Original Research Article

A study to determine the value of pre operative hyperbilirubinemia as a predictor of complicated appendicitis

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ABSTRACT

Background: Acute appendicitis is a common acute abdominal condition that all surgeons confront. The early detection of patients who could go in for complication is critical so that appropriate treatment can be initiated to reduce mortality. There is no pre-operative investigation which accurately point out the patients who are going to develop severe disease. Hence this prospective study was done to identify whether preoperative bilirubin level can predict the severity of the disease.

Methods: The study was conducted in the Department of General Surgery, Sree Gokulam Medical College and Research Foundation, Venjaramoodu, Trivandrum on 100 consecutive patients who were clinically diagnosed as acute appendicitis. These patients were evaluated with Alvarado score. In addition, preoperative bilirubin level and liver enzymes were estimated. Ultrasound abdomen was done preoperatively routinely. After surgery histopathology was studied. The parameters which showed statistically significant results for predicting complications were analyzed.

Results: In this prospective study on 100 consecutive patients, acute appendicitis was found more commonly in males, 57 (57%) cases than in females, 43 (43%) cases. Among the cases 56 were acute appendicitis, 13 perforated, 11 gangrenous and 20 suppurative appendicitis. In our study, there was significant correlation of preoperative hyperbilirubinemia with complications of appendicitis.

Conclusions: 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

Acute appendicitis is the commonest cause of ‘acute surgical abdomen’. Appendicectomy is the most frequently performed urgent abdominal operation and is often the first major procedure performed by a surgeon in training. Diagnosis of appendicitis is based on history, examination, laboratory values and imaging. In some cases, the signs and symptoms are variable and a diagnosis can be difficult to make. Delay in diagnosis of acute appendicitis leads to perforation and peritonitis and increased mortality. Incidence of perforation ranges 50-90% in various series.

To supplement clinical diagnosis and to reduce the frequency of unnecessary appendicectomy, the importance of laboratory investigations like white blood cell (WBC) counts and C-reactive protein (CRP) values has been stressed. The use of ultrasonography (USG) as a diagnostic tool for appendicitis has been widely known and studied. Scores combining clinical features and laboratory investigations have also been developed and are good enough to reach the diagnosis. Available scoring
systems are the Alvarado score and the Modified Alvarado score.7,8

Now there is no confirmatory laboratory marker for the pre-operative diagnosis of acute appendicitis and appendicular perforation.

Importance of raised total bilirubin has not been stressed in acute appendicitis and appendicular perforation. Bacterial invasion in appendix leads to transmigration of bacteria and release of pro-inflammatory cytokines such as TNF- alpha, IL-6 and cytokines which in turn reach the liver via the portal system and may produce inflammation, abscess or dysfunction of liver either directly or indirectly by altering the hepatic blood flow.9,10

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/ suppuration/perforation in acute appendicitis.

METHODS

The study was conducted in Department of General Surgery, Sree Gokulam Medical College and Research Foundation, Venjaramoodu, Trivandrum. This was a prospective observational study of 100 consecutive cases.

All 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.7 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). The data was uploaded in Microsoft excel sheet and analyzed using ROC curve and Kappa test. The study had a sample size of 100 patients and the study duration was 18 months from November 2013 to May 2015.

RESULTS

In our study 57 (57%) were males and 43 (43%) were females. Out of the 100 cases 44 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. 62 cases had elevated bilirubin preoperatively in which 35 cases were having complications like gangrene, suppuration and perforation. Out of the 62 cases that had elevated bilirubin preoperatively 31 (50%), 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) | 56    | 56         |
| Perforated appendicitis    | 13    | 13         |
| Gangrenous appendicitis    | 11    | 11         |
| Suppurative appendicitis   | 20    | 20         |
| Total                  | 100   |            |

Table 2: Distribution of cases based on preoperative elevated bilirubin.

| Type of appendicitis | Bilirubin elevated | Normal bilirubin | Total |
|---------------------|--------------------|------------------|-------|
| Acute appendicitis (uncomplicated) | 27          | 29               | 56    |
| Gangrenous appendicitis    | 9             | 2                | 11    |
| Suppurative appendicitis   | 15            | 5                | 20    |
| Perforated appendicitis    | 11            | 2                | 13    |
| Total                  | 62            | 38               | 100   |

35 of the 44 cases of complicated appendicitis had elevated total bilirubin levels preoperatively. Of the 35 cases of preoperative hyperbilirubinemia, in 21 (47.7%) cases the bilirubin level came back to normal levels within 72 hours of appendicectomy. Out of the 100 patients 8 (8%) had alkaline phosphatase less than 46, 90 (90%) were between 46-116 and only 2 (2%) patients had alkaline phosphatase more than 116. Out of 100 cases 46 patients had a total leucocyte count more than 11000 (Table 3).

Table 3: Total leucocyte count.

| TLC (cells/mm³) | Number | Percentage |
|-----------------|--------|------------|
| <4000           | 2      | 2          |
| 4000-11,000     | 52     | 52         |
| >11,000         | 46     | 46         |

In our study CRP was positive in 81 cases (>0.6 mg/l). In hundred cases Alvarado score had a mean of 6.5, maximum being 10 and minimum being 2. On histopathology, 56 were acute appendicitis, 13 were perforated appendicitis, 11 were gangrenous appendicitis, 20 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 1.55 mg/dl had the best sensitivity and specificity (Table 4).
It was done using a ROC curve. Area under the curve was 0.852, (0.72-0.98) 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 0.66 and p value was <0.001. It showed substantial agreement. Taking preoperative total bilirubin value 1.55 mg/dl as cut off in predicting perforated appendicitis the sensitivity was 69.2, specificity was 94.6 with an accuracy of 89.9.

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

| Total bilirubin (mg/dl) | Perforated appendicitis | Acute appendicitis | Total |
|------------------------|-------------------------|-------------------|-------|
| ≥1.55                  | 9                       | 3                 | 12    |
| <1.55                  | 4                       | 53                | 57    |
| Total                  | 13                      | 56                | 69    |

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

| Total bilirubin | Suppurative appendicitis | Acute appendicitis | Total |
|-----------------|--------------------------|-------------------|-------|
| Elevated        | 15                       | 27                | 42    |
| Normal          | 5                        | 29                | 34    |
| Total           | 20                       | 56                | 76    |

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 1.80 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 cutoff 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 | Total |
|-------------------------|--------------------------|-------------------|-------|
| ≥1.45                   | 11                       | 5                 | 16    |
| <1.45                   | 9                        | 51                | 60    |
| Total                   | 20                       | 56                | 76    |

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 0.741, (0.59-0.89) with 95% CI and a p=0.001. Kappa test was done with preoperative bilirubin value of 1.45 mg/dl to find agreement between histopathology finding and total bilirubin. Kappa was 0.49 and a p<0.001 which showed, moderate agreement. Taking preoperative total bilirubin value as 1.45 mg/dl as cut off in predicting gangrenous appendicitis the sensitivity was 55, specificity was 91.1 with an accuracy of 81.6.

DISCUSSION

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.11

In our study majority of patients with appendicitis were male 57 (57%) which was similar to studies by Chaudary et al and Atahan et al.12,13 In a study by D’Souza et al elevated total bilirubin preoperatively showed significant diagnostic value of complicated appendicitis.14

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 69.2 and specificity of 94.6 in our study in case of perforation.15

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.16 From our study preoperative hyperbilirubinemia was a predictor of complicated appendicitis similar to a study by Fabio Silva et al.17

In the study of 471 patients by Emmanuel et al, hyperbilirubinemia was found in 34% patients with appendicitis. In our study 62 (62%) patients had hyperbilirubinemia. 44 patients in our study had complicated appendicitis out of which 35 (79.5%) 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%.18

CONCLUSION

From our prospective study of 100 consecutive patients of acute appendicitis, in our study 62 (62%) patients had hyperbilirubinemia. 44 patients in our study had complicated appendicitis out of which 35 (79.5%) patients had hyperbilirubinemia. Taking preoperative total bilirubin value 1.55 mg/dl as cut off in predicting perforated appendicitis the sensitivity was 69.2, specificity was 94.6 with an accuracy of 89.9. 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. Taking preoperative total bilirubin value as 1.45 mg/dl as cut off in predicting gangrenous appendicitis the sensitivity was 55, specificity was 91.1 with an accuracy of 81.6. Thus, inclusion of total bilirubin estimation in routine preoperative laboratory investigations of acute appendicitis can help in predicting the complications.

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