

Prospective observational determination of the value of pre-operative hyperbilirubinemia as a predictor of complicated appendicitis

¹Dr. Gundla Vamshi Krishna, ²Dr. Nachagiri Madhava, ³Dr. Srinivas Talla

^{1,2}Assistant Professor, General Surgery, RVM Institute of Medical Sciences & Research Centre, Laxmakkapally, Telangana, India

³Associate Professor, General Surgery, RVM Institute of Medical Sciences & Research Centre, Laxmakkapally, Telangana, India

Corresponding Author:

Dr. Nachagiri Madhava (rvims.ri@gmail.com)

Abstract

Aim: The aim of this study to determine the value of pre-operative hyperbilirubinemia as a predictor of complicated appendicitis.

Material and methods: The study was a prospective observational study conducted in the Department of General Surgery....., India for the period of 1 year. Total 60 patients who were diagnosed to have appendicitis and admitted in surgery department and who underwent appendicectomy were included in the study. Clinical examination, blood routine examination, Alvarado score, ultrasound abdomen, histopathology examination, pre and post-operative values of total bilirubin, direct bilirubin and indirect bilirubin were studied.

Results: In our study 35 (58.33%) were males and 25 (41.67%) were females. Out of the 60 cases 26 were complicated. 37 cases had elevated bilirubin preoperatively in which 21 cases were having complications like gangrene, suppuration and perforation. Out of the 37 cases that had elevated bilirubin pre-operatively 19 (51.35%), the bilirubin level came down to normal limits after 72 hours of appendicectomy. On histopathology, 34 were acute appendicitis, 8 were perforated appendicitis, 6 were gangrenous appendicitis, 12 were suppurative appendicitis. From the study of sensitivity and specificity of pre-operative total bilirubin values in predicting perforated appendicitis, it was found that preoperative total bilirubin value of 1.59 mg/dl had the best sensitivity and specificity. Taking preoperative total bilirubin value 1.59 mg/dl as cut off in predicting perforated appendicitis the sensitivity was 68.8, specificity was 95.1 with an accuracy of 90.2.

Conclusion: Patients with appendicitis with elevated bilirubin levels have more chance for complications like perforation, gangrene and suppuration.

Keywords: Acute appendicitis, gangrenous appendix, hyperbilirubinemia, perforated appendix

Introduction

Appendicitis commonly occurs in young adults (the highest incidence, approximately 40%, in 2nd decade of life i.e. 10-19 years and 70% of the subjects are less than 30 years old) [1, 2]. Acute appendicitis is relatively rare at the extreme of age [3, 4]. Most subjects with acute appendicitis present with classic signs and symptoms for the ease of diagnosis. But in some

atypical presentation's diagnostic confusion and delay in treatment may occur. Crohn's disease, ectopic pregnancy, diverticulitis, endometriosis, mittelschmerz, mesenteric adenitis, omental torsion, pelvic inflammatory diseases, ruptured ovarian cyst, urinary tract infection may mimic acute appendicitis. Worldwide mean value for difference in diagnostic error rate, ranges from 12 to 23% and 24-42% respectively in men and women. Error occurs mostly in whites (74%), while it is lesser in darker complexions (5%) [3].

Surgical delay in a prompt management of the subjects with appendicitis (not with perforation, in particular), either due to delay in presentation (particularly in males with retrocaecal or retroileal position) or misjudgment, leads to dread complications like gangrenous changes and perforation of the appendix. Gangrene or perforation further leads to more complications like appendicular abscess formations, localized/generalized peritonitis, fecal fistula formation, intestinal obstruction due to adhesion formation, portal pyemia, sepsis and sterility in women of child-bearing age (though recent studies denies it as a major risk factor) with overall increased morbidity and prolonged hospital stay [5]. In adults, the incidence of appendicular perforation is 13-37% [6]. The risk is higher in extreme of ages (45% in under 5 years age group and 51% in over 65 years age group) [1, 4]. The mortality rate for uncomplicated, non-perforated appendicitis is 0.1-0.5% while that of perforated appendicitis is much higher, ranging from 3% overall to as high as 15% in elderly subjects [1]. On the contrary, in case of diagnostic difficulties and atypical presentations if appendectomy is performed based on clinical suspicion only, may increase the number of unnecessary appendectomies (up to 20%) [7]. The rate of negative appendectomy (mostly due to pelvic inflammatory conditions) is 35 to 45% in women of child bearing age [8]. Unnecessary appendectomy carries a small risk of wound sepsis and the subsequent adhesive intestinal obstruction and occurrence of incisional hernia.

In spite of numerous advances in the diagnosis, evolved in the last 125 years, still now acute appendicitis continues to be a diagnostic challenge for surgeons and it remains mostly a clinical Diagnosis. Total bilirubin levels upon admission can be used in conjunction with other diagnostic tests such as ultrasonography and routine investigations to help determine the presence of complicated appendicitis and aid in proper clinical management. Present study was conducted to assess relationship between hyperbilirubinemia and acute appendicitis and to find out whether elevated bilirubin levels have a predictive potential for diagnosis of gangrene/suppurative/perforation in acute appendicitis.

Material and methods

The study was a prospective observational study conducted in the Department of General Surgery....., India for the period of 1 year, after taking the approval of the protocol review committee and institutional ethics committee.

Methodology

Total 60 patients who were diagnosed to have appendicitis and admitted in surgery department and who underwent appendicectomy were included in the study. Appendicectomy performed incidentally, patients with appendicular lump, history of alcoholic liver disease, hemolytic or liver diseases associated with hyperbilirubinemia, history of viral hepatitis, Gilbert's disease, Dubin Johnson syndrome were excluded. Data was collected by interview with the participant with help of structured proforma, clinical examination, blood routine examination, Alvarado score, ultrasound abdomen, histopathology examination, pre and post-operative values of total bilirubin, direct bilirubin and indirect bilirubin [9]. The upper limit of normal value in our laboratory for total bilirubin was 1.4 mg/dl (direct-0.3 mg/dl, indirect-1.1 mg/dl).

Results

In our study 35 (58.33%) were males and 25 (41.67%) were females. Out of the 60 cases 26 were complicated (Table 1). In our study acute appendicitis were classified as complicated as uncomplicated. Complications included perforated appendix, gangrenous appendix and appendicitis with suppuration. 37 cases had elevated bilirubin preoperatively in which 21 cases were having complications like gangrene, suppuration and perforation. Out of the 37 cases that had elevated bilirubin pre-operatively 19 (51.35%), the bilirubin level came down to normal limits after 72 hours of appendicectomy (Table 2).

Table 1: Distribution of acute appendicitis in complicated and uncomplicated cases

Type of appendicitis	Number	Percentage
Acute appendicitis (uncomplicated)	34	56.67
Perforated appendicitis	8	14.17
Gangrenous appendicitis	6	10
Suppurative appendicitis	12	19.17
Total	60	100

Table 2: Distribution of cases based on preoperative elevated bilirubin

Type of appendicitis	Bilirubin elevated	Normal bilirubin	Total
Acute appendicitis (uncomplicated)	16	18	34
Gangrenous appendicitis	4	2	6
Suppurative appendicitis	10	2	12
Perforated appendicitis	7	1	8
Total	37	23	60

21 of the 26 cases of complicated appendicitis had elevated total bilirubin levels preoperatively. Of the 21 cases of preoperative hyperbilirubinemia, in 24 cases the bilirubin level came back to normal levels within 72 hours of appendicectomy. Out of the 60 patients 5 patients had alkaline phosphatase less than 23, 54 cases were between 46-116 and only 1 patients had alkaline phosphatase more than 116. Out of 60 cases 26 patients had a total leucocyte count more than 11000 (Table 3).

Table 3: Total leucocyte count

TLC (cells/mm ³)	Number
<4000	1
4000-11,000	33
>11,000	26

In our study CRP was positive in 49 cases (>0.6 mg/l). In hundred cases Alvarado score had a mean of 6.7, maximum being 11 and minimum being 3. On histopathology, 24 were acute appendicitis, 8 were perforated appendicitis, 6 were gangrenous appendicitis, 12 were suppurative appendicitis. From the study of sensitivity and specificity of pre-operative total bilirubin values in predicting perforated appendicitis, it was found that preoperative total bilirubin value of 1.59 mg/dl had the best sensitivity and specificity (Table 4).

It was done using a ROC curve. Area under the curve was 0.844, (0.74-0.96) with 95% CI and a p value of <0.001. Kappa test was done with preoperative bilirubin value of 1.55 mg/dl to find agreement between histopathology finding and total bilirubin. Kappa was 0.68 and p value was <0.001. It showed substantial agreement. Taking preoperative total bilirubin value 1.59 mg/dl as cut off in predicting perforated appendicitis the sensitivity was 68.8, specificity was 95.1 with an accuracy of 90.2.

Table 4: Predictive power of pre-operative total bilirubin in predicting perforated appendicitis over acute appendicitis

Total bilirubin (mg/dl)	Perforated appendicitis	Acute appendicitis
±1.55	5	3
<1.55	4	31
Total	9	34

Table 5: Predictive power of pre-operative total bilirubin in predicting gangrenous appendicitis over acute appendicitis

Total bilirubin	Suppurative appendicitis	Acute appendicitis
Elevated	9	16
Normal	3	18
Total	12	34

From the study of sensitivity and specificity of pre-operative total bilirubin values in predicting gangrenous appendicitis, it was found that preoperative total bilirubin value of 1.77 mg/dl had the best sensitivity and specificity (Table 5). It was done using a ROC curve. Area under the curve was 0.811, (0.63-0.99) with 95% CI and a $p < 0.001$. Kappa test was done with preoperative bilirubin value of 1.80 mg/dl to find agreement between histopathology finding and total bilirubin. Kappa was 0.69 and a p value of < 0.001 which showed, substantial agreement. Taking preoperative total bilirubin value 1.80 mg/dl cut off in predicting gangrenous appendicitis the sensitivity was 63.6, specificity was 98.2 with an accuracy of 92.5.

Table 6: Predictive power of pre-operative total bilirubin in predicting suppurative appendicitis over acute appendicitis

Total bilirubin (mg/dl)	Suppurative appendicitis	Acute appendicitis
±1.45	6	3
<1.45	15	31
Total	11	34

From the study of sensitivity and specificity of pre-operative total bilirubin values in predicting suppurative appendicitis, it was found that preoperative total bilirubin value of 1.45 mg/dl had the best sensitivity and specificity (Table 6). It was done using a ROC curve. Area under the curve was 0.752, (0.58-0.92) with 95% CI and a $p = 0.001$. Kappa test was done with preoperative bilirubin value of 1.47 mg/dl to find agreement between histopathology finding and total bilirubin. Kappa was 0.47 and a $p < 0.001$ which showed, moderate agreement. Taking preoperative total bilirubin value as 1.47 mg/dl as cut off in predicting gangrenous appendicitis the sensitivity was 57, specificity was 90.7 with an accuracy of 82.4.

Discussion

In acute appendicitis or appendicular perforation, inflammatory response causes appendix to become more edematous and ischemic. This causes transmigration or translocation of bacteria, toxins and cytokines leading to endotoxemia/bacteraemia. Invasion of bacteria into the hepatic parenchyma interferes with the physiology of excretion of bile and leads to hyperbilirubinemia. Hyperbilirubinemia in sepsis is a well-recognised entity and gram-negative bacteria are the usual culprits. Hyperbilirubinemia occurs in appendicitis as a result of bacteraemia and endotoxins in the blood. This could happen in complicated appendicitis which is similar to findings in our study^[10].

In our study majority of patients with appendicitis were male 35 (58.33%) which was similar to studies by Chaudary *et al.* and Atahan *et al.* [11, 12]. In a study by D'Souza *et al.* elevated total bilirubin preoperatively showed significant diagnostic value of complicated appendicitis [13].

In a study by Sand *et al.*, the mean bilirubin was 1.5 ± 0.9 mg/dl in patients with appendicular perforation. The sensitivity was 0.70 and specificity was 0.86 compared to a sensitivity of 0.68 and specificity of 0.95 in our study in case of perforation [14].

In a study of 157 patients by Estrada *et al.* patients with suppuration were significantly more likely to have hyperbilirubinemia. Appendicular perforation was 3 times higher for patients with hyperbilirubinemia when compared to normal bilirubin levels [15]. From our study preoperative hyperbilirubinemia was a predictor of complicated appendicitis similar to a study by Fabio Silva *et al.* [16].

In the study of 471 patients by Emmanuel *et al.*, hyperbilirubinemia was found in 34% patients with appendicitis. In our study 74 (61.67%) patients had hyperbilirubinemia. 26 patients in our study had complicated appendicitis out of which 21 patients had hyperbilirubinemia. For patients with appendicitis in Emmanuel *et al.* study with hyperbilirubinemia, specificity for perforation was 70% compared to our study in which the specificity was 94.6% [17].

Conclusion

Patients with appendicitis with elevated bilirubin levels have more chance for complications like perforation, gangrene and suppuration.

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