

Original Research Article

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

Arun Lal, Thomas K. Thomas*, R. Dayananda Babu, Deepak Paul

Department of General Surgery, Sree Gokulam Medical College and Research Foundation, Venjaramoodu, Kerala, India

Received: 12 July 2020

Revised: 24 July 2020

Accepted: 27 July 2020

***Correspondence:**

Dr. Thomas K. Thomas,

E-mail: thomassgmc57@gmail.com

Copyright: © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

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'.^{1,2} Appendectomy 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.^{3,4}

To supplement clinical diagnosis and to reduce the frequency of unnecessary appendectomy, the importance of laboratory investigations like white blood cell (WBC) counts and C-reactive protein (CRP) values has been stressed.⁵ The use of ultrasonography (USG) as a diagnostic tool for appendicitis has been widely known and studied.⁶ 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/suppurative/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 appendectomy were included in the study. Appendectomy 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 appendectomy (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 appendectomy. 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/mm ³)	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.

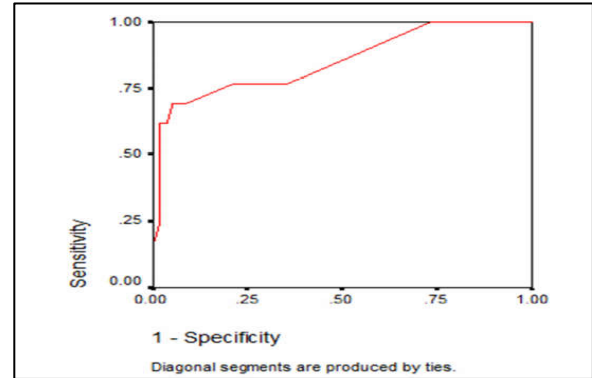


Figure 1: ROC curve for finding cut off value of preoperative total bilirubin for predicting perforated appendicitis.

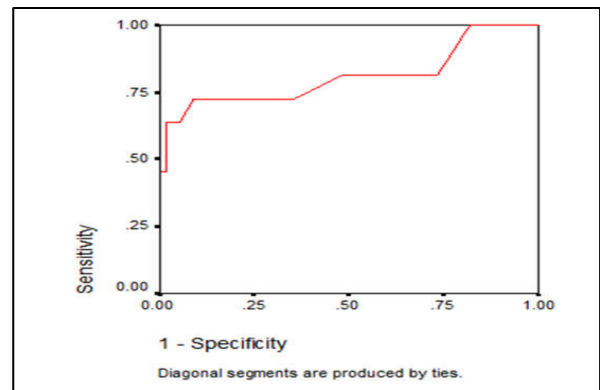


Figure 2: ROC curve for finding cut off value of preoperative total bilirubin for predicting gangrenous appendicitis.

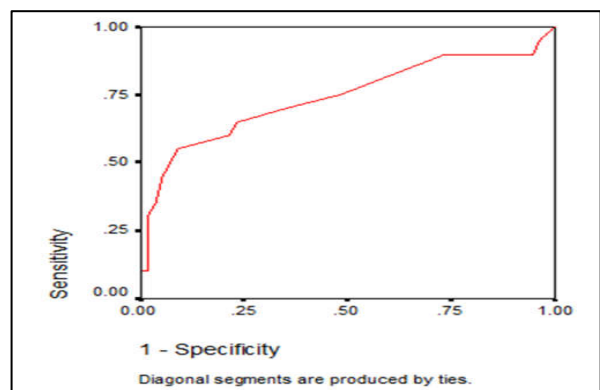


Figure 3: ROC curve for finding cut off value of preoperative total bilirubin for predicting suppurative appendicitis.

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.

ACKNOWLEDGEMENTS

Author would like to thank the department of general surgery for supporting him in this study.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Khan AQ, Patil A, Pawar P. Role of hyperbilirubinemia as a diagnostic predictor of appendicular perforation. *Int J Sci Res.* 2014;3(12):2012-5.
2. Smink DS, Soybel DI. Appendix and appendectomy. In: Maingot's Abdominal Operations. 11th ed. New York McGraw Hill; 2007: 589-612.
3. Von Titte SN, McCabe CJ, Ottinger LW. Delayed appendectomy for appendicitis: causes and consequences. *Am J Emerg Med.* 1996;14(7):620-2.
4. Temple CL, Huchcroft SA, Temple WJ. The natural history of appendicitis in adults. A prospective study. *Ann Surg.* 1995;221(3):278.
5. Grönroos JM, Grönroos P. A fertile-aged woman with right lower abdominal pain but unelevated leukocyte count and C-reactive protein. *Langenbeck's Arch Surg.* 1999;384(5):437-40.
6. Puylaert JBCM, Rutgers PH, Lalisang RI, de Vries BC, van der Werf SDJ, Dörr JPJ, et al. A prospective study of ultrasonography in the diagnosis of appendicitis. *N Engl J Med.* 1987;317(11):666-9.
7. Alvarado A. A practical score for the early diagnosis of acute appendicitis. *Ann Emerg Med.* 1986;15(5):557-64.
8. Kalan M, Talbot D, Cunliffe WJ, Rich AJ. Evaluation of the modified Alvarado score in the diagnosis of acute appendicitis: a prospective study. *Ann R Coll Surg Engl.* 1994;76(6):418.
9. Berg RD, Garlington AW. Translocation of *Escherichia coli* from the gastrointestinal tract to the mesenteric lymph nodes in gnotobiotic mice receiving *Escherichia coli* vaccines before colonization. *Infect Immun.* 1980;30(3):894-8.
10. Juric I, Primorac D, Zagar Z, Biocić M, Pavić S, Furlan D, et al. Frequency of portal and systemic

- bacteremia in acute appendicitis. *Pediatr Int.* 2001;43(2):152-6.
11. Whitehead MW, Hainsworth I, Kingham JG. The causes of obvious jaundice in South West Wales: perceptions versus reality. *Gut.* 2001;48(3):409-13.
 12. Chaudhary P, Kumar A, Saxena N, Biswal UC. Hyperbilirubinemia as a predictor of gangrenous/perforated appendicitis: a prospective study. *Ann Gastroenterol Q Publ Hell Soc Gastroenterol.* 2013;26(4):325.
 13. Atahan K, Üreyen O, Aslan E, Deniz M, Çökmez A, Gür S, et al. Preoperative diagnostic role of hyperbilirubinaemia as a marker of appendix perforation. *J Int Med Res.* 2011;39(2):609-18.
 14. D'Souza N, Karim D, Sunthareswaran R. Bilirubin; a diagnostic marker for appendicitis. *Int J Surg.* 2013;11(10):1114-7.
 15. Sand M, Bechara FG, Holland-Letz T, Sand D, Mehnert G, Mann B. Diagnostic value of hyperbilirubinemia as a predictive factor for appendiceal perforation in acute appendicitis. *Am J Surg.* 2009;198(2):193-8.
 16. Estrada JJ, Petrosyan M, Barnhart J, Tao M, Sohn H, Towfigh S, et al. Hyperbilirubinemia in appendicitis: a new predictor of perforation. *J Gastrointest Surg.* 2007;11(6):714-8.
 17. Silva FR, da Rosa MI, Silva BR, Simon C, Alexandre MC, Medeiros LR, et al. Hyperbilirubinaemia alone cannot distinguish a perforation in acute appendicitis. *ANZ J Surg.* 2016 ;86(4):255-9.
 18. Emmanuel A, Murchan P, Wilson I, Balfe P. The value of hyperbilirubinaemia in the diagnosis of acute appendicitis. *Ann R Coll Surg Engl.* 2011;93(3):213-7.

Cite this article as: Lal A, Thomas TK, R. Babu D, Paul D. A study to determine the value of pre operative hyperbilirubinemia as a predictor of complicated appendicitis. *Int Surg J* 2020;7:2848-52.