



Research Article

CORRELATIONAL STUDY OF HYPERBILIRUBINEMIA AS A DIAGNOSTIC PREDICTOR FOR PERFORATION IN ACUTE APPENDICITIS

D Rishi Papanaidu^{1*}, Chinta Priyanka²

Article Information

Received: 27th November 2023
Revised: 24th March 2024
Accepted: 11th April 2024
Published: 30th April 2024

Keywords

Acute appendicitis,
appendicular perforation,
bilirubin, hyperbilirubinemia

ABSTRACT

Background: Appendicitis is an acute and life-threatening situation if not treated promptly encountered in surgery practice. Even today, most cases of appendicitis are diagnosed by clinical findings and imaging. Scanty information is available to diagnose the perforation of the appendix using serological tests; hence, an attempt is made. The present study aimed to find out the correlation of hyperbilirubinemia as a diagnostic predictor for perforation in acute appendicitis patients. **Methods:** This prospective observational study was conducted among patients diagnosed with acute appendicitis attending OPD of the general surgery department of Narayana Medical College Hospital. The duration of the study is between January 2023 and December 2023. A total of 400 patients with a diagnosis of either acute appendicitis or perforation were recruited into the study, and they collected blood samples for estimation of hyperbilirubinemia. **Results:** In the study population of 400 patients, 72 cases were diagnosed as appendicular perforation, and 328 patients had acute appendicitis. The cut-off value of hyperbilirubinemia was taken as serum bilirubin >1.0 mg/dl. Out of 72 cases of appendicular perforations, 64 patients have hyperbilirubinemia (89%), while in the acute appendicitis patients group, 82 of 328 patients have elevated serum bilirubin (25%). The observed mean values of serum bilirubin in the two groups were 1.74 and 0.89, and the difference in the standard error of the mean value of the two groups is statistically significant at a P-value of <0.001. **Conclusions:** Patients who presented with acute appendicitis symptoms and had serum bilirubin values >1.0 mg/dl had a higher probability of appendicular perforation. Hence, measuring serum bilirubin can be considered an additional diagnostic tool to existing clinical diagnosis and radiological evaluation for more precision in diagnosis.

INTRODUCTION

Pain abdomen is the most common surgical emergency presentation to casualty. Acute appendicitis is one of the most

common etiologies in pain abdomen patients [1]. Even today, diagnostic evaluation's mainstay is clinical examination [2]. Despite clinicians' vast experience, there is every possibility of

¹Department of Surgery, Narayana Medical College, Nellore, Andhra Pradesh, India

²Department of Radiology, Narayana Medical College, Nellore, Andhra Pradesh, India

*For Correspondence: drpriyankachinta@gmail.com

©2024 The authors

This is an Open Access article distributed under the terms of the Creative Commons Attribution (CC BY NC), which permits unrestricted use, distribution, and reproduction in any medium, as long as the original authors and source are cited. No permission is required from the authors or the publishers. (<https://creativecommons.org/licenses/by-nc/4.0/>)

either over- or under-diagnosis, which is quite common. With the available serological investigations, precision in diagnosing appendicular pathology is lacking [3]. Available literature suggests bilirubin can be used as a predictor of diagnosis of appendicular pathology [4].

Recent studies used hyperbilirubinemia to differentiate appendicular perforation and acute appendicitis based on serum bilirubin values. Most of these studies are retrospective studies and have one or more limitations in their study design, and very limited prospective studies are available on this serum biomarker [5]. Outcomes in different appendicular pathology are variable; patients who are presented with acute appendicitis requiring surgical intervention will have good recovery, but when it comes to patients who are diagnosed with perforated appendix may have life-threatening complications, including the death of the patient [6,7]. The majority of recently introduced diagnostic modalities like ultrasonography, and helical abdominal CT-scanning have yielded favorable outcomes [8] in patients with painful abdomen, minimizing the surgical interventions in case of non-appendicular origin abdominal pains, but the main hindrance is these equipment are not affordable or scarcity of availability of equipment in the majority of hospitals [9,10]. So, the estimation of serum bilirubin is considered to find a widely available diagnostic tool to diagnose various appendicular pathologies. A meticulously planned prospective study design incorporating estimation of serum bilirubin at the time of presentation to the hospital and prospectively patients' diagnosis established with radiological evaluation and intra-operative surgical diagnosis was corroborated. Finally, the correlation was established, if any existed, between hyperbilirubinemia and appendicular pathology.

MATERIALS AND METHODS

This prospective study was conducted in the department of general surgery among patients diagnosed with acute appendicitis attending the OPD and emergency surgical ward of the general surgery department of Narayana Medical College Hospital. The duration of the study is between January 2023 and December 2023.

All subjects signed informed consent prior to enrollment, and the protocol was approved by the Institution's ethics committee (NMC/ADM/ETHICS/approval/007/12/2022). All provisions of the Declaration of Helsinki were meticulously followed while

performing this study. 400 cases were recruited into the study who fulfilled the inclusion and exclusion criteria. The criteria for selecting patients were based on the history of presentation, physical examination, and imaging modalities like ultrasound or CT Scan of the abdomen; the specificity of Ultra Sound was (54.2%) compared with the specificity of CT (97.2%). Hematological and biochemical investigations, including CBP, Liver function tests, and Renal Function Tests.

Inclusion criteria:

1. Study subjects who were 10 years to 75 years old. (Appendicitis is uncommon below 10 years children, >75 years)
2. Patients of Both the genders
3. Patients who are clinically diagnosed with acute appendicitis.
4. Patients who underwent surgery
5. Patients whose intra-operative findings corroborate with histopathology findings of specimens suggestive of appendicitis
6. Patients who are willing to give informed consent.

Exclusion criteria:

1. Conservatively treated appendicitis Patients were excluded.
2. Patients who were previously diagnosed with liver diseases like cholelithiasis, HBsAg positive, malignancy of the hepatic system, etc were excluded from the study
3. Chronic alcoholism and drug intake causing cholestasis were excluded.
4. Hemolytic disease
5. Congenital or acquired biliary disease.
6. Patients less than 10 years of age and more than 75 were also excluded from the study
7. Patients who were Not willing to give informed consent

After the recruitment of study participants into the study, details of the patient were entered into predesigned proforma comprising details of socio-demographic details, CBC, liver function tests, blood urea, serum creatinine, HBs Ag, HCV antibody, details of ultrasonography, clinical findings, and details of histopathological findings of the specimen after surgery. Serum bilirubin values were calibrated as per WHO guidelines at 0.1-0.3 mg/dl of direct bilirubin and 0.2-0.8 mg/dl of indirect bilirubin, which comes to 0.3-1.0 mg of total bilirubin.

Statistical Analysis

Statistical analysis was done by using the SPSS statistical software program package (SPSS version 25.0 for Windows, Armonk, NY: IBM Corp.). Quantitative data are represented as mean \pm SD. For uniformly distributed data variables, a student t-test for two groups was performed to evaluate the Means of the two groups. The correlation of bilirubin levels was estimated by standard error of means by using Kolmogorov-Smirnov normality tests to test the normality of data. Means for normally distributed data were compared using the student's test for two groups.

RESULTS

Of the 400 study population, 220 (55%) were males, and 180 (45%) were female patients. In this study sample, 19% of the total sample suffered from appendicular perforation, and 81% had acute appendicitis. Most of the study population belonged to the 20-30 age group, and the frequency of both appendicitis and appendicular perforation decreased as the age of patients increased. The complete details of these socio-demographics are described in Table 1.

Table 1: Distribution of age study participants of appendicular perforation and acute appendicitis.

Condition	Age (Years)	Bilirubin > 1	Bilirubin < or = 1	Total
Acute Appendicitis	11-20	22	81	103
	21-30	29	104	133
	31-40	13	43	56
	41-50	10	12	22
	51-60	5	2	7
	61+	3	4	7
	Total	82	246	328
Appendicular Perforation	11-20	16	0	16
	21-30	29	2	31
	31-40	7	3	10
	41-50	5	0	5
	51-60	4	2	6
	61+	3	1	4
	Total	64	8	72

Out of 400 study samples, 72 patients were presented with appendicular perforation, and 328 patients presented with appendicitis. Of 72 patients who presented with appendicitis, 64 had hyperbilirubinemia (>1 mg/dl), and out of 328 patients with appendicitis diagnosis, only 82 presented with

hyperbilirubinemia (>1mg/dl). These findings signify that hyperbilirubinemia is more common with the perforation of the appendix (Table 2)

Table 2: Depicting the study population Distribution based on the serum bilirubin levels

	Bilirubin (mg %) > 1	< or = 1	Total
Acute Appendicitis	82	246	328
Appendicular Perforation	64	8	72
Total	146	254	400

Table 3: Correlation of serum bilirubin levels of two groups

	N	Mean Bilirubin Level (mg %)	Standard Error of Mean
Acute Appendicitis	328	0.89 \pm 0.38	0.0156
Appendicular Perforation	72	1.74 \pm 0.79	0.1263

In the cases with appendicular perforation, the observed mean value of serum bilirubin is 1.74, whereas the observed serum bilirubin mean value of appendicitis is 0.89. The difference in the standard error of mean value is statistically significant at a P-value of <0.001 between the two study population groups (table 3)

DISCUSSION

Out of 400 study samples, 72 patients were presented with appendicular perforation, and 328 patients presented with appendicitis. Of 72 patients who presented with appendicitis, 64 had hyperbilirubinemia (>1 mg/dl), and out of 328 patients with appendicitis diagnosis, only 82 presented with hyperbilirubinemia (>1mg/dl). Most of the study population belongs to the 21-30 years age group, both in the appendicitis group (133/328) and the perforation group (31/72). Our study findings are comparable to the findings of the studies done by Abedalqader et al., which revealed that the most common age group suffering from appendicitis and appendicular perforation belongs to 21-30 years [1], and Bolmers et al. also mention that the most common age group affected is <30 years [2]. In the study population of 400 patients, 220 (55%) were males and 180 (45%) were female. In this study sample, 19% of the total sample suffered from appendicular perforation, and 81% of the study

sample had acute appendicitis. The above-mentioned values depict appendicitis, and appendicular perforation was more common in the male gender when compared to the female gender in the distribution of the study population. These findings are similar to the study conducted by Bakshi S et al., who mentioned a study sample distribution of men 51.38% and women 48.61% [3]. Out of 400 study samples, 72 patients were presented with appendicular perforation, and 328 patients presented with appendicitis. Of 72 patients who presented with appendicular perforation, 64 had hyperbilirubinemia (>1 mg/dl) (89%), and out of 328 patients with appendicitis diagnosis, only 82 presented with hyperbilirubinemia(>1mg/dl) (25%). These findings signify hyperbilirubinemia, which is more common with the perforation of the appendix. Our findings are from a study by Kumar et al., who proposed that 73% and 23% of the study sample had hyperbilirubinemia [8].

In our study, In cases of appendicular perforation, the observed mean value of serum bilirubin is 1.74, similar to a study done by Cheekuri et al. [11]. The study revealed that the serum bilirubin value of the study population was 1.5 mg/dl. In another study done by Motie et al.[12] and Sifri et al. [13] revealed a serum bilirubin value of 1.4 mg/dl and 1.7 mg/dl, respectively, and they used hyperbilirubinemia as a parameter to diagnose a perforated appendix.in our study sample, the observed serum bilirubin mean value of appendicitis is 0.89, and this value is similar to the mean bilirubin value obtained by Sandstrom A et al.,[10] They proposed a bilirubin of 0.925md/dl in their study population of acute appendicitis. In our study in the acute appendicitis group, serum bilirubin cutoff point value is fixed between 0.3 -1.0 mg/dl for acute appendicitis and >1.0 mg/dl for appendicular perforations, which were used as sensitive parameters for differentiating two categories of the study sample. The outcome values of serum bilirubin yielded in our study were 1.74 mg/dl in the appendicular perforation group and 0.89 mg/dl in the acute appendicitis group, which slightly differs from the study findings of study done by Chaudhary et al. with the reported mean value of 0.9 mg/dl in patients of appendicular perforation and a mean bilirubin value of 1.5 mg/dl in non-perforated appendicitis [14].

CONCLUSIONS

Patients with serum bilirubin values of >1.0 mg% and clinical symptoms suggestive of appendicular pathology should be considered to have a higher chance of perforating the appendix

than those with normal serum bilirubin values. These findings suggest that the measurement of serum bilirubin levels can be considered an adjuvant tool for the clinical diagnosis of appendicular pathologies.

Limitations

The current study should be read with the following limitations kept in mind,

1. The current study uses a relatively small sample size of people who have attended hospitals for treatment. Hence, its findings cannot be extrapolated to the general population.
2. No verifiable data about other contributing factors for elevated bilirubin is available in most patients as they were presented for emergency management

Future implications

Studies are done with larger sample sizes of diverse population groups and incorporating various confounding factors that can contribute to hyperbilirubinemia while selecting patient populations are needed to establish the existence of a correlation between hyperbilirubinemia and outcomes of appendicular pathologies more precisely. Estimating serum bilirubin is easily available and can minimize unnecessary surgical interventions in places with scarce facilities.

FINANCIAL ASSISTANCE

Nil

CONFLICT OF INTEREST

The authors declare no conflict of interest

AUTHOR CONTRIBUTION

Rishi Papa Naidu collected data and interpreted the statistical values. He and Chinta Priyanka designed the study and contributed to drafting and editing the manuscript. Both authors wrote the final draft, which was read and approved by both authors.

REFERENCES

- [1] Abedalqader T, Bakir M, AlJohani F, Altahan T, Amer SM, Almustanyir S. Acute Abdomen Secondary to Granulomatous Appendicitis: A Rare Case of Complicated Appendicitis. *Cureus*, **14**, e23247 (2022).
- [2] Akbulut S, Koç C, Şahin TT, Şahin E, Tuncer A, Demyati K, Şamdancı E, Çolak C, Yılmaz S. An investigation into the factors predicting acute appendicitis and perforated

- appendicitis. *Ulus Travma Acil Cerrahi Derg*, **27**, 434-42 (2021).
- [3] Khalid SY, Elamin A. The Diagnostic Accuracy of Hyperbilirubinemia in Predicting Appendicitis and Appendiceal Perforation. *Cureus*, **15**, e48203 (2023).
- [4] Küçükakçali Z, Akbulut S, Çolak C. Value of fecal calprotectin in prediction of acute appendicitis based on a proposed model of machine learning. *Ulus Travma Acil Cerrahi Derg*, **29**, 655-62 (2023).
- [5] Wu Z, Zhao L, Liu Y, Qian S, Wu L, Liu X. Fibrinogen as a Marker of Overall and Complicated Acute Appendicitis: A Systematic Review and Meta-Analysis. *J Surg Res*, **280**, 19-26 (2022).
- [6] Bakshi S, Mandal N. Evaluation of role of hyperbilirubinemia as a new diagnostic marker of complicated appendicitis. *BMC Gastroenterol*, **21**, 42 (2021).
- [7] Moris D, Paulson EK, Pappas TN. Diagnosis and Management of Acute Appendicitis in Adults: A Review. *JAMA*, **326**, 2299-311 (2021).
- [8] Pogorelić Z, Lukšić AM, Mihanović J, Đikić D, Balta V. Hyperbilirubinemia as an Indicator of Perforated Acute Appendicitis in Pediatric Population: A Prospective Study. *Surg Infect (Larchmt)*, **22**, 1064-71 (2021).
- [9] Hajibandeh S, Hajibandeh S, Hobbs N, Mansour M. Neutrophil-to-lymphocyte ratio predicts acute appendicitis and distinguishes between complicated and uncomplicated appendicitis: A systematic review and meta-analysis. *Am J Surg*, **219**, 154-63 (2020).
- [10] Chin X, Mallika Arachchige S, Orbell-Smith JL, Da Rocha D, Gandhi A. Conservative Versus Surgical Management of Acute Appendicitis: A Systematic Review. *Cureus*, **16**, e52697 (2024).
- [11] Flum DR, Davidson GH, Monsell SE, Shapiro NI, Odom SR, Sanchez SE et al. A Randomized Trial Comparing Antibiotics with Appendectomy for Appendicitis. *N Engl J Med*, **383**, 1907-19 (2020).
- [12] Wang CH, Yang CC, Hsu WT, Qian F, Ding J, Wu HP et al. Optimal initial antibiotic regimen for the treatment of acute appendicitis: a systematic review and network meta-analysis with surgical intervention as the common comparator. *J Antimicrob Chemother*, **76**, 1666-75 (2021).
- [13] Zagales I, Sauder M, Selvakumar S, Spardy J, Santos RG, Cruz J, Bilski T, Elkbuli A. Comparing Outcomes of Appendectomy Versus Non-operative Antibiotic Therapy for Acute Appendicitis: A Systematic Review and Meta-Analysis of Randomized Clinical Trials. *Am Surg*, **89**, 2644-55 (2023).
- [14] de Almeida Leite RM, Seo DJ, Gomez-Eslava B, Hossain S, Lesegretain A, de Souza AV, Bay CP et al. Nonoperative vs Operative Management of Uncomplicated Acute Appendicitis: A Systematic Review and Meta-analysis. *JAMA Surg*, **157**, 828-34 (2022).