table 2: Sex distribution of cases in study group.

Sex	No. of cases	Percentage
Male	70	70
Female	30	30
Total	100	100

Male cases were more as compare to female.

Table 3: Incidence of hyperbilirubinemia distribution of cases in study group.

Incidence of hyperbilirubinemia	No. of cases	%
Present	66	66
Absent	34	34
Total	100	100

Table 4: Severity of acute appendicitis distribution of cases in study group.

Severity of acute appendicitis	No. of cases	%
1-4 (Unlikely to be appendicitis)	2	2
5-6 (Probable cases of appendicitis)	30	30
7 and above (Acute appendicitis)	68	68
Total	100	100

Out of 100 cases 66 patient showing hyperbilirubinemia with acute appendicitis.

Table 5: Histopathological finding distribution of cases in study group.

HPE finding	No. of cases	Percentage
Acute Appendicitis	69	69
Suppurative appendicitis	27	27
Chronic Appendicitis	2	2
Normal Appendicitis	2	2
Total	100	100

100 cases operated for acute appendicitis.

69 cases as per histological findings suggestive of acute appendicitis. 27 cases as per histological findings suggestive of Suppurative appendicitis. 2 cases as per histological findings suggestive of Chronic Appendicitis. 2 cases as per histological findings suggestive of Normal Appendicitis.

In the study 66 cases showed hyperbilirubinemia with Mean Alvarado score 6.27 and SD 0.921.

Table 6: Comparison of Alvarado score according to incidence of hyperbilirubinemia in study group.

	Incidence	of hyperbiliru				
Parameter	Present (n=66) Absent (n=34)		MW test Z Value	P Value		
	Mean	SD	Mean	SD		
Alvarado score	6.27	0.921	5.09	0.514	6.44	< 0.0001

In the study 34 cases showed acute appendicitis but normal levels of bilirubin with Mean Alvarado score 5.09 and SD 0.514. So, Alvarado score and bilirubin can predict the severity of appendicitis.

Patients with hyperbilirubinemia will show more Alvarado score as compare to normal bilirubin. In present study it was significant.

In present study Mean bilirubin level for acute appendicitis were 1.50 in the cases with Alvarado score 7 and above. And SD 0.70.

In present study Mean bilirubin level for probable cases of appendicitis were 1.10 in the cases with Alvarado score 5-6 And SD 0.77.

In present study Mean bilirubin level unlikely to be appendicitis cases were 0.35 in the cases with Alvarado score 1-4 And SD 0.212.

Table 7: Comparison of Sr. Bilirubin according to severity of acute appendicitis in study group.

Severity of	Sr.	Bilirubir	- F	P	
Acute Appendicitis	N	Mean	SD	Value	Value
1-4 (Unlikely to be appendicitis)	2	0.35	0.212		
5-6 (Probable cases of appendicitis)	30	1.10	0.77	5.29	0.007
7 and above (Acute appendicitis)	68	1.50	0.70		

Increase in the bilirubin can predict the severity of appendicitis, we found bilirubin is significant marker in case of appendicitis. In present study it was significant.

Table 8: Comparison of CRP level according to severity of acute appendicitis in study group.

Severity of		CRP level			P .
Acute Appendicitis	n	Mean	SD	F Value	Value
1-4 (Unlikely to be appendicitis)	2	14.15	5.303		
5-6 (Probable cases of appendicitis)	30	76.05	110.574	0.33	0.72
7 and above (Acute appendicitis)	68	79.28	112.585		

In present study CRP for acute appendicitis Mean 79.28 and SD 112.585 and in probable cases of appendicitis Mean 76.05 and SD 110.574. It was not significant.

Table 9: Comparison of TLC according to severity of acute appendicitis in study group.

Severity of	TL	С		F	Р
Acute Appendicitis	n	Mean	SD	Value	Value
1-4 (Unlikely to be appendicitis)	2	12250	2474.87		
5-6 (Probable cases of appendicitis)	30	7169	935.66	43.70	<0.0001
7 and above (Acute appendicitis)	68	12704.56	3185.13		

In present study Mean TLC level for acute appendicitis were 12704.56 in the cases with Alvarado score 7 and above. In present study Mean TLC level for probable cases of appendicitis were 7169 in the cases with Alvarado score 5-6. In present study Mean TLC level unlikely to be appendicitis cases were 12250 in the cases with Alvarado score 1-4. So, increase in the TLC can predict the severity of appendicitis, we found TLC is significant marker in case of appendicitis. In present study it was significant.

Table 10: Association between incidence of hyperbilirubinemia and HPE finding in study group.

HPE finding	Incidence hyperbilin	Total	
	Present	Absent	
Acute appendicitis	49	20	69
Suppurative appendicitis	13	14	27
Chronic appendicitis	2	0	2
Normal appendicitis	2	0	2
Total	66	34	100

69 cases with HPE finding of acute appendicitis 49 shows hyperbilirubinemia. 27 cases with HPE finding of suppurative appendicitis 13 shows hyperbilirubinemia. 2 cases with HPE finding of chronic appendicitis 2 shows hyperbilirubinemia. 2 cases with HPE finding of normal appendicitis 2 shows hyperbilirubinemia.

Table 11: Comparison of TLC according to HPE finding in study group.

HPE		TLC		F	P
finding	n	Mean	SD	Value	Value
Acute appendicitis	69	11249.57	3752.38		
Suppurative appendicitis	27	10675.19	3819.32	0.24	0.80
Chronic appendicitis	2	10250	353.55	0.34	0.80
Normal appendicitis	2	9265	1039.45		

In present study Comparison of TLC according to HPE finding Mean for acute appendicitis was 11249.57 and mean for chronic appendicitis was 10250. So as per present study TLC increases with the severity of appendicitis. So, comparisons of TLC according to HPE finding were significant in predicting the severity of appendicitis.

Table 12: Comparison of Sr. Bilirubin according to HPE finding in study group.

HPE finding	N	Sr. Bili Mean	rubin SD	F Value	P Value
Acute appendicitis	69	1.44	0.533	Value	v aruc
Suppurative appendicitis	27	1.19	0.625	1.04	0.38
Chronic appendicitis	2	1.05	0.071	1.04	0.38
Normal appendicitis	2	1.00	0.007		

In present study showing Comparison of Sr. Bilirubin according to HPE finding shows increase in level of bilirubin can predict the type of appendicitis according to HPE.

In present study Comparison of Sr. Bilirubin according to HPE finding in study group were significant.

#### DISCUSSION

The most important step in the management of appendicitis is reaching the decision about operative intervention. Appendicectomy is a routine surgical procedure.<sup>8</sup>

If Acute Appendicitis is diagnosed correctly and treated early there is less associated morbidity and mortality.<sup>8</sup>

A study of 100 cases of suspected appendicitis admitted to Dr. D Y Patil hospital was made between May 2015 to September 2017 adopting through clinical examination with investigation to make a diagnosis of acute appendicitis.

In present study 70 male and 30 female patients, so male preponderance observed in the study. In present study 66 cases were positive for hyperbilirubinemia and 34 were negative with acute appendicitis.

Emmanuel mentioned a specificity of hyperbilirubinemia for appendicular perforation to be 70% with a positive predictive value of 91%. There was a total of 2 cases unlikely to be appendix category, 30 cases in probable appendicitis category and 68 cases in acute appendix category.

In present study negative appendix was not involved. The age for acute appendicitis was 21-30 years. Male highest incidence was observed.

Acute Appendicitis and its complication can be challenge for the surgeon, the role of hyperbilirubinemia in the workup of the patients with appendicitis has been studied.<sup>3-5</sup>

In meta-analysis Anderson concluded that most diagnostic information comes from a history of migratory pain, clinical assessment confirming peritoneal irritation and inflammation. Apart from Total Count and CRP, Bilirubin has also been investigated as a marker for Acute Appendicitis. 10,11

Anderson reported that appendicitis is unlikely when all inflammatory variables are normal. Sengupta et al reported a Normal Predictive Value of 100% for TLC and CRP in Acute Appendicitis, concluding that patients experiencing lower abdominal pain with normal TLC and CRP are unlikely to have appendicitis. As per Shaw V et al both TLC and CRP can be normal range this may because lag in changes of inflammatory variables with the time of the onset of symptoms. 13,14

In 1969 miller and Irvine reported that a series of 120 cases of acute appendicitis, jaundice was noted in 7.5% and correlated with positive peritoneal culture for Escherichia coli. 15 potential mechanism that result in hyperbilirubinemia in acute appendicitis could be either due to increased hemolysis by *E. coli* and therefore increased bilirubin load or due to endotoxin induced cholestasis. 16.17

In present study, authors found that bilirubin and white cell count have predictive value for appendicitis. In present study, the mean total count for acute appendicitis was 12704, and the mean total count for probable case of appendicitis was 7169. Study by Zuhoor K et al the mean for acute appendicitis was found to be 9400. So there

was increase in total count with increase in severity of the appendicitis noted in present study.

In present study, the mean CRP for acute appendicitis was 79.28. In present study, the mean CRP for probable case of appendicitis was 76.05. So, there was observation of CRP was not statistically significant.

Study by Tuker A et al CRP level ranged from 1-453mg/l with a mean of 56.53±86.49mg/l.<sup>18</sup> The presence of raised CRP was not statistically significant. So, it was observed in present study that CRP was not statistically significant for diagnosing the appendicitis. So, TLC count was more significant indicator of acute appendicitis than CRP for predicting the severity of appendicitis.<sup>18</sup>

In present study, the mean total bilirubin for acute appendicitis was 1.50. In present study, the mean total bilirubin in probable cases of appendicitis was 1.10.

The study done by Sand et al reported a relatively high incidence of hyperbilirubinemia (24.9%) from an analysis of 538 acute appendicitis patients, of whom 50.7% were verified as having perforated appendicitis.<sup>19</sup>

In a study by Noh et al, bilirubin showed highest specificity in diagnosing complicated cases at 75% compared to WBC (19%) and CRP (35%).<sup>20</sup>

Patel et al have reported a sensitivity of 65.33% for hyperbilirubinemia in acute uncomplicated cases and 92% for complicated appendicitis. Another study Ghimire P et al has stated that 57.7% patients with hyperbilirubinemia had gangrenous or perforated appendix. 22

The study done by Khan S et al there was hyperbilirubinemia in 86.6% of the patient of acute appendicitis bilirubin ranged from 1.2mg/dl-8.4mg/dl.<sup>4</sup> So Authors observed that bilirubin can be important investigation for diagnosing the Appendicular infection. However, when all three values i.e., total count, CRP, bilirubin is combined, we may safely predict about the severity of the appendix infection.

In present study total count with bilirubin levels may suffice in distinguishing severity of appendicitis. In present study ALVARADO SCORE with bilirubin levels may suffice in distinguishing severity of appendicitis.

The study done Ghimire et al have found a statistically significant difference between the gangrenous and uncomplicated appendicitis patients in Alvarado score, total leucocyte count and total bilirubin level.<sup>22</sup>

The study done Hong et al reported that the univariate analysis demonstrated significant differences for TLC (p<0.0001), total bilirubin (p<0.0001) and Alvarado score (p<0.0001). The multivariate analysis demonstrated that

total bilirubin and Alvarado score have statistically significant diagnostic value for perforated appendicitis. <sup>23</sup>

There are limitations for this study that selected study groups were based on histological diagnosis and the patients who were admitted with possible appendicitis but not operated were not included, patients with negative appendicitis were not included. The timing of the blood tests with the onset of symptoms could not be retrieved accurately. Such timing can affect the level of the symptoms could not be retrieved accurately. Large study is needed to investigate the value Bilirubin among other signs in predicting appendicitis.

#### **CONCLUSION**

From present study authors conclude that hyperbilirubinemia can be considered as a supportive index to diagnose the acute appendicitis. Hyperbilirubinemia can be a diagnostic marker for acute appendicitis.

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Ethical approval: The study was approved by the

Institutional Ethics Committee

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