Role of hyperbilirubinemia as a diagnostic marker for acute appendicitis : a hospital based study from Tamil Nādu

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ABSTRACT

Background & objectives: The rise of bilirubin levels can enhance the precision of clinical diagnosis for acute appendicitis and, significantly, aid in the anticipation and prevention of potential complications associated with this condition. The aim of this study was to examine the correlation between hyperbilirubinemia and acute appendicitis, and to assess its validity as a diagnostic indicator for acute appendicitis. **Methods:** A total of one hundred patients, exhibiting symptoms of right iliac fossa pain that clinically indicate appendicitis or appendicular perforation, and falling within the age range of 21 to 50 years, were included in the study using successive sampling. Routine laboratory examinations were conducted in all individuals. The measurement of serum bilirubin levels was conducted in all patients using a fully automated analyser system. **Results:** The levels of total bilirubin (mg/dl) were 0.90±0.34 mg/dl in simple cases, 2.15±0.83 mg/dl in cases of perforated appendicitis, and 2.47±1.23 mg/dl in cases of perforated appendicitis. Among a total of 85 instances, 26 cases exhibited a bilirubin level over 1mg/dl. Furthermore, in the subset of gangrenous appendicitis cases (n=3), all cases demonstrated a bilirubin level exceeding 1mg/dl. Similarly, among the 12 cases of perforated appendicitis, 11 cases exhibited a bilirubin level exceeding 1mg/dl. **Conclusions:** The presence of elevated total serum bilirubin levels in the absence of elevated liver enzymes serves as a reliable signal for appendicular perforation. The measurement of total serum bilirubin shows potential as a novel and effective laboratory indicator for the diagnosis of appendicular perforation.

Key words: appendicitis, diagnosis, lesion, clinical suspicion, serum bilirubin level

INTRODUCTION

Appendicitis is a prevalent etiology of stomach pain that necessitates urgent surgical intervention. The prevalence of this condition is seldom during infancy and among the elderly, but is more prevalent among children, teenagers, and young people. Appendicitis affects approximately 8% of individuals residing in Western countries during the course of their lifespan.[1] The highest occurrence rate of acute appendicitis is observed throughout the second and third decade of an individual's life. The occurrence of this condition is infrequent during infancy, but its prevalence tends to rise

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during childhood and early adulthood. The prevalence of appendicitis is comparable between males and females before to reaching puberty. The male-female ratio in the population of teenagers and young adults experiences an increase to a ratio of 3:2 by the age of 25. The prevalence of appendicectomy is 12% among males and 25% among females, with roughly 7% of individuals experiencing appendectomy due to acute appendicitis at some point in their lives.[2,3]

The primary etiology of acute appendicitis is widely attributed to luminal obstruction. Faecoliths commonly serve as the primary etiological factor for blockage. The microbial composition of the normal appendix closely resembles that of the normal colon.[4] The clinical diagnosis of acute appendicitis is mostly reliant on clinical evaluation. However, relying solely on clinical suspicion to make a choice for surgery can result in the unnecessary removal of a healthy appendix in a significant proportion of patients, ranging from 15% to 50%. The accurate identification of Appendicitis continues to pose a challenge, despite the progress made in laboratory and radiographic examinations. The variability in the number of appendectomies resulting in the subsequent discovery of a normal appendix ranges from 15% to 50%.[5] Additionally, postoperative problems can arise in up to 50% of these patients. It appears that a prudent course of action would be to promptly perform an appendectomy upon suspicion of the problem.[6]

The rise of bilirubin levels can contribute to the precision of clinical diagnosis for acute appendicitis and, more significantly, aid in the anticipation and prevention of potential complications associated with this condition. In contrast to non-perforated acute appendicitis, which can be effectively treated through appendectomy with minimal postoperative recuperation, the presence of perforated appendicitis or suppurative appendicitis can give rise to a range of complications that may lead to potentially fatal circumstances.[7] The study was done to investigate the role of hyperbilirubinemia as a novel diagnostic tool for predicting the occurrence of gangrenous or perforated appendicitis. The objective of this study was to examine the correlation between hyperbilirubinemia and acute appendicitis, as well as assess its validity as a diagnostic indicator for acute appendicitis.

MATERIALS AND METHODS

This study was conducted at the Department of Surgery, Government Kilpauk Medical College Hospital in Chennai, India. It focused on 100 patients aged between 21 and 50 years who were diagnosed with acute appendicitis. The study period spanned from May 2021 to April 2022, and participants were selected using consecutive sampling. All individuals experiencing discomfort in the right iliac fossa, which is clinically indicative of appendicitis or appendicular perforation, were enrolled in the study. Patients with a documented medical history of Jaundice or liver disease, positive HbsAg, cholelithiasis, and suspected hepatobiliary system malignancy were evaluated and determined to be free of the latter condition.

The surgeons noted the clinical indications of acute appendicitis and recorded the duration of the symptoms upon admission. Informed consent was acquired from all individuals who were registered as cases. The preliminary diagnosis of acute appendicitis will be established in patients experiencing pain in the right iliac fossa, relying on a

comprehensive assessment of their medical history, clinical manifestations, and pertinent clinical information. A series of standard laboratory tests were conducted. The measurement of serum bilirubin levels was conducted in all patients using a fully automated analyser system.

The categorical variables were reported in terms of number and percentage (%), while the continuous variables were reported as mean ± standard deviation (SD) and median. The comparison of quantitative data was conducted using an Independent t-test between the two groups. On the other hand, the comparison of qualitative factors was performed using either a Chi-Square test or a Fisher Exact test. A p-value less than 0.05 was deemed to be statistically significant. The data was inputted into a Microsoft Excel spreadsheet, and subsequent analysis was conducted using the Statistical Package for Social Sciences (SPSS) version 21.0.

RESULTS

In our investigation, it was observed that 22.00% of the patients were within the age category of 13 to 20. A total of 56.00% of the patient population falls between the age range of 21-30 years. The average age of presentation was 25.92±9.13 years. The study population consisted predominantly of male adults, comprising 58% of the total sample, while female adults accounted for 42% of the participants. (Table 1)

Table 1: Distribution of cases according to age and sex

Age group (years)	**No. of patients**	**Percentage**
21- 20	22	22.00%
21 to 30	56	56.00%
31 to 40	10	10.00%
41 to 50	12	12.00%
Sex		
Male	58	58.00%
Female	42	42.00%

A total of 76 cases of acute appendicitis and 8 cases of perforated/gangrenous appendicitis were identified in the USG findings.

The mean total bilirubin level in uncomplicated cases was 0.90±0.34 mg/dl, whereas in cases of perforated appendicitis it was 2.15±0.83 mg/dl and in cases of severe appendicitis it was 2.47±1.23 mg/dl. During the perioperative period, a total of 100 patients were examined. Among these patients, 85 had physical symptoms indicative of acute appendicitis, whereas 12 presented with a ruptured appendix and 3 displayed a gangrenous appendix. (Table 2)

Table 2: Distribution of cases according status of appendicitis & bilirubin levels

Parameters	**Uncomplicated (n=85)**	**Perforated Appendicitis**	**Gangrenous appendicitis**	**p-value**

Total bilirubin(mg/dl)	0.90±0.34	2.15±0.83	2.47±1.27	0.001
Direct bilirubin(mg/dl)	0.58±0.31	1.71±0.73	2.00±1.38	0.001
Indirect bilirubin(mg/dl)	0.32±0.17	0.51±0.18	0.44±0.12	0.001

Histopathological analysis revealed that out of the total sample size, 85 patients were diagnosed with acute appendicitis, whereas 3 patients exhibited gangrenous appendicitis and 12 patients presented with perforated appendicitis. In a study of acute appendicitis, a total of 85 cases were examined. Among these instances, 26 had a bilirubin level exceeding 1mg/dl. In the subset of gangrenous appendicitis, all three cases had a bilirubin level exceeding 1mg/dl. Similarly, in the subset of perforated appendicitis, 11 out of 12 cases had a bilirubin level exceeding 1mg/dl. (Table 3)

Table 3: Histopathological diagnosis & bilirubin levels

Histopathological diagnosis	**Total Bilirubin**		**Total**	**P value**
	<1mg/dl	**>1mg/dl**		
Acute appendicitis	59	26	85	0.001*
Gangrenous appendicitis	0	3	3	
Perforated appendicitis	1	11	12	

DISCUSSION

In our investigation, it was observed that 22.00% of the patients were within the age category of 13 to 20. A total of 56.00% of the patient population falls between the age range of 21-30 years. The average age of presentation was 25.92±9.13 years. The study population consisted predominantly of male adults, comprising 58% of the total sample, while female adults accounted for 42% of the participants. The average age of males was 23.86 years, while the average age of females was 28.44 years. In a study conducted by Muzna Iftikhar et al.[8], it was observed that the age range of participants ranged from 12 to 60 years, with a mean age of 24.16 ± 11.69 years.

In our investigation, the levels of total bilirubin (mg/dl) were observed to be 0.90±0.34 mg/dl in cases without complications, 2.15±0.83 mg/dl in cases of perforated appendicitis, and 2.47±1.23 mg/dl in cases of perforated appendicitis. The SGOT level in uncomplicated instances was found to be 33.15±9.06 IU/L, whereas in cases of perforated appendicitis, it was observed to be 58.33±17.62 IU/L. Additionally, in cases of perforated appendicitis, the SGOT level was measured to be 51.33±25.40 IU/L.

In a study involving 85 cases of acute appendicitis, it was observed that 26 cases exhibited a bilirubin level over 1mg/dl. Among the 3 cases of gangrenous appendicitis, all cases demonstrated a bilirubin level exceeding 1mg/dl. Similarly, among the 12 cases of perforated appendicitis, 11 cases exhibited a bilirubin level exceeding 1mg/dl. Ramaswami YB and Muzna Iftikhar et al. also observed a similar trend, where hyperbilirubinemia was identified as a diagnostic indicator for difficult appendicitis (specifically gangrenous and perforated cases) in 36 patients (19.46%), while uncomplicated (simple) acute appendicitis was diagnosed in 149 patients (80.54%).[9] The utilization of hyperbilirubinemia as a diagnostic marker has the potential to address the

issues of limited resources and diagnostic modalities, while also facilitating the identification of complex instances of AA. This, in turn, can inform surgical decision-making by prioritizing those cases that are deemed more challenging, as opposed to cases that are initially identified as simple. Therefore, it is possible to partially prevent the complications that arise as a result of gangrenous and perforated appendicitis.

In a study conducted by Tuker et al., the C-reactive protein (CRP) levels were seen to vary between 1-453 mg/l, with a mean value of 56.53±86.49 mg/l. The statistical significance of the occurrence of elevated C-reactive protein (CRP) levels was not seen. The current study findings indicate that there was no statistically significant association between C-reactive protein (CRP) levels and the diagnosis of appendicitis. The total leukocyte count (TLC) demonstrated a higher level of significance as a predictor for acute appendicitis compared to C-reactive protein (CRP) in predicting the severity of the condition.[10]

The research conducted by Sand et al. (year) revealed a notable prevalence of hyperbilirubinemia, with around 24.9% of the 538 patients diagnosed with acute appendicitis exhibiting this condition. Furthermore, it was found that 50.7% of the patients had confirmed cases of perforated appendicitis.[11] In a study conducted by Noh and colleagues, it was found that bilirubin demonstrated the best level of specificity (75%) in the diagnosis of difficult cases, as opposed to white blood cell count (19%) and C-reactive protein (35%).[12] In their study, Patel et al. (year) found that the sensitivity for detecting hyperbilirubinemia in acute uncomplicated cases was 65.33%, but it was 92% for complex appendicitis.[13]

According to a study conducted by Ghimire et al., it was shown that 57.7% of patients diagnosed with hyperbilirubinemia also presented with gangrenous or perforated appendix.[14] In the study conducted by Khan et al., it was shown that 86.6% of the patients diagnosed with acute appendicitis exhibited hyperbilirubinemia. The bilirubin levels in these patients ranged from 1.2mg/dl to 8.4mg/dl. The authors noted that bilirubin can serve as a significant diagnostic tool for investigating Appendicular infection. However, when the total count, CRP, and bilirubin readings are combined, it is possible to make a reliable prediction regarding the severity of the appendix infection.

The research conducted by Ghimire et al. has identified a statistically significant distinction between patients with gangrenous appendicitis and those with simple appendicitis in terms of their Alvarado score, total leukocyte count, and total bilirubin level.[15] The study conducted by Hong et al. found that the univariate analysis revealed statistically significant differences for TLC ($p<0.0001$), total bilirubin ($p<0.0001$), and Alvarado score ($p<0.0001$). The results of the multivariate analysis indicate that both total bilirubin levels and the Alvarado score exhibit statistically significant diagnostic value in identifying cases with perforated appendicitis.

This study has many limitations. Firstly, the study groups were chosen based on histological diagnosis, which may introduce bias. Additionally, patients who were admitted with suspected appendicitis but did not undergo surgery were not included in the study, thus affecting the generalizability of the findings. Furthermore, patients with negative appendicitis were also not included, which could impact the comprehensiveness of the results. The correct retrieval of the timing of blood tests in relation to the onset of symptoms

was not possible. The timing of events may have an impact on the accuracy of symptom retrieval. A comprehensive investigation is required to assess the significance of Bilirubin, together with other indicators, in the prediction of appendicitis.

CONCLUSION

An elevated level of total blood bilirubin, in the absence of raised liver enzymes, serves as a reliable signal for appendicular perforation. The measurement of total serum bilirubin shows potential as a novel laboratory indicator for the detection of appendicular perforation. Patients who exhibit clinical signs and symptoms of appendicitis, along with the presence of hyperbilirubinemia, should be recognized as having an increased likelihood of appendicular perforation. This suggests that the measurement of total blood bilirubin levels holds predictive value in the diagnosis of appendicular perforation.

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AUTHORS' CONTRIBUTION

All the authors have contributed equally.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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