

A Comparative Study of Hyperbilirubinemia in Predicting Appendicitis and its Complications

Chethan L

Author's Affiliation: Associate Professor, Department of Surgery, Sridevi Institute of Medical sciences and Research Hospital, Tumkur, Karnataka 572106, India.

How to cite this article:

Chethan L/A Comparative Study of Hyperbilirubinemia in Predicting Appendicitis and its Complications/ New Indian J Surg. 2021;12(3): 33-38.

Abstract

Background: Acute appendicitis is the most common general surgical emergency in young adults. Diagnosis of Appendicitis still remains a dilemma in spite of the advances in various laboratory and radiological investigations. Importance of hyperbilirubinemia or elevated Serum Bilirubin and its association in acute appendicitis and its complication as been postulated recently. The present study was undertaken to assess relationship between hyperbilirubinemia in predicting appendicitis and its complication.

Methods: The present study was conducted in the Department of Surgery, SIMS & RH ,Tumkur during the period of August 2019 to August 2020. A total of 100 patients with clinical diagnosis of acute appendicitis or Appendicular perforation were studied. The serum bilirubin and LFTs were carried out in all the patients.

Results: In this study, males (56%) outnumbered females (44%). Of the 100 patients, 91% were diagnosed as acute appendicitis clinically while 9% were diagnosed with Appendicular perforation. Post-operatively 82% were confirmed as acute appendicitis while 18% were diagnosed with Appendicular perforation. Of 82 patients with acute appendicitis, 74.39% had raised bilirubin levels, while 25.6% had normal levels. 18 patients were diagnosed as Appendicular perforation, 15 patients (83.33%)

had raised bilirubin levels, while the remaining 03 patients (16.66%) had normal levels.

Conclusion: The Sensitivity and Specificity of serum bilirubin as a marker in predicting acute appendicitis and Appendicular perforation was 74.39% and 83.33% respectively. Serum bilirubin levels appears to be a promising new laboratory marker for diagnosing acute appendicitis, however diagnosis of appendicitis is essentially still - clinical. Patients with clinical signs and symptoms of appendicitis and with hyperbilirubinemia double the normal range (Raise in Direct Bilirubin being still higher) should be identified as having a higher probability of Appendicular perforation suggesting, serum bilirubin levels have a predictive potential for the diagnosis of Appendicular perforation.

Keywords: Appendicitis; Serum bilirubin; Appendicular perforation; Hyperbilirubinemia.

Objectives

The objectives of the study were

1. To study the association between hyperbilirubinemia and acute appendicitis.
2. To evaluate whether elevated bilirubin levels have a predictive potential for the diagnosis of Appendicular perforation.

Introduction

The most common cause of acute surgical abdomen is Appendicitis. The most commonly performed abdominal surgery is appendicectomy. The

Corresponding Author: Chethan L, Associate Professor, Department of Surgery, Sridevi Institute of Medical sciences and Research Hospital, Tumkur, Karnataka 572106, India.

E-mail: drchethan29@gmail.com

diagnosis of acute appendicitis is based on clinical history and physical examination. It is difficult to diagnose in cases of retrocaecal or retroileal appendix. 15-30% of appendectomy specimen found to be normal. In order to decrease the negative appendectomy, various diagnostic modalities used like laboratory investigations like White Blood Cells, CR reactive Protein, ultrasonogram and CT scan etc., have been emphasised. Many number of scoring system were developed to arrive the diagnosis. These scoring systems are based on clinical features, laboratory investigations. Some examples are Alvarado, Modified alvarado, Ripasa. Still the negative appendectomy rate remains constant. Studies show that serum bilirubin is raised in acute appendicitis and appendicular perforations. But the significance of which is not stressed. In uncomplicated appendicitis and complicated appendicitis there is transmigration of bacterial endotoxins and cytokines into the bloodstream. The cytokines reach the liver through the superior mesenteric vein and may lead to inflammation, abscess and liver dysfunction which leads to elevated bilirubin levels. In view of the above context, the present study was undertaken to assess the relationship between Hyperbilirubinemia and acute appendicitis and to see whether elevated bilirubin levels have a predictive potential for the diagnosis of appendicular perforation.

Materials and Methods

The study was conducted in the Department of General Surgery, SIMS & RH, Tumkur during the period of August 2019 to August 2020. A total of 100 patients with clinical diagnosis of acute appendicitis or appendicular perforation were studied.

Selection criteria

Inclusion

- All clinically and radiologically diagnosed cases of acute appendicitis and its complication.

Exclusion

- All patients with hepatic disorders.
- Patients with history of chronic alcohol intake.
- Patient with history of hepatotoxic drug intake.
- HbsAg positive and or with a past history of jaundice.
- All patients with cancer of hepato-biliary system.

- All patient with cholelithiasis, hemolytic disease, Acquired or Congenital Biliary disease.

Statistical Analysis

The data obtained was tabulated on Microsoft excel spreadsheet and analysed as below.

- Patients with clinical diagnosis of acute appendicitis having hyperbilirubinemia were expressed in percentage
- Mean of the level of elevation of Serum bilirubin was calculated for patients with clinical diagnosis of acute appendicitis.
- Patients with clinical diagnosis of appendicular perforation having hyperbilirubinemia were expressed in percentage
- Mean of the level of elevation of serum bilirubin were calculated for patients with clinical diagnosis of appendicular perforation.
- A hypothesis was made based on the observation of the level of the two means.
- Also, sensitivity, specificity, positive predictive value, negative predictive value and Odds ratio was determined.

Results

A total of 100 patients with clinical diagnosis of acute appendicitis or appendicular perforation admitted in the Department of General surgery, SIMS & RH, Tumkur were studied.

As per the study, the age group 11-20 years is most commonly affected (45%) followed by age group 21-30 (31%). The youngest patients of this study were of 8 years old while the oldest patient was a 70 year lady.

Table 1: Distribution of patients by age.

Age groups (years)						
≤10	11-20	21-30	31-40	41-50	51-60	61-70
8	45	31	8	3	4	1

Table 2: Liver Function Tests.

Parameters	Mean	SD
Total Bilirubin(mg/ dl)	1.6	0.8
Direct Bilirubin (mg/ dl)	1.1	0.55
Indirect Bilirubin(mg/ dl)	0.5	0.25
SGOT(U/L)	27.8	13.9
SGPT(U/L)	25.97	12.98
ALP(U/L)	80.86	40.43

The mean Total bilirubin of all 100 patients was 1.6 ± 0.8 mg/dL (range, 0.7 - 2.3 mg/dL) while the Direct bilirubin was 1.1 ± 0.55 mg/dL (range, 0.3-1.7 mg/dL). The mean SGOT and SGPT were 27.8 ± 13.9 U/L (range, 15.7-40.1 U/L) and 25.97 ± 12.98 U/L (range, 14.9 - 35.9 U/L). The mean ALP values were 80.86 ± 40.43 U/L (range, 59.2 -102.4 /L).

Table 3: Total bilirubin levels.

Total bilirubin (mg/dl)	Number	Percentage
<1.0	24	24
≥ 1.0	76	76
Total	100	100

24 patients (24%) of all 100 patients were found to have normal bilirubin levels (≤ 1.0 mg/dL), while 76 patients (76%) had raised bilirubin levels (> 1.0 mg/dL).

Table 4: Bilirubin levels in patients with uncomplicated acute appendicitis as diagnosis.

Total bilirubin (mg/dL)	Distribution in Patients with uncomplicated Acute Appendicitis	
	Number	Percentage
>1.0	61	74.39
≤ 1.0	21	25.6
Total	82	100.0

Of 82 patients diagnosed as uncomplicated acute appendicitis, 61 patients (74.39%) had raised bilirubin levels (> 1.0 mg/dL), while the remaining 21 patients (25.6%) had normal levels (≤ 1.0 mg/dL).

Table 5: Bilirubin levels in patients with Appendicular perforation diagnosis.

Total bilirubin (mg/dl)	Distribution in Patients with Appendicular perforation	
	Number	Percentage
>1.0	15	83.33
≤ 1.0	03	16.66
Total	18	100

18 patients diagnosed as Appendicular perforation, 15 patients (83.33%) had raised bilirubin levels (> 1.0 mg/dL), while the remaining 03 patients (16.66%) had normal levels (≤ 1.0 mg/dL).

Table 6: Histopathological diagnosis.

Diagnosis	Distribution (n= 100)	
	Number	Percentage
Acute appendicitis	82	82
Appendicular perforation	18	18
Total	100	100

Histopathologically, 82 patients (82%) were confirmed as Acute appendicitis while 18 patients

(18%) were diagnosed with Appendicular perforation.

Table 7: Comparison of mean serum bilirubin levels in patients with acute appendicitis and Appendicular perforation.

Bilirubin (mg/dl)	Diagnosis			
	Acute Appendicitis		Appendicular Perforation	
	Mean	SD	Mean	SD
Total bilirubin	1.5	0.75	1.8	0.9
Direct bilirubin	0.8	0.4	1.1	0.55
Indirect bilirubin	0.6	0.3	0.80	0.40

The mean bilirubin levels in patients diagnosed with Acute appendicitis was 1.5 ± 0.75 mg/dL (range, 0.75 - 2.05 mg/dL) while in patients diagnosed with Appendicular perforation was 1.8 ± 0.9 mg/dL (range, 0.74 - 3.06 mg/dL). The Direct bilirubin and Indirect bilirubin in patients diagnosed with Acute appendicitis were 0.8 ± 0.4 mg/dL and 0.6 ± 0.3 respectively. The Direct bilirubin and Indirect bilirubin in patients diagnosed with Appendicular perforation were 1.1 ± 0.55 mg/dL and 0.80 ± 0.40 mg/dL respectively.

Table 8: Correlation of acute appendicitis and Appendicular perforation with total serum bilirubin levels.

Serum bilirubin (mg/dl)	Final Diagnosis (n=100)			
	Acute Appendicitis (n=82)		Appendicular Perforation (n=18)	
	Number	%	Number	%
>1.0	61	74.39	15	83.33
≤ 1.0	21	25.6	03	16.66
Total	82	100	18	100

61 patients (74.39%) of the total patients diagnosed with Acute appendicitis (n=82) were found to have elevated bilirubin levels (> 1.0 mg/dL) while 21 patients (25.6%) had normal bilirubin levels (≤ 1.0 mg/dL). Similarly, 15 patients (83.33%) of the total patients diagnosed with Appendicular perforation (n=18) were found to have elevated bilirubin levels (> 1.0 mg/dL) while 03 patients (16.66%) had normal bilirubin levels (≤ 1.0 mg/dL).

Table 9: Accuracy of serum bilirubin as a marker in predicting Appendicular perforation.

	Accuracy
Sensitivity	74.39%
Specificity	83.33%
Positive Predictive Value	80.26%
Negative Predictive Value	12.5%
Odds Ratio	0.58

The Sensitivity and Specificity of serum bilirubin as a marker in predicting acute appendicitis and Appendicular perforation was 74.39% and 83.33% respectively. Similarly the Positive predicative value and Negative predicative value for the same is 80.26% and 12.5% respectively. The Odds ratio was calculated to be 0.58.

Discussion

Acute appendicitis is the most common cause of “acute abdomen” in young adults. Appendectomy is the most frequently performed emergency abdominal operation and is often the first major procedure performed by a surgeon in Training.¹ About 8% of people in Western countries have appendicitis at some time in their lifetime.²

In teenagers and young adults, the male - female ratio increases to 3:2 at age 25. The lifetime rate of appendectomy is 12% for men and 25% for women, with approximately 7% of all people undergoing appendectomy for acute appendicitis during their lifetime.^{3,4} Obstruction of the lumen is believed to be the major cause of acute appendicitis.⁵ Faecoliths are the usual cause of obstruction. Less-common causes are hypertrophy of lymphoid tissue, tumors, intestinal parasites.⁵ The bacteriology of normal appendix is similar to that of normal colon. The principal organism seen in normal appendix, in acute appendicitis, and in perforated appendicitis are *Escherichia Coli* and *Bacteroids fragilis*. However a wide variety of both facultative and anaerobic bacteria may be present.⁵

The diagnosis of acute appendicitis is essentially clinical; however, a decision to operate based on clinical suspicion alone can lead to the removal of a normal appendix in 15 to 50% of cases.⁶ The premise that it is better to remove a normal appendix than to delay diagnosis does not stand up to close scrutiny, particularly in the elderly¹ as such procedures are associated with complications in 50% cases.⁷ Hence, the diagnosis of Appendicitis still remains a dilemma in spite of the advances in various laboratory and radiological investigations. A new tool to help in the diagnosis of acute appendicitis would thus be welcome.

Serum Bilirubin level elevation will help in the accuracy of clinical diagnosis of acute appendicitis and more importantly help in foreseeing and preventing impending complications of acute appendicitis.

Importance of hyperbilirubinemia and its association in acute appendicitis has being postulated recently. There are only a few case

reports in the available literature that describe the finding of hyperbilirubinemia in patients of acute appendicitis.⁸ It is hypothesized that an association exists between hyperbilirubinemia and acute appendicitis and its complications.⁸

The present study was undertaken to study the relationship between hyperbilirubinemia and acute appendicitis and to evaluate whether elevated bilirubin levels have a predictive potential for the diagnosis of Appendicular perforation.

This study was conducted in the Department of General Surgery, SIMS & RH, Tumkur over a period of one year from August 2019 to August 2020 on 100 patients with clinical diagnosis of Acute appendicitis and Appendicular perforation.

In the present study of the 100 patients enrolled for the study, 56 patients (56%) were males while the remaining 44 patients (44%) were females. The mean age in our study population (100 patients) was 23.1 ± 11.99 years (range, 11.11-35.09 years). This is consistent with the quoted incidence of Appendicitis in the literature where it is most frequently seen in patients in their second through fourth decades of life.^{3,4} The average age group in males 24 ± 11.93 years (range, 12.07 -35.93 years) was slightly higher than females 23.1 ± 11.93 years (range, 11.17 -35.03 years).

Hyperbilirubinemia (> 1.0 mg/dL) in our study was found in 76 patients (76%) of all the 100 patients (n=100) enrolled in the study, while 24 patients (24%) had normal bilirubin levels (≤ 1.0 mg/dL). Estrada et al⁸ had found hyperbilirubinemia in 59 (38%) of 157 patients studied with acute appendicitis.

The mean total serum bilirubin of all 100 patients was 1.6 ± 0.8 mg/dL (range, 0.7 - 2.3 mg/dL), which was above the normal range (≤ 1.0 mg/dL) considered for the study, hence indicating the occurrence of hyperbilirubinemia. The mean of Direct bilirubin was 1.1 ± 0.55 mg/dL (range, 0.3-1.7 mg/dL) while that of Indirect bilirubin was 0.5 ± 0.25 mg/dL (range, 0.3 - 0.7 mg/dL). Our finding was consistent with hyperbilirubinemia found in a study conducted by Khan S,⁹ who found average level of serum bilirubin in his study population to be 2.38 mg/dL.

All patients were found to have SGOT and SGPT within the normal range, thus excluding any associated liver pathology (Exclusion criteria). The mean SGOT and SGPT were 27.8 ± 13.9 U/L (range, 15.7-40.1 U/L) and 25.97 ± 12.98 U/L (range, 14.9 - 35.9 U/L). The mean ALP values were 80.86 ± 40.43 U/L (range, 59.2 -102.4 U/L).

In our study population of 100 patients, 91 patients (91%) were diagnosed as acute appendicitis pre-operatively while 09 patients (9%) were diagnosed with Appendicular perforation.

The diagnosis was confirmed post-operatively by histopathological reports (HPR) and those differing from the pre-operative diagnosis were excluded from the study.

Amongst the patients diagnosed with Acute appendicitis without perforation (n=82), 61 patients (74.39%) were found to have elevated bilirubin (>1.0 mg/dL) while only 21 patients (25.6%) had normal bilirubin levels (\leq 1.0 mg/dL). In patients diagnosed with Appendicular perforation (n=18), 15 patients (83.33%) had bilirubin elevated (>1.0 mg/dL), while only 3 patients (16.66%) had normal levels (>1.0 mg/dL). Thus, Hyperbilirubinemia was found in most of the patients diagnosed with acute appendicitis (74.39%) or Appendicular perforation (83.33%).

On Ultrasonography, 69 patients (69%) were diagnosed as Acute appendicitis, 13 patients (13%) as Appendicular perforation and 18 patients (18%) were reported as normal ultrasonographic findings. Ultrasonography was 82% sensitive for appendicitis and/or Appendicular perforation, hence Ultrasonography is a helpful tool in diagnosing appendicitis or perforation.

The mean bilirubin levels in patients diagnosed with Acute appendicitis was 1.5 ± 0.75 mg/dL (range, 0.75 - 2.05 mg/dL) while in patients diagnosed with Appendicular perforation was 1.8 ± 0.9 mg/dL (range, 0.74 - 3.06 mg/dL). Hence, we see that patients with Appendicular perforation had higher levels of bilirubin as compared to that of acute appendicitis. So we infer that, patients with features suggestive of appendicitis with higher values of bilirubin, are more susceptible of having Appendicular perforation than those with normal or slightly elevated total serum bilirubin.

Sand et al¹⁰ in his study found the mean bilirubin levels in patients with Appendicular perforation to be significantly higher than those with a non-perforated appendicitis.

Sensitivity and Specificity of bilirubin in predicting acute appendicitis and Appendicular perforation diagnosis was 74.39% and 83.33% respectively. Similarly Positive predictive value and Negative predictive value of bilirubin in predicting acute appendicitis and Appendicular perforation diagnosis was 80.26% and 12.5% respectively. The Odds ratio was calculated to be 0.58.

The sensitivity in our study was more than that by Sand et al¹⁰ in which, he found the sensitivity and specificity in his study of hyperbilirubinemia for predicting Appendicular perforation to be 70% and 86.0% respectively.

Conclusion

The present study suggests:

- Serum bilirubin levels appears to be a promising new laboratory marker for diagnosing acute appendicitis. Its level come out to be a credible aid in diagnosis of acute appendicitis and would be helpful investigation in decision making.
- Patients with clinical signs and symptoms of appendicitis and with hyperbilirubinemia higher than the normal range have a higher probability of Appendicular perforation suggesting, serum bilirubin levels have a predictive potential for the diagnosis of Appendicular perforation.

Acknowledgement

I Acknowledge my sincere thanks to Professor Dr. Narendra Kumar. I also thank other staff members and my colleagues for their help and suggestions. My deep sense of gratitude to my wife Dr. Shilpasri. Y.M and other family members.

Declaration

Funding: None

Conflict of interest: None Declared

Ethical Approval: Approved

References

1. O'Connell PR. "The Vermiform Appendix". In: Williams NS, Bulstrode CJK, O'Connell PR (Ed.). Bailey and Love's - Short practice of surgery. 25 ed. London: Arnold; 2008; p. 1204-8.
2. John Maa. "The Appendix". In Townsend CM, Beauchamp RD, Evers BM, Mattox KL, eds. Sabiston Textbook of Surgery. 18th ed. Philadelphia, Pa: Saunders Elsevier; 2008. p: 1333-1347.
3. Addiss DG, Shaffer N, Fowler BS, Tauxe RV. The epidemiology of appendicitis and appendectomy in the United States. *Am J Epidemiol* 1990; 132 (5): 910-25.
4. Flum DR, Morris A, Koepsell T, Dellinger EP. Has misdiagnosis of appendicitis decreased over time? A population-based analysis. *JAMA* 2001; 286 (14): 1748-53.

5. Bernard M. Jaffe and David H. Berger. "The Appendix". In Brunicaudi F, Andersen D, Billiar T, Dunn D, Hunter J, Matthews J, et al. Schwartz's Principles of Surgery. 9th ed. New York: McGraw Hill; 2009. p.1073- 1092.
6. Deutsch A, Shani N, Reiss R. Are some appendectomies unnecessary: an analysis of 319 white appendices. J R Coll Surg Edinb 1983; 28: 35-40.
7. Piper R, Kager E, Nasman P. Acute appendicitis a clinical study of 1018 cases of emergency appendectomy. Acta Chir Scand. 1982; 148:51-62.
8. Estrada JJ, Petrosyan M, Krumenacker J Jr, Huang S, Moh P. Hyperbilirubinemia in Appendicitis: A New Predictor of Perforation. Journal of Gastrointestinal Surgery 2007; 11: 714-5.
9. Khan S. Evaluation of hyperbilirubinemia in acute inflammation of appendix: A prospective study of 45 cases. KUMJ 2006; 4(3) 15: 281-9.
10. Sand M, Bechara GF, 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 Aug;198(2):193-8.

