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Original Research Article

C-reactive protein and total serum bilirubin as a predictor of perforated appendicitis: a cross sectional study

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ABSTRACT

Background: C-reactive protein (CRP) and bilirubin have been used as adjuncts for diagnosis of appendicitis. This study assessed the diagnostic value of these markers in patients with suspected acute appendicitis.
Methods: CRP values and total serum bilirubin among the patients who presented with acute appendicitis were compared among patients who had perforated appendix and non- perforated appendix. The diagnostic value of CRP and TSB markers as a predictor for perforation were compared in terms of Sensitivity, specificity, PPVs and NPV and the diagnostic accuracy assessed by AUC using receiver operating characteristic (ROC) curve analysis.
Results: This study showed sensitivity is 72.50%, specificity of 92.23%, positive predictive value of 78.38% for a raised CRP. The sensitivity of TSB for predicting perforation is 77.50 and the values of specificity, PPV and NPV of the same are 87.38 %, 70.45% and 90.91% respectively. The area under curve was more for CRP than TSB indicating that CRP is better predictor for perforation in appendicitis as compared to the TSB.
Conclusions: Thus, serum CRP and total serum bilirubin (TSB) can be used as useful markers for early diagnosis and prediction of perforation in cases of acute appendicitis.

Keywords: Appendicitis, C-reactive protein, Perforated appendicitis, Total serum bilirubin

INTRODUCTION

Despite appendicitis being a common disease, its presentation is not always typical and misdiagnosis is therefore not uncommon.[1] It is further complicated by perforation, abdominal abscess, urinary retention, small bowel obstruction and peritonitis causing an increase in morbidity and even mortality of the patients due to delay in diagnosis and surgery for this condition.

On the other hand, too aggressive surgical approach may lead to an increased rate of negative appendectomies. The incidence of perforated appendicitis in adults has been reported from 13–37% or higher.[2,3] No reliable specific marker as predictor of perforation in acute appendicitis has been identified, but few recent studies have shown significant role of hyperbilirubinemia and CRP as a predictor of perforation in acute appendicitis.[4,5] Appendicitis has been shown to have a strong association with hyperbilirubinemia. It has been hypothesized that following appendicitis inflammatory agents like IL-6, TNF α and cytokines usually migrate to the liver via the superior mesenteric vein producing inflammation, abscess or dysfunction of the liver and also alter the hepatic blood flow and normal physiological flow of the bile causing hyperbilirubinemia.[6,7]

C-reactive protein is an acute-phase protein. Normal concentration in healthy human serum is usually lower than 10 mg/l, slightly increasing with aging. Higher levels are found in late pregnancy, mild inflammation and viral infections (10-40 mg/l), active inflammation,

bacterial infection (40-200 mg/l), severe bacterial infections etc.[8] Though various imaging modalities like computed tomography (CT) scan, magnetic resonance imaging (MRI) and ultrasonography may help in early diagnosis of perforated appendix, they may not be readily available in many health centres of the third world and developing countries.

In such condition clinical and laboratory investigations may be the only, cheaper and readily available options for diagnosis. This study is an effort to establish the role of hyperbilirubinemia and CRP as predictive factors for complicated appendicitis with perforation, abscess formation or gangrenous change.

METHODS

The present study is prospective study conducted by the department of Surgery from April 2011to March 2012. 150 consecutive cases of acute appendicitis were included in the study.

The patients in whom appendectomy performed incidentally or for other indications; age below 15 years; history of alcoholic liver disease; hemolytic or liver diseases associated with hyperbilirubinemia; history of gastrointestinal or hepatopancreatobiliary malignancy in the past and unwilling patients were excluded from the study. These were subjected to investigation to support the diagnosis.

Investigation included total leukocytes count, differential leukocytes count, ultrasound, liver function tests (LFT) and CRP. Informed consent was obtained from all participants. These cases were operated and clinical diagnosis was confirmed by histopathological examination which is considered as a gold standard.

Based on histopathological examination patients we categorized the patients as negative (acute appendicitis without perforation or gangrene) and positive (acute appendicitis with perforation and/or gangrene). Their clinical and investigative data were compiled and analysed by using spss 17 version.

RESULTS

Present study results showed that the maximum participants were in age group of 11-30 years of age. out of the total, 84 (56%) were male participants. Pain in right iliac fossa 150 (100%) was the main complaint in almost all the patient.

Table 1: Characteristics of study population.

Variables		Number	Percentage
Age group in years	0-10	8	5.33
	11-20	59	39.33
	21-30	50	33.34
	31-40	21	14.00
	41-50	7	4.66
	>50	5	3.34
Sex	Male	84	56
	Female	66	44
Presenting complaints	Pain in RIF	150	100.00
	Nausea	93	62.00
	Vomiting	82	54.67
	Fever	46	30.67
	Anorexia	89	59.33
Clinical signs	Mc Burney's tenderness	150	100.00
	Psoas test	27	18.00
	obturator test	21	14.00
	Rovsing sign	58	38.67
	Cough sign	39	26.00
	Rebound tenderness	76	50.67
	Local rigidity	68	45.33
Alvarado Score	5-6	51	34.00
	7-8	47	31.33
	9-10	52	34.67

The next most common complaint was nausea 93 (62%) followed by anorexia 89 (59.33%) and vomiting 82 (54%). Amongst all signs, tenderness at Mc Burney,s point was the most common one, followed by Rebound tenderness 76 (50%), local rigidity 68 (45%) and Rovsing sign 58 (39%).

Table 2: Association between CRP, TSB and perforated appendix.

Variable		Perforated/gangrenous appendix 40 (27.98%)	Non- perforated appendix 103 (72.02%)	Total 144 (100%)	x^2 value	df	P value
CRP	Positive	29 (78.37%)	8 (21.63%)	37 (100%)	62.94	1	<0.05
	Negative	11 (10.37%)	95 (89.63%)	106 (100%)			
TSB	Positive	31 (70.45%)	13 (29.55%)	44 (100%)	56.93	1	<0.05
	Negative	09 (9.09%)	90 (90.91%)	99 (100%)			

Table 3: Sensitivity, Specificity, PPV and NPV Of CRP and TSB in predicting perforation.

Variable	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
CRP	72.50	92.23	78.38	89.62
TSB	77.50	87.38	70.45	90.91

About 51 (34%) patients were scored between 5-6 as per Alvarado score, 47 (31.33%) in range of 7-8 and 52 (34.67%) were scored between 9-10. Positive CRP level as greater than 60 mg/dl.

Total serum bilirubin as more than 1.2 mg/dl. Out of all in whom the CRP was positive, about 29 (78.37%) patients had either perforated or gangrenous appendicitis as compared to 8 (21.63%) in whom the appendix was non-perforated.

About 31 (70.45%) patients of perforated appendicitis had positive values for total serum bilirubin levels as compared to only 13 (29.55%) of non-perforated appendix had the positive TSB Values. Differences between the two groups i.e. Perforated and non-perforated appendix in relation to the positive CRP, TSB values are statistically significant (P Value <0.05).

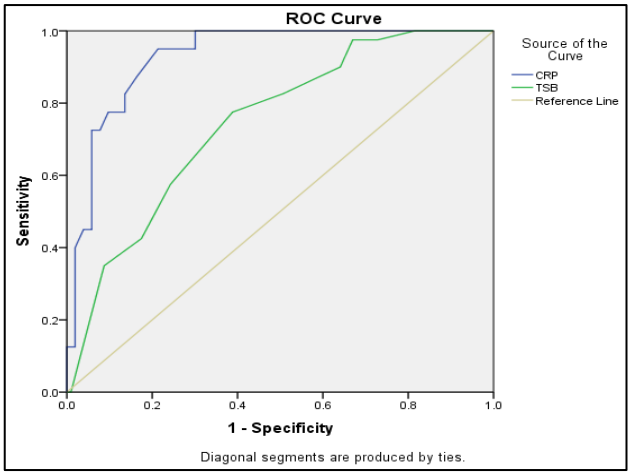

Figure 1: Receiver operating characteristic curves for C-reactive protein (CRP) and bilirubin (TSB) in predicting perforated appendicitis.

This study showed sensitivity is 72.50%, specificity of 92.23%, positive predictive value of 78.38% for a raised CRP. The sensitivity of TSB for predicting perforation is 77.50 and the values of specificity, PPV and NPV of the same are 87.38%, 70.45% and 90.91% respectively.

Table 4: Area under curve in ROC for CRP and TSB.

Lab investigations	AUC	Std. error	Asymptotic sig.	Significance
CRP	0.929	0.021	0.000	HS
TSB	0.745	0.043	0.000	HS

The area under curve was more for CRP than TSB indicating that CRP is better predictor for perforation in appendicitis as compared to the TSB.

DISCUSSION

The objective of present study was to evaluate role of total serum bilirubin (TSB) and C-reactive protein (CRP) individually as predictor of perforation in acute appendicitis. This can be achieved by comparing both in terms of Area Under Curve in ROC, sensitivity, specificity, positive predictive value and negative predictive value. CRP was identified as an acute-phase protein. Physiologically, CRP enhances cell-mediated immunity by promoting phagocytosis, accelerating chemotaxis and activating platelets. CRP is reliable early indicator of inflammation or injury.[9,10] The levels of CRP (C-reactive protein) usually increase around 8 hours after the onset of injury and usually reach their peak levels around 2-4 days and are found to be elevated as long as there is persisting infection or injury. In present study population, elevated serum CRP was present in 37 (34.90%) patients. Amongst the non-perforated cases the elevated serum CRP was present in only 8 (21.63%) cases as compared to perforated one where 29 (78.37%) had positive CRP level with statistically significant difference. Also, there is statistically significant difference TSB levels in the two groups; i. e. perforated and non-perforated appendicitis. Our finding is consistent with findings of study done by Kaya B. which documented a statistically significant difference in elevated CRP, between patients of acute appendicitis with perforation and without perforation.[11] In a study done by Mcgowanet al. they found that the biochemical markers (bilirubin, CRP and white cell count were significantly higher in perforation ($P < 0.001$).[12] Findings are similar with a study done by Hyoung-Min Moon, in which sensitivity of TSB is lower than CRP and specificity of CRP is more for diagnosing perforated appendicitis.[13] In several studies, the sensitivity of C-reactive protein for the diagnosis of acute appendicitis was 40-87%, the specificity was 53-82%, and diverse results were reported.[14] Bilirubin is not commonly known to be a relevant marker in appendicitis. Bilirubin levels in adults is usually raised due to liver or gallbladder problems.In appendicitis, especially in perforated one, compromised appendix wall integrity leads to translocation of bacteria and endotoxins from the appendix lumen into the portal system which leads Inflammatory cytokines to travel to the liver, inducing intrahepatic cholestasis. Present study

showed the specificity of hyperbilirubinemia of 87.34% for predicting the perforation in appendicitis. TSB is useful marker with slightly higher sensitivity than CRP for, but a lower specificity. Present study findings are similar to a study done by Chaudhary P.[15] AUC in ROC is more for CRP than TSB indicating CRP as better predictor in perforated appendicitis than TSB. Same findings are reported in a study done by Mujahid Ahmad Mir. Diagnostic Value of Total Leucocyte Count (TLC), C-reactive Protein (CRP) and bilirubin in patients with suspected acute appendicitis.[16] The diagnosis of appendicitis is still based on a patient's clinical presentation, and the judgement of the emergency surgeon. A correct pre-operative diagnosis is necessary to reduce unnecessary operations which will not only put the extra cost the but also the risk of complications associated with the surgery. This can be achieved by simpler blood investigations like CRP and TSB. This will help surgeon to proceed with the cases of acute appendicitis and to understand prognosis.

CONCLUSION

Thus, serum CRP and total serum bilirubin (TSB) can be used as useful markers for early diagnosis and prediction of perforation in cases of acute appendicitis. CRP would be a better marker for early diagnosis of perforation than TSB. But, larger study is recommended to validate the present observations as small sample size is the limitation of the study.

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