

Original Research Article

Diagnostic accuracy of hyperbilirubinemia in preoperative diagnosis of acute perforated appendix

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ABSTRACT

Background: Delayed diagnosis of perforated appendicitis is a life threatening condition. All these cases warrant expeditious surgical intervention. Hyperbilirubinemia can play a vital role in early diagnosis of perforated appendix and thereby reduce mortality, morbidity and prolonged hospital stay. The aim of this study is to compare the levels of bilirubin in simple appendicitis and perforated appendicitis.

Methods: This was a single center retrospective study of 100 patients who attended Surgery OPD with right iliac fossa pain during the period between July 2017 and June 2018.

Results: During the period of study, 100 patients were selected of which 18 (18%) subjects were diagnosed having perforated appendix and 82 (82%) cases were having non-perforated appendix. The mean serum bilirubin levels were 1.65 ± 0.83 among subjects diagnosed having perforated appendix whereas it was 0.82 ± 0.36 among subjects having non-perforated appendix. Further raised levels of bilirubin levels in blood were detected among 20 cases, of which 17 cases were diagnosed having perforated appendix. Out of total 20 cases in whom hyperbilirubinemia was observed, only 3 cases were having non-perforated appendix. Of total 80 cases in which normal Bilirubin levels in blood were detected, only 1 case had perforated appendix.

Conclusions: Preoperative serum bilirubin levels are promising tool with high diagnostic accuracy in preoperative diagnosis of acute perforated appendix when used together with clinical correlation.

Keywords: Acute perforated appendix, Hyperbilirubinemia, Unwanted appendisectomies

INTRODUCTION

Appendicitis is one of the most common clinical conditions encountered by general surgeons in our country. It presents as pain abdomen especially in the region of right iliac fossa. Many a times, atypical clinical presentation may pose a diagnostic challenge in front of us.^{1,2} It may also result in unnecessary appendectomy. Prevalence of such cases may range up to 20%. Literature has reported the rate of negative appendectomies as 35 to 45% in young women of child bearing age in whom condition mimics to pelvic inflammatory disease very closely.³

Scientific fraternity has devised a variety of methods or tests to evaluate the various aspects of appendicitis so that the frequency of unwanted appendectomies may be reduced. In this scenario, a variety of laboratory parameters like white blood cell (WBC) counts, C-reactive protein (CRP) values have been utilized.⁴ Accuracy of abdominal ultra-sonogram for diagnosing appendicitis have also been evaluated by various researchers.^{5,6} Apart from this, various scores combining clinical features and lab investigations have also been developed and evaluated.⁷⁻⁹

The present study will make a modest attempt to find the relationship between serum bilirubin levels and appendicitis and its predictive potential for the diagnosis of complicated appendicitis. Therefore, keeping scenario of resource-constrained settings with limited lab and radiological facilities in mind, it was planned to assess the practical utility of serum bilirubin levels in preoperative diagnosis of subjects having acute perforated appendix. Thus, the aim of the study was to evaluate diagnostic accuracy of hyperbilirubinemia in preoperative diagnosis of acute perforated appendix.

METHODS

The present study was conducted by the Department of General Surgery of a tertiary care teaching center at Aarupadai Veedu Medical College and Hospital, Puducherry, India. Patients seeking care at surgery OPD with pain in Right iliac fossa during the period from July 2017 to June 2018 formed the study population. Subjects with clinical diagnosis of acute appendicitis were included in the study. Patients having alcoholic liver disease, Hemolytic or liver disease associated with hyperbilirubinemia, gastrointestinal or hepatopancreaticobiliary malignancy in past and subjects having appendicular lump were excluded from this study.

The surgeon noted clinical features of acute appendicitis. In all patients with pain in right iliac fossa, the provisional diagnosis of acute appendicitis was made on the basis of history, clinical signs and relevant clinical data. Routine laboratory investigations were carried out like Haemoglobin, TLC count, neutrophil count, serum bilirubin, liver enzymes, which include SGPT (alanine transaminase), SGOT (aspartate transaminase), ALP (Alkaline phosphatase), Urine routine microscopy, X-Chest PA, X-ray abdomen erect, Ultrasonography abdomen and pelvis.

For the purpose of this study, patients were classified in the two groups, (1) subjects diagnosed having perforated appendix and (2) subjects with non-perforated appendix. Serum Bilirubin levels were measured at the time of operation of appendix. Later on diagnostic accuracy of hyperbilirubinemia was assessed in diagnosing the cases with perforated appendix.

The study adhered to the tenets of the declaration of Helsinki for research in humans. All the proforma were manually checked and edited for completeness and consistency and were then coded for computer entry. After compilation of collected data, analysis was done by dividing subjects into 2 groups, subjects diagnosed with or without perforated appendix. Diagnostic accuracy of hyperbilirubinemia was calculated by sensitivity, specificity, positive predictive value and negative predictive value.

These attributes were calculated with the help of following standardized formulas.¹⁰⁻¹²

Sensitivity: Probability that a test result will be positive when the disease is present (true positive rate) = $a / (a+b) \times 100$

Specificity: Probability that a test result will be negative when the disease is not present (true negative rate) = $d / (c+d) \times 100$

Positive predictive value: Probability that the disease is present when the test is positive = $a / (a+c) \times 100$

Negative predictive value: Probability that the disease is not present when the test is negative = $d / (b+d) \times 100$.

RESULTS

Data of a total of 100 patients was analyzed and presented in this study. Out of total, 18 (18%) subjects were diagnosed having perforated appendix whereas remaining 82 cases were having non-perforated appendix. Mean serum bilirubin levels were 1.65 ± 0.83 among subjects diagnosed having perforated appendix whereas it was 0.82 ± 0.36 among subjects having non-perforated appendix (Table 1).

Table 1: Comparison of serum bilirubin levels among study subjects.

Study subjects	Serum bilirubin levels	
	Mean	Standard deviation
Subjects diagnosed having perforated appendix	1.65	0.83
Subjects with non-perforated appendix	0.82	0.36

Raised levels of bilirubin levels in blood were detected among 20 cases, of which 17 cases were diagnosed having perforated appendix. Out of total 20 cases in whom hyperbilirubinemia was observed, only 3 cases were having Non-Perforated Appendix. Of total 80 cases in which normal Bilirubin levels in blood were detected, only 1 case had perforated appendix (Table 2).

Table 2: Status of bilirubinemia with the condition of appendix at the time of operation.

Bilirubin levels in blood	Condition of appendix at the time of operation		Total
	Perforated appendix	Non-perforated appendix	
Raised	17 (a)	3 (b)	20 (a+b)
Normal	1 (c)	79 (d)	80 (c+d)
Total	18 (a+c)	82 (b+d)	100 (a+b+c+d)

Sensitivity of hyperbilirubinemia in diagnosing perforated appendix was calculated to be 94.4%.

Specificity was 96.3%. Positive predictive value of the test was 85% whereas Negative predictive value of hyperbilirubinemia in diagnosing perforated appendix was calculated to be 98% (Table 3).

Table 3: Diagnostic accuracy of hyperbilirubinemia in diagnosing perforated appendix.

Parameter of diagnostic accuracy	Formula	Calculation	Value (%)
Sensitivity	$a / (a+b) \times 100$	$17 / (17+1) \times 100$	94.4
Specificity	$d / (c+d) \times 100$	$79 / (3+79) \times 100$	96.3
Positive predictive value	$a / (a+c) \times 100$	$17 / (17+3) \times 100$	85.0
Negative predictive value	$d / (b+d) \times 100$	$79 / (1+79) \times 100$	98.0

DISCUSSION

The appendix was first described in 1521 and inflammation of the appendix has been known to be a clinical problem since 1759.¹³ The term 'appendicitis', however, was not used until Reginald Fitz described this condition in 1886.¹⁴ One of the commonest clinical presentations that require emergency surgery is acute appendicitis. It is rare in infancy and amongst the elderly, but is common in children, teenagers and young adults.

Recent studies have found bilirubin to be a potential marker for acute appendicitis.^{15,16} The underlying mechanism for hyperbilirubinemia is thought to be due to compromised appendix wall integrity that leads to translocation of bacteria and endotoxin into the portal system. This will disrupt the excretion of bilirubin into bile canaliculi. Serum total bilirubin increases as the infection becomes more severe.¹⁷ Pro-inflammatory cytokine and nitric oxide also play a role in triggering intrahepatic cholestasis.¹⁸

In the current study, mean serum bilirubin levels were 1.65 ± 0.83 among subjects diagnosed having perforated appendix whereas it was 0.82 ± 0.36 among subjects having non-perforated appendix. Thus, it can be stated that mean serum bilirubin levels were quite higher in patients with perforated appendicitis compared to non-perforated.

Mean bilirubin level was 2.026 mg/dl (SD: 0.71 mg/dl) in acute appendicitis with perforation which was significantly higher than those with non-perforated appendix ($p < 0.001$) compared to Michael Sand et al the mean bilirubin in perforated appendix was 1.5 mg/dl (SD-0.9 mg/dl) which was significantly higher than those of non-perforated group ($p < 0.05$).¹⁹ This observation is in cohort with previous study done by McGowan DR.²⁰ This study shows the odds of appendiceal perforation which are two times higher (odds ratio 2.27) for patients with

hyperbilirubinemia compared to those with normal bilirubin levels. This finding is similar with a retrospective study conducted by USC Medical Center, Los Angeles that found patients with gangrene and perforation were significantly more likely to have hyperbilirubinemia than those with acute appendicitis.²¹

In this study we observed that, sensitivity of hyperbilirubinemia in diagnosing perforated appendix was calculated to be 94.4%. Specificity was 96.3%. Positive predictive value of the test was 85% whereas Negative predictive value of hyperbilirubinemia in diagnosing perforated appendix was calculated to be 98%. Salamat Khan in his study found specificity, sensitivity, positive predictive value, negative predictive value and overall diagnostic accuracy of 100%, 80%, 100%, 14% and 81.14% respectively, here false positive result was nil and false negative was 18.5%.²² Atahan et al in his study showed specificity, sensitivity, positive predictive value, negative predictive value of 87.21%, 77.77%, 45.16% and 96.66% respectively.²³

Many studies looked at the level of 17 $\mu\text{mol/l}$ as the cut-off value to predict perforated appendix.^{2,24} In view of the multiple findings on sensitivity and specificity, hyperbilirubinemia gave some value as a predictor of perforated appendix. Researchers suggested that bilirubin level should be assessed together with clinical sign and symptoms.²⁵

CONCLUSION

In light of above discussion, it can be concluded that preoperative serum bilirubin levels are promising tool with high diagnostic accuracy in preoperative diagnosis of acute perforated appendix. It should be used together with clinical findings and other routine laboratory tests to improve clinical decision-making by the clinician.

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