



“ELEVATED SERUM BILIRUBIN LEVELS - DIAGNOSTIC MARKER OF COMPLICATED APPENDICITIS - A RETROSPECTIVE COHORT STUDY”

General Surgery

Dr S Mansur Basha*

M.S. Assistant Professor , Department Of General Surgery , Kurnool Medical College
*Corresponding Author

Dr J Sahrudai

3 Rd Year Postgraduate , Department Of General Surgery , Kurnool Medical College

Dr N Ramesh Naik

3 Rd Year Postgraduate , Department Of General Surgery , Kurnool Medical College

Dr G Ananth Nivesh

3 Rd Year Postgraduate , Department Of General Surgery , Kurnool Medical College

ABSTRACT

Introduction : One of the most frequent emergency surgery is an appendectomy. Complicated appendicitis can result from delayed diagnosis and treatment. There is currently no conclusive predictive factor for the diagnosis of complicated appendicitis. The purpose of the study is to evaluate the potential predictive value of a high blood bilirubin level for complex appendicitis. **Methods :** Patients diagnosed with acute appendicitis between March 2023 and December 2023 were included in a retrospective cohort study. Patients' informed written consent was obtained, and preoperative biochemical parameters such as elevated white blood cell count ($>11000/\text{cubic millimeter}$) and serum bilirubin level ($>1.4 \text{ mg/dl}$) were examined. Appendicitis cases diagnosed with the aid of the Alvarado score and undergoing surgery were taken in study. Based on the histopathological report, the cases were classified into two groups: Uncomplicated and complicated. **Results:** Seventy-two percent of the 68 individuals who were enrolled in the study had a mean age of 25.3 ± 6.5 years. Of those who experienced appendicitis, 75 percent had an uncomplicated case and 25 percent had a difficult case. The straightforward group's mean bilirubin was $0.9 \pm 0.3 \text{ mg/dl}$, while the complicated group's mean was $1.7 \pm 0.4 \text{ mg/dl}$ ($P < 0.05$). Hyperbilirubinemia had an 82.3 and 84.3% sensitivity and specificity in predicting complex appendicitis, respectively. **Conclusion:** According to the study, there is a greater chance of complicated appendicitis in patients with acute appendicitis and a higher serum bilirubin level. Serum bilirubin levels aid in the early detection of complex appendicitis and the planning of prompt and effective treatment. Therefore, the study shows that when evaluating patients with suspected acute appendicitis, bilirubin should be employed in addition to clinical examination and other laboratory procedures.

KEYWORDS

Acute Appendicitis, hyperbilirubinemia , complicated.

INTRODUCTION

One of the most frequent surgical emergencies worldwide is acute appendicitis, and appendectomy is one of the most popular emergency procedures [1]. 40% of instances of appendicitis occur in patients between the ages of 10 and 29 [2]. This makes it a disease of the young. Globally, it affects men comparatively more often than women. The lifetime risk of Acute appendicitis for an individual is 6.7% for women and 8.6% for men [3]. Research has indicated that only 7.46% of surgical pathology patients had an Acute appendicitis case that was confirmed by histopathology [4]. Nonetheless, Acute appendicitis clinical diagnosis continues to be a prevalent surgical issue. The prevalence of incorrect appendicitis diagnoses (15.3%) has not changed despite the growing use of computed tomography and ultrasonography, as the rate of appendicular perforation [2]. Life-threatening complications may arise if appendicitis is not diagnosed and treated promptly [5]. Increased rates of perforation, post-operative morbidity, death, and length of hospital stay are the outcomes of the delay. As soon as the problem is suspected, appendectomy appears to be a safe alternative, however this approach may lead to an increase in needless appendectomies [6].

There are a number of scoring systems used for diagnostic purposes, including the Alvarado score, the pediatric version of the Alvarado score, and the more recent Appendicitis Inflammatory Response (AIR) score. These have been shown to be helpful in diagnosing Acute appendicitis [7-9] and take into account clinical signs and symptoms in addition to hematological markers including leucocytosis and C-reactive protein. The Alvarado score was utilized in our study to make the appendicitis diagnosis. But no consistently accurate marker or scores for anticipating Acute appendicitis problems have been found [10]. There is a great deal of disagreement over the best way to treat appendicitis. Antibiotic nonoperative management may be possible, according to several studies [11,12]. In order to avoid needless surgery, patients in many institutions who have an unclear diagnosis but do not develop peritonitis are generally treated with a trial of observation. Combined with clinical symptoms, an Acute appendicitis -specific biochemical test may determine whether patients are at risk for complex appendicitis and should be evaluated for surgery. Therefore, a novel marker for complex Acute appendicitis would be really appreciated.

It has been suggested by Estrada et al. [13] that elevated serum bilirubin could serve as a distinct indicator for perforated or gangrenous appendicitis. Elevated serum bilirubin levels have been linked to complicated appendicitis in multiple investigations, indicating that this illness may be predicted by elevated bilirubin levels [14]. But a systematic review by Gavrilidis et al. [15] issued a warning, saying that hyperbilirubinemia might not be a reliable predictor of perforation in appendicitis cases on its own. This study intends to examine the possible relevance of hyperbilirubinemia as a predictor of complex appendicitis in light of the contradictory results.

MATERIALS AND METHODS

Study design : Retrospective Cohort study

Sample size : 68

Duration of study : March 2023 - December 2023

In the emergency room, patients were clinically assessed with a thorough history and physical examination. Serum bilirubin and other standard preoperative hematological and biochemical parameters were determined in the hospital laboratory using an auto-analyzer equipment. More than 1.4 mg/dl of total bilirubin was considered hyperbilirubinemia. A white blood cell (WBC) count of more than 11,000 was considered elevated. These numbers match the upper bounds of the reference ranges that the institution's hospital laboratory uses for normalcy. Based on the hospital laboratory's reference levels, the results were classified as either "normal" or "raised (hyperbilirubinemia)."

Following the appendectomy in these cases, intraoperative results were documented. The specimen was placed in a 10% formalin solution and sent for histological analysis. Every case's histopathological report could be located.

The patients who underwent conventional open appendectomy were grouped into two categories on the basis of the histo- pathological reports:

Group 1 or uncomplicated appendicitis

Uncomplicated appendicitis was defined as the presence of an inflamed appendix, in the absence of gangrene, perforation, or abscess around the appendix.

Group 2 or complicated appendicitis

Complicated appendicitis was defined as gangrenous or perforated appendicitis or appendicular abscess[17].

Complicated appendicitis was defined as perforation of the appendix, gangrenous appendicitis, and/or abscess noted on radiological studies upon hospital admission, operative reports, or the pathology of the results of the surgical specimen.

Inclusion Criteria

All the patients admitted in Department of Surgery of our institution with diagnosis of Acute appendicitis using the Alvarado score and operated for Acute appendicitis.

Exclusion Criteria

1. Patients with a history of alcoholic liver disease and chronic liver disease.
2. Patients with hemolytic or liver diseases associated with hyperbilirubinemia.
3. History of gastrointestinal or hepatopancreaticobiliary malignancy in the past.
4. Patients with positive HBsAg and HCV status.
5. Patients with choledocholithiasis.
6. Patients under going interval appendectomy.

RESULTS**Sociodemographic characteristics**

The mean age of the patients was 25.3 years with a SD of 6.5 years. The age of the patients with appendicitis ranged from 14 to 45 years. Seventy two percent of the included patient were male while 28 % were females. The proportion of complicated appendicitis was 25 % in the study. The details of the demographic distribution are shown in Table 1.

Table : 1

Sociodemographic characteristics of included patients	
Variables	n (%)
Age (in years	25.3 ± 6.5
Sex	
Male	49 (72%)
Female	19 (28%)
Type of Appendicitis	
Uncomplicated	51 (75%)
Complicated	17 (25%)

Clinical and laboratory findings

In our study, the duration of pain was observed to be longer in complicated cases (2.41 days) as compared to uncomplicated cases (1.68 days). However, this difference did not reach statistical significance. The mean WBC count was higher in complicated cases (15.52 thousand cells/mm³) compared to uncomplicated cases (13.19 thousand cells/mm³), but the difference was not statistically significant. On the other hand, the mean bilirubin level was found to be significantly different between the two groups of appendicitis (P = 0.0002).

(). The details of the clinical and lab findings of the included patient are shown in Table 2.

Table : 2

Clinical and lab findings of included patient			
	Uncomplicated	complicated	P value
Duration of pain(in days)	1.6 ± 0.7	2.4 ± 1.0	0.04
Mean WBC level (Thousand cells/mm ³)	13.19 ± 5.3	15.52 ± 4.6	0.01
Mean bilirubin levels (mg/dl)	0.9 ± 0.3	1.7 ± 0.4	0.0002

Hyperbilirubinemia as a predictor of complicated appendicitis

Among the 17 patients with complicated appendicitis, 82.3% of them developed hyperbilirubinemia as detailed in Table 3. Table 4 presents the sensitivity and specificity of hyperbilirubinemia in predicting complicated appendicitis, which were found to be 82.3 and 84.3%, respectively. Similarly, the positive predictive value and negative predictive value of hyperbilirubinemia in predicting complicated appendicitis were 63.6 and 93.4 %, respectively. A bilirubin level above 1.4 mg/dl was used as the cutoff for determining hyperbilirubinemia. To assess the accuracy of bilirubin in predicting complicated appendicitis, ROC analysis was performed. The test result

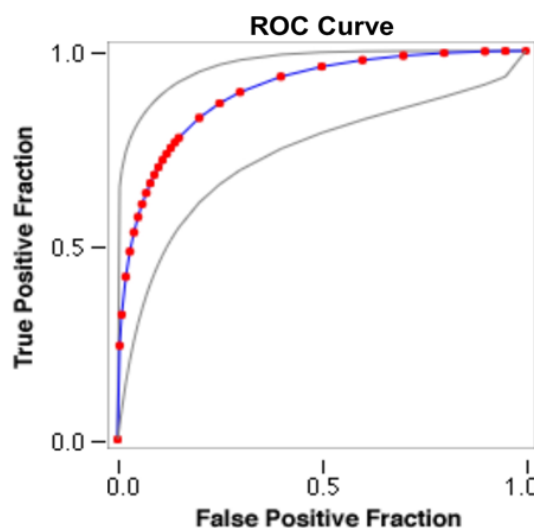
of the ROC curve showed that the area under the curve (AUC) was 0.897 which was statistically significant with a P-value <0.05 (Fig. 1). In this study, hyperbilirubinemia was observed in 32.35 % of the AA cases. These findings suggest that bilirubin can serve as a diagnostic test to distinguish complicated appendicitis.

Table : 3

Cross-tabulation of bilirubin level with type of appendicitis			
	Complicated Appendicitis		
Hyperbilirubinemia	Yes	No	Total
Yes	14 (82.3%)	08 (15.6%)	22 (32.35%)
No	03 (17.6%)	43 (84.3%)	46
Total	17	51	68

Table : 4

Sensitivity and Specificity calculation	
Sensitivity	82.3
Specificity	84.3
Positive predictive value	63.6
Negative predictive value	93.4

**ROC Curve****DISCUSSION**

Although it can afflict people at any age, appendicitis most frequently strikes those between the ages of 10 and 29 [18,19]. The age range of 14 to 45 years for the participants in our study who had Acute appendicitis supports the idea that it can happen at any age. With a median age of 25 , more than half of the Acute appendicitis patients in our study were in the 18- to 28-year-old age range. These results are consistent with those of studies conducted in Nepal [20], Pakistan [21], and Ireland [22]. Nonetheless, another investigation found that the median age was higher [13, 23]. The burden of Acute appendicitis was greater among male than female in our study (72 % of the cases), which was consistent with other studies around the world, where the burden among male ranged from 52 to 78% [18,20,21,23–25].

This study's overall classification of Acute appendicitis cases as complicated was 25%, which is similar to studies done in the US [13,18] but different from a study done in Pakistan, where 59.2% of all Acute appendicitis cases were classified as complicated [21]. Compared to cases with simple appendicitis, complex cases had a significantly longer mean duration of pain upon hospital presentation (2.4 days vs 1.6 days). This could be explained by the patient's delayed presentation, which resulted in complications. This was statistical significance. In our study, difficult cases of appendicitis had a higher total leukocyte count than simple cases, but the difference was not statistically significant.

Our study's comparison of bilirubin levels revealed a sensitivity of 82.3% and specificity of 84.3%, which is in line with research findings from studies carried out in Nepal, the US, the UK, and Ireland [20,22,26,27]. There was a statistically significant difference in mean bilirubin levels between uncomplicated (0.9 mg/dl) and complicated (2.4 mg/dl) cases of Acute appendicitis . The study set a cutoff level of

bilirubin levels above 1.4 mg/dl to identify hyperbilirubinemia. According to an Irish investigation, hyperbilirubinemia was more common in cases of difficult Acute appendicitis than in cases of uncomplicated Acute appendicitis [22]. Moreover, the region under the curve in ROC demonstrated statistical significance, suggesting that hyperbilirubinemia may function as a predictor of complex Acute appendicitis. This result is consistent with previous research showing hyperbilirubinemia to be a predictor of complex Acute appendicitis [13, 22, 27, 28]. There are several known causes of hyperbilirubinemia in Acute appendicitis. One method that has been linked to bacteria like *Escherichia coli* is hemolysis [29]. Another mechanism is the decreased hepatic absorption and excretion of bilirubin and bile salts as a result of the production of the cytokines IL6 and TNF α brought on by endotoxemia [30]. The most frequent bacteria found in intraperitoneal fluids in Acute appendicitis [22] is *E. coli*, which is linked to lipopolysaccharide endotoxemia. Bacterial invasion of the portal venous system, liver, and eventually the artery system is facilitated by elevated levels of bacteria in the appendix combined with ischemia [13]. It is assumed that endotoxemia linked to appendicitis and portal bacteremia are the causes of hyperbilirubinemia in Acute appendicitis.

One helpful marker of complex appendicitis (perforation, gangrene, or abscess) is an increased total serum bilirubin level. This result showed that in order to avoid septicemia and peritonitis, prompt intervention was necessary. An increased total bilirubin level can offer important information when paired with clinical signs and symptoms, supporting the decision to perform an early appendectomy. Children with difficult Acute appendicitis tend to have mean values of blood total bilirubin that are greater than those with uncomplicated cases, according to a comprehensive study by Montero et al. [14]. Researchers discovered that serum total bilirubin has a strong diagnostic yield for differentiating between children's complex and uncomplicated appendicitis. Additionally, they advised exercising caution when interpreting the results because of the significant heterogeneity across the papers that made up the review.

It's crucial to recognize this study's limitations, though. This study had a small sample size and was conducted at a single center. There was no patient follow-up in this trial; only the in-hospital outcomes were documented. Serum bilirubin levels taken at the time of admission can be useful when combined with more sophisticated diagnostic procedures like CT scanning and ultrasounds, which can help identify complicated appendicitis and facilitate appropriate therapeutic care.

CONCLUSION

According to the study, individuals with Acute appendicitis and elevated serum bilirubin levels are more likely to experience a complex case of appendicitis. Morbidity and death from complex appendicitis can be reduced with early detection. Serum bilirubin level aids in the prediction of complex appendicitis, allowing for the timely and appropriate planning of treatment. Therefore, the study shows that when evaluating individuals with suspected Acute appendicitis, bilirubin should be employed in addition to clinical evaluation and other laboratory studies.

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