



Original Article

Evaluation of Significance of Total Bilirubin and C-Reactive Protein in Suspected Cases of Acute Appendicitis

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Abstract

Aims: To evaluate the importance of serum CRP level and Total bilirubin levels in the diagnosis of acute appendicitis, by comparing with final histopathologic diagnosis.

Materials and Methods: This study was done in 100 patients admitted in Father Muller Medical College Hospital from November 2013 to November 2014. Patient with history of acute abdominal pain, in whom acute appendicitis was suspected based on detailed history and physical examination and will be posted for appendicectomy based on decision by surgeon. Serum C-Reactive Protein estimation and Total Bilirubin levels was measured preoperatively in suspected cases of appendicitis. Diagnosis was confirmed by intraoperative and histopathological findings. Operative finding and HPE of appendicectomy specimen and serum CRP and Serum Total bilirubin results will be documented and studied. Collected data will be analysed by frequency, percentage, mean, standard deviation and by sensitivity, specificity, positive predictive value, negative predictive value. Results were confirmed by chi-square test.

Results: In our study, out of the 100 patients who were operated, 85 patients had appendicitis and 15 were normal according to intraoperative and histopathological findings. Present study of serum CRP and surgeon's diagnosis reveals sensitivity - 75.29%, specificity - 93.33%, PPV - 98.46% and NPV - 40% and study of serum bilirubin and surgeon's diagnosis reveals sensitivity - 58.82%, specificity - 93.33%, PPV - 98.03% and NPV - 73.68%. There was a statistical significance between serum CRP and acute appendicitis, & serum total bilirubin and acute appendicitis.

Conclusion: In our study, serum CRP & total bilirubin levels are useful in the diagnosis of acute appendicitis and supports surgeon's clinical diagnosis of acute appendicitis. Negative appendicectomy rate can be decreased, if appendicectomy is avoided in cases where serum CRP or Total bilirubin is negative. Serum CRP levels are reliable inflammatory markers that could be used to support the clinical diagnosis of appendicitis. Serum Total bilirubin is a marker for acute appendicitis with a good positive predictive value.

Keywords: Appendicitis, CRP, Total bilirubin.

INTRODUCTION

Acute appendicitis is considered to be the most common cause of acute surgical abdomen presenting to emergency department and Emergency Appendectomy is the most common procedure done.^{1,2}

Approximately 7% of the population will suffer from acute appendicitis during their lifetime hence considerable effort has been directed towards early diagnosis and treatment.^{3,4,5} The mortality rate is less than 1% but may be as high as 20% in certain populations, such as the elderly.

Classic clinical findings and laboratory parameters usually allow for accurate diagnosis and treatment. However, some patients have atypical and varied presentations leading to misdiagnosis. Diagnostic difficulty in patients with atypical and varied clinical presentation has resulted in unnecessary appendectomies, which have been reported to be with average of about 20 % in the surgical literature.

Attempts to increase the diagnostic accuracy in acute appendicitis included computed tomography, ultrasonography and various scoring systems. Despite recent advances in radiographic imaging and diagnostic laboratory investigations, the diagnosis of appendicitis is still difficult. On one hand normal appendix at appendectomy represents misdiagnosis and on the other hand a diagnostic delay of appendicitis may lead to complications like perforation, peritonitis and septicemia. No single sign, symptom or diagnostic test accurately makes the diagnosis of appendiceal inflammation in all cases.

Despite improvements in diagnostic methods, negative appendectomy rates still remain between 10 and 30% in acute appendicitis.¹ Cost-effective and easily applicable diagnostic methods with fair results are required to reduce negative appendectomy rates.

MATERIALS AND METHODS

Method of collection of data

All patients above the age of 18 years and below 50 years diagnosed clinically to have Acute Appendicitis and posted for Appendectomy in

Department of General Surgery, Father Muller Medical College Hospital. This correlative study was performed on 100 consecutive patients who were operated on for treatment of acute appendicitis. Patient with history of acute abdominal pain, in whom acute appendicitis was suspected based on detailed history and physical examination and will be posted for appendectomy based on decision by surgeon. The patients thus selected after purposive sampling method will be included in the study after obtaining their consent. Blood samples will be drawn from all patients diagnosed clinically as having acute appendicitis for C-reactive protein estimation and Total Bilirubin levels. Serum CRP concentrations and Total Bilirubin levels were measured before the surgery. Normal CRP levels range from 0 to 6 mg/l and Normal serum bilirubin levels ranges from 0.3 - 1.0 mg/dl.

Depending on results of the examination by a surgeon, patients underwent surgery for treatment of acute appendicitis. Operative findings and histopathological examination of appendectomy specimens established the exact diagnosis. A histological criterion for the diagnosis of acute appendicitis is polymorphous leucocytic infiltration of the muscularis mucosa.

Operative finding and histopathological examination of appendectomy specimen and serum CRP, and Serum Total bilirubin results was documented and studied. The results of Serum CRP and Serum Total bilirubin were correlated with the operative and histopathological examination using chi-square test. Collected data was analysed by frequency, percentage, mean, standard deviation and by sensitivity, specificity, positive predictive value, negative predictive value.

Exclusion criteria:

All patients documented to have a past history of Jaundice or Liver disease

Hemolytic disease

Acquired or Congenital biliary disease

All patients with positive HBsAg

All patients with cholelithiasis

All patients with malignancy of hepato-biliary system

RESULTS

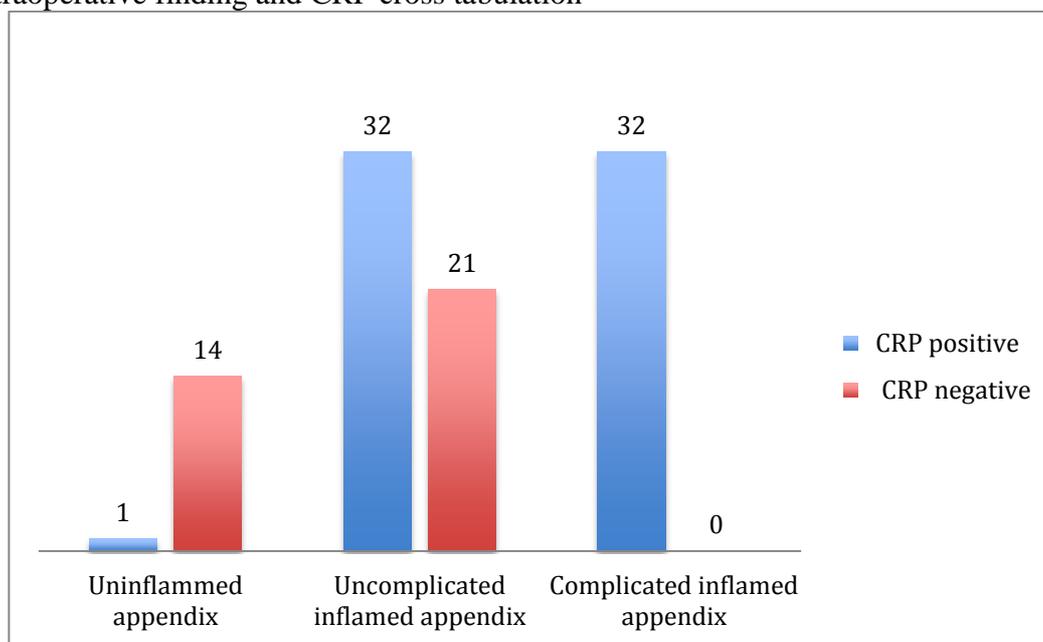
Table 1: Age incidence

Age	Frequency	Percentage
< 20	3	3%
21-30	70	70%
31-40	12	12%
41-50	15	15%
Total	100	100%

Table 2: Intraoperative Finding and CRP Cross Tabulation

	CRP positive	CRP negative	Total
Uninflamed appendix	1	14	15
Uncomplicated inflamed appendix	32	21	53
Complicated inflamed appendix	32	0	32
Total	65	35	

Figure 1: Intraoperative finding and CRP cross tabulation



Chi square statistic is 26.39, the P value is 0. This result is significant. P=<0.05(significant)

Table 3: Sensitivity, specificity, positive predictive value and negative predictive value of CRP

	Appendicitis positive	Appendicitis negative	TOTAL
CRP positive	64(a)	01 (b)	65
CRP negative	21 (c)	14 (d)	35
TOTAL	85	15	

a= True positive b= False positive

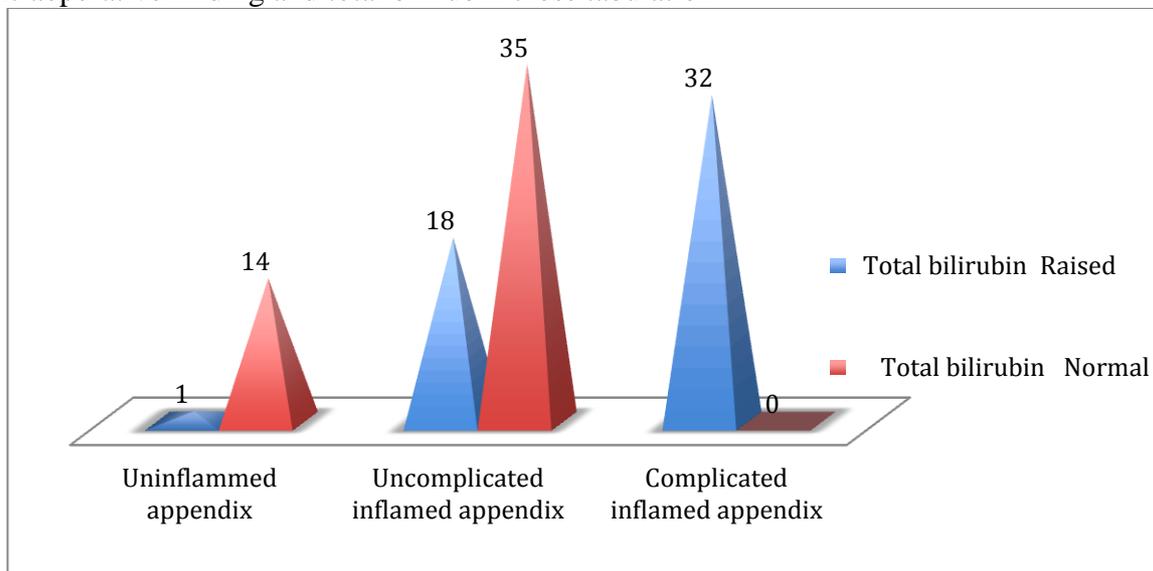
c= False negative d= True negative

- Sensitivity(a / a+c) = 64 /85= 75.29% , Specificity (d / b+d)= 14/15 = 93.33%
- Positive predictive value (a / a+b) = 64/ 65= 98.46%
- Negative predictive value (d / c+d)= 14/ 35= 40%

Table 4: Intraoperative finding and total bilirubin cross tabulation

	Total bilirubin raised	Total bilirubin normal	Total
Uninflamed appendix	1	14	15
Uncomplicated inflamed appendix	18	35	53
Complicated inflamed appendix	32	0	32

Fig 2. : Intraoperative finding and total bilirubin cross tabulation



P=<0.05(significant)Chi-square statistics is 13.8793. The P value is 0.000195. The result is significant

Table 5: Sensitivity, specificity, positive predictive value and negative predictive value of total bilirubin

	Appendicitis positive	Appendicitis negative	Total
Total bilirubin positive	50(a)	01 (b)	51
Total bilirubin negative	35 (c)	14 (d)	49
Total	85	15	

a= True positive b= False positive

c= False negative d= True negative

• Sensitivity(a / a+c) = 50 /85= 58.82%,Specificity (d / b+d)= 14/15 = 93.33%

• Positive predictive value (a / a+b) = 50/ 51= 98.03%

• Negative predictive value (d / c+d)= 14/ 49= 73.68%

In 85 patients of acute appendicitis serum CRP was elevated in 64 and normal in 21 patients. Serum Total bilirubin was elevated in 50 and normal in 35 patients. Of the 15 patients with normal appendix, serum CRP was normal in 14 patients and elevated in 1 patient. And similarly serum Total bilirubin was normal in 14 patients and elevated in 1 patient. Preoperative CRP values were false negative in 21 patients with appendicitis and false positive in 1 patient with normal appendix. Preoperative serum Total bilirubin was false negative in 35 patients with appendicitis and false positive in 1 patient with normal appendix.

The difference of true and false results between CRP's test and surgeon's diagnosis was statistically significant. Similarly, The difference of true and false results between serum Total bilirubin value and surgeon's diagnosis was statistically significant.

DISCUSSION

Acute appendicitis remains a common abdominal emergency throughout the world. Early and accurate diagnosis of acute appendicitis is required to reduce the morbidity and mortality associated with delayed diagnosis and its complications. Appendicitis still poses a

diagnostic challenge and many methods have been investigated to try to reduce removal of a normal appendix without increasing the perforation rate.

Radiological methods such as ultrasonography and computed tomography are being used. In an attempt to increase the diagnostic accuracy, several scoring systems have been devised. The present study was undertaken to reach an accurate diagnosis in the fastest and cheapest way.

In this study the diagnostic value of the serum CRP levels and Total bilirubin levels in patients with clinical suspicion of acute appendicitis was investigated.

Following the onset of the infection, an increase occurs in the synthesis of some hepatic proteins as an acute phase response. Serum concentrations of acute phase proteins augment in 8-12 hours after the onset of infection. One of these, CRP, is a marker of acute phase response, which can be used as an indicator of disease. Elevation of serum concentrations of CRP indicates the presence of acute appendicitis.

Recently, elevation in serum bilirubin was reported, but the importance of the raised total bilirubin has not been stressed in appendicitis. 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 and may produce inflammation, abscess or dysfunction of liver either directly or indirectly by altering the hepatic blood flow.

Thus the present study was undertaken to evaluate the credibility of Hyperbilirubinaemia and elevated CRP levels as a diagnostic marker for acute uncomplicated appendicitis and complicated appendicitis.

In our study of 100 patients (53 male, 47 female), on histopathological examination 85 patients had acute appendicitis, with a negative appendicectomy rate of 15%. In similar studies done by Khan I⁶, Ohmann C⁷, and Arian GM⁸, negative appendicectomy rates of 14%, 14.3% and 16.1% respectively were observed.

The mean age in our study population (100 patients) was 29.19. Majority of the patients in present study were in 2nd and 3rd decades of life. In our study, serum CRP estimation in diagnosis of acute appendicitis yielded a sensitivity of 75.29% and specificity of 93.33%. This is comparable to the results of study done by Asfar⁹ where sensitivity and specificity were 86.6% and 93.6% respectively. This is also supported by study done by Shakhartreh where sensitivity and specificity were 95.5% and 88.9% respectively¹⁰. CRP is elevated in any cause of acute inflammation. But if clinical suspicion of appendicitis is not confirmed, CRP estimation provides the clue for acute appendicitis. In this study CRP and acute appendicitis were highly associated and statistically significant (p value<0.05). This study proves the adjunct value of serum CRP estimation in suspected cases of acute appendicitis.

The development of jaundice in sepsis is well recognized and has been associated with a variety of causative bacteria, gram-negative bacteria being most commonly implicated. Several mechanisms leading to hyperbilirubinaemia in systemic infections have been described. Hemolysis causes an increased bilirubin load and has been associated with several bacteria including *Escherichia coli*.¹¹ Another mechanism is reduced hepatic uptake and canalicular excretion of bilirubin caused by endotoxaemia.¹² Hyperbilirubinaemia presumably occurs in appendicitis as a result of bacteraemia or endotoxaemia, which could occur both in simple appendicitis and perforated or gangrenous appendicitis.

In our study on evaluating Serum Total bilirubin in suspected cases of appendicitis, it was found to have elevated bilirubin in 50 patients and normal in 35 patients out of 85 patients with histopathologically proven appendicitis. In our study, serum Total bilirubin estimation in diagnosis of acute appendicitis yielded a sensitivity of 58.82% and specificity of 93.33%. In this study, no case with complicated appendicitis

(appendicular perforation or abscess formation) had normal serum total bilirubin.

Patients with hyperbilirubinaemia were significantly more likely to have acute appendicitis than those with a normal bilirubin. The sensitivity of hyperbilirubinaemia for appendicitis was 58.82%, which was lower than in other studies. However, we found that hyperbilirubinaemia had a high specificity of 93.33% and positive predictive value of 98.03%. In our study, serum Total bilirubin and acute appendicitis were associated and were statistically significant (p value < 0.05)

Therefore, in suspected cases of appendicitis elevation of Serum bilirubin or CRP can be used as a criterion to diagnose and manage acute appendicitis. Both sensitivity and specificity of elevated total Serum bilirubin level and CRP in acute appendicitis with perforation and/or gangrene is higher.

Serum CRP levels and Total bilirubin can be used with clinical examination and other laboratory investigations in the assessment of patients with suspected acute appendicitis for accurate diagnosis. Negative appendectomy rate can be decreased, if appendectomy is avoided in cases where serum CRP or Total bilirubin is negative.

Bilirubin is a marker for acute appendicitis with a good positive predictive value. It is also a valuable indicator of patients more likely to have appendiceal perforation or gangrene. Serum CRP levels are reliable inflammatory markers that could be used to support the clinical diagnosis of appendicitis.

No single clinical or laboratory test is able to reliably predict acute appendicitis. Rather, a combination of history, clinical examination and laboratory and radiological investigations is used to make the diagnosis and decide appropriate management.

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