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Original Research Article

Hyperbilirubinemia as a predictor of the severity of acute appendicitis - an observational study

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ABSTRACT

Background: Appendicitis is the most common acute abdominal condition requiring emergency surgery, with a lifetime risk of 6%. Appendectomy continues to be one of the commonest procedures in general surgery, accounts for approximately 1% of all surgical operation. Despite the increased use of ultrasonography, computed tomography scanning and laparoscopy, the rate of misdiagnosis of appendicitis has remained constant (15.3%). The aim of this study was to whether Serum Bilirubin can be considered as a new laboratory marker to aid in the diagnosis of acute appendicitis and if so, does it have the predictive capacity to warn us about complicated appendicitis.
Methods: This was prospective observational study done in Mahatma Gandhi Medical College and Research Institute, Pondicherry between November 2014 and August 2016. About 110 patients of acute appendicitis who had undergone appendicectomy were studied. Data was collected and analyzed critically.
Results: Males 66 (60%) outnumbered females 44 (40%) and overall mean age was 26.61±12.37 years. Of the 110 patients, 9% were normal appendix, 59.09% were confirmed as acute appendicitis while 31.81% were diagnosed with complicated appendicitis on biopsy. The Sensitivity and Specificity of serum bilirubin as a marker in predicting Acute appendicitis and complicated appendicitis was 47.6% and 90.9% respectively. Similarly, the Positive predicative value and Negative predicative value for the same was 88.5% and 61.5% respectively with odds ratio 12.4 with significant p value <0.0001.
Conclusions: Serum bilirubin is easily available test and cheap and can be estimated from the sample of blood drawn for routine blood investigations. Patients with clinical signs and symptoms of appendicitis and with hyperbilirubinemia should be identified as having a higher probability of complicated appendicitis. Hence, serum bilirubin levels have a predictive potential for the diagnosis of severity of acute appendicitis and need for early appendicectomy. If total serum bilirubin is added to already existing laboratory tests, then the diagnosis of complicated appendicitis in clinically suspected cases can be made with fair degree of accuracy, the need for CECT and MRI can be reduced and unnecessary delay in appendicectomy can be avoided.

Keywords: Appendectomy, Hyperbilirubinemia, Ruptured appendicitis

INTRODUCTION

Acute appendicitis is the most common cause of "acute surgical abdomen".[1,2] Appendicectomy is the emergency abdominal operation most frequently performed and is often the first major procedure performed by a surgeon in training.[1] Despite advances in the radiological and laboratory investigations, the diagnosis of appendicitis remains a dilemma. Based on a combination of history, physical examination and laboratory studies experienced clinicians accurately diagnose appendicitis about 80% of the time.[3] Most patients with acute appendicitis can be easily diagnosed, but in some cases the sign and symptoms are variable and a firm diagnosis can be

difficult. This is particularly true where the appendix is retrocaecal or retroileal. The percentage of appendicectomies performed, where normal appendix found, varies from 15-50% and postoperative complications can occur in up to 50% of these patients.[4,5] Delay in diagnosis of acute appendicitis leads to perforation and peritonitis with increased mortality. Appendicular perforation ranges 50-90% in various series.[6,7]

The importance of laboratory investigations like White Blood Cell (WBC) counts and C-reactive protein (CRP) etc. values has been stressed to supplement the clinical diagnosis and to reduce the frequency of unnecessary appendicectomy.[8] The importance of Ultrasonography (USG) as a diagnostic tool for appendicitis has been widely known and studied.[9-10] Various scores combining clinical features and laboratory investigations, have also been developed to reach the diagnosis, such as the Alvarado score and the Modified Alvarado score.[11,12]

However, till now there is no confirmatory laboratory marker for the pre-operative diagnosis of acute appendicitis and appendicular perforation. Elevation in serum bilirubin was reported recently, but the importance of the raised total bilirubin has not been stressed in acute appendicitis and appendicular perforation.[13] It is well established that when microorganisms invade the body, leukocytes defend it and leads to increase in the leukocyte count. Microbial invasion in the appendix leads to transmigration of microbe and the release of pro-inflammatory cytokines such as TNF-alpha, IL6 and cytokines. They reach the liver through Superior mesenteric vein (SMV), either directly or indirectly by altering the hepatic blood flow, produce inflammation, abscess or dysfunction of liver.[14-15] In view of the above context, the present study was undertaken to find out the role of serum bilirubin as a laboratory marker to aid in the diagnosis of acute appendicitis and to evaluate whether elevated bilirubin levels have a predictive potential for the diagnosis of the severity of Appendicitis.

METHODS

This was a prospective observational study, which was conducted at the Mahatma Gandhi Medical College and Research Institute. Patients were briefed about the study and their consent was taken. A total of 110 patients clinically diagnosed as appendicitis from August 2014 to August 2016 at Mahatma Gandhi Medical College and research institute, Pondicherry and had undergone apppedicectomy, either emergency or elective were analyzed. The aim of the study was to find out the role of serum Bilirubin as a laboratory marker to aid in the diagnosis of acute appendicitis and to evaluate whether elevated bilirubin levels have a predictive potential for the diagnosis of the severity of Appendicitis. All patients diagnosed as acute appendicitis clinically on admission and operated for the same and after surgery for who histopathological report available were included in the study. Patients with known pre-existing liver disease, hemolytic disease, cholelithiasis/choledecholithiasis or medication influencing liver function were excluded from analysis.

A complete history and thorough clinical examination for all selected patients were carried out. All patients had undergone routine investigations such as routine blood investigations (i.e. complete blood count, total leukocyte count), ultrasound abdomen, liver enzymes, which include -serum bilirubin (total and direct bilirubin), SGPT (Alanine transaminase), SGOT (Aspartate transaminase), ALP (Alkaline phosphatase). Once pre-operative clinical diagnosis of appendicitis, all patients were subjected to surgery. The removed appendix was sent for histopathological examination. Normal values per local laboratory references were TLC between 4500 to 11000/µL, total bilirubin ≤1 mg/dL, SGOT≤35 U/L, SGPT ≤40 U/L, ALP≤140 U/L. Histopathological findings were divided into three groups: Normal appendix, Acute appendicitis and complicated appendicitis

All slides were reported by a single pathologist. The data regarding patient diagnosis, investigations, and histopathological report is collected in a specially designed case recording form and transferred to a master chart for analysis.

Statistical analysis was carried out using SPSS version 19.0 (IBM SPSS, US) software with Regression Modules installed. Descriptive analyses were reported as mean and standard deviation of continuous variables. Paired t test and independent t test were used to analyze the data.

RESULTS

Table 1 revealed that a total of 110 patients who underwent appendicectomy were studied. In the studied population males 66 (60%) outnumbered females 44 (40%) and overall mean age was 26.61±12.37 years.

Table 1: Demographic profile.

Age	Male	Female	Total
13-20	27 (61%)	14 (39%)	41
21-30	22 (57.9%)	16 (42.1%)	38
31-40	7 (50%)	7 (50%)	14
41-50	6 (50%)	6 (50%)	12
51-60	1 (50%)	1 (50%)	2
>60	3 (100%)	0	3
Total	**66 (60%)**	**44 (40%)**	**110**
Mean age in years	**26.61±12.30**	**26.97±12.37**	**26.86±12.37**

Table 2 shows the histopathological diagnosis of the patients in the study. Out of the 110 patients, 9% were found out to be normal appendix, 59.09% were confirmed as acute appendicitis while 31.81% were diagnosed with complicated appendicitis.

Table 2: Histopathological diagnosis.

Histopathology	Number	Percentage
Normal appendix	10	9.10%
Acute appendicitis	65	59.09%
Complicated appendicitis	35	31.81%
Total	**110**	

Table 3 showed the comparison of mean serum bilirubin levels in patients with different histopathological diagnoses. The mean total bilirubin levels in patients diagnosed with normal appendix, Acute appendicitis was 1.125±0.44 mg/dL while in patients diagnosed with complicated appendicitis was 1.56±0.44mg/dL.

Table 3: Comparison of mean serum bilirubin levels in patients with normal appendix, acute appendicitis and complicated appendicitis.

Bilirubin	Normal appendix	Acute appendicitis	Complicated appendicitis
Mean total bilirubin	0.75 ±0.45	O.94±0.44	1.56±0.44

Table 4: Serum bilirubin versus histopathology report.

Histology	Total bilirubin (≤1 mg/dl)	(>1 mg/dl)	Total
Normal appendix	8 (15.4%)	2(3.4%)	10
Acute appendicitis	40 (76%)	25(43.2%)	65
Perforated or gangrenous appendix	4 (7.6%)	31(53.4%)	35

Table 4 highlights the incidence of hyperbilirubinemia among the study population with different histopathological diagnosis. Compared to histopathology, 2 patients (3.4%) of normal appendix, 25 patients (43.2%) of acute appendicitis, 31 patients (53.4%) of perforated appendix were having hyperbilirubinemia (>1mg/dl). Table 5 shows the statistical correlation of serum bilirubin level to the histopathology of appendix. The Sensitivity and Specificity of serum bilirubin as a marker in predicting Acute appendicitis and complicated appendicitis was 47.6% and 90.9% respectively. Similarly, the Positive predicative value and Negative predicative value for the same was 88.5% and 61.5% respectively with odds ratio 12.4 with significant p value <0.0001.

Table 5: Comparison of serum bilirubin levels versus histopathology of appendix.

Tests	Normal vs acute appendicitis	Normal vs complicated appendix	Acute vs complicated appendix
Sensitivity	92.5%	94%	47.6%
Specificity	16.66%	66.66%	90.9%
PPV	38.45%	88.5%	88.5%
NPV	80%	80%	61.5%
P Value	0.25	<0.0001	<0.0001

Table 6: Accuracy of serum bilirubin as a marker in diagnosing complicated appendicitis.

Accuracy of serum bilirubin	
Sensitivity	94%
Specificity	66.66%
PPV	88.5%
NPV	80%

Findings in Table 6 patients show that patients with clinical signs and symptoms of appendicitis with hyperbilirubinemia should be identified as having a higher probability of complicated appendicitis suggesting, serum bilirubin levels have a predictive potential for the diagnosis of severity of acute appendicitis and need for early appendicectomy.

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, cytokines leading to endotoxemia/bacteraemia. Invasion of bacteria into the hepatic parenchyma interferes with the physiology of excretion of bile and leads to hyperbilirubinemia. In present study, the mean total serum bilirubin of all 110 patients was 1.125±0.44 mg/dL (range, 0.3-2.4 mg/dL), which was above the normal range considered for the

study, hence indicating the occurrence of hyperbilirubinemia. Our finding was consistent with hyperbilirubinemia found in a study conducted by Khan S et al, who found average level of serum bilirubin in his study population to be 2.38 mg/dL.[16]

Sand et al in his study found the mean bilirubin levels in patients with appendicular perforation to be significantly higher than those with acute appendicitis.[17] The specificity in our study was more than that by Sand et al in which, he found the sensitivity and specificity in his study of hyperbilirubinemia for predicting appendicular perforation to be 70% and 86.0% respectively.[16] Khan S et al in his study concluded that elevated total serum bilirubin, without severe abnormalities in the value of liver enzymes is a good indicator of acute appendicitis.[16] Estrada J et al in his study found significant relationship between the presence or absence of appendicular gangrene and perforation with the presence of hyperbilirubinemia.[18] Present study showed that the Sensitivity and Specificity of bilirubin in diagnosing complicated appendicitis and normal appendix was 94% and 66.66% respectively. Similarly, Positive predictive value and Negative predicative value of bilirubin in predicting complicated appendicitis and normal appendix was 88.5% and 80% respectively. (P value <0.0001).

CONCLUSION

Serum bilirubin is easily available test and cheap and can be estimated from the sample of blood drawn for routine blood investigations. If total serum bilirubin is added to already existing laboratory tests, then the diagnosis of complicated appendicitis in clinically suspected cases can be made with fair degree of accuracy, the need for CECT and MRI can be reduced and unnecessary delay in appendicectomy can be avoided.

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REFERENCES

1. O'Connell PR. The Vermiform Appendix. CJK, O'Connell PR (Ed.). Bailey and Love's - Short practice of surgery. 26th ed. London: Arnold: 2012:1199-203.
2. Smink DS, Soybel DI. Appendix and Appendectomy In: Zinner MJ, Stanley W (eds) Maingot'sabdominal operations. 12th ed. Ashley: McGraw Hill. 2012:589-612.
3. John Maa. The Appendix. Beauchamp. RD, In Evers Townsend BM, Mattox KL, eds. Sabiston Textbook of Surgery. 18th ed. Philadelphia, Pa: Saunders Elsevier. 2008:1333-47.
4. Deutsch AA, Shani N, Reiss R. Are some some appendectomies unnecessary? An analysis of 319 white appendices. J R Coll Surg Edinb. 1983;28(1):35-40.
5. Pieper R, Kager L, Näsman P. Acute appendicitis: a clinical study of 1018 cases of emergency appendectomy. Acta Chir Scand. 1982;148(1):51-62.
6. Von Titte SN, McCabe CJ, Ottinger LW. Delayed appendectomy for appendicitis: causes and consequences. Am J Emerg Med. 1996;14(7):620-2.
7. Temple CL, Huchcroft SA, Temple WJS. Natural History of appendicitis in adult: A prospective study. Ann Surg. 1995;221:78.
8. Grönroos JM, Grönroos P. A fertile-aged woman with right lower abdominal pain but unelevated leukocyte count and C-reactive protein: acute appendicitis is very unlikely. Langenbecks Arch Surg. 1999;384:437-40.
9. Puylaert JBCM, Rutgers PH, Lalisang RI, de Vries BC, van der Werf SD, Dörr JP, et al. A prospective study of ultrasonography in the diagnosis of appendicitis. N Engl J Med. 1987;317:666-9.
10. Lim HK, Lee WJ, Lee SJ, Namgung S, Lim JH. Focal appendicitis confined to the tip: diagnosis at US. Radiology. 1996;200:799-801.
11. Alvarado A. A practical score for early diagnosis of acute appendicitis. Ann Emerg Med. 1986;15:557-64.
12. Kalan M, Tabbot O, Cunlife WJ, Rich AJ. Evaluation of the modified Alvrado score in the diagnosis of acute appendicitis. A prospective study. Ann R Cool Surg Engl. 1994;76:418-9.
13. Khan S Evaluation of hyperbilirubinemia in acute inflammation of appendix: a prospective study of 45 cases Kathmandu Univ Med J (KUMJ). 2006;4(3):281-9.
14. Juric I, Primorac D, Zagar Z, Biocic Frequency of portal and systemic bacteremia in acute appendicitis. Pediatr Int. 2001;43(2):152-6.
15. Wang P, Chudhary IH. Mechanism of hepatocellular dysfunction during hyper dynamic sepsis. Am J Physiol Regul Integr Comp Physiol. 1996;270:927-38.
16. Khan S. Elevated serum Bilirubin in Acute Appendicitis: a new Diagnostic tool. Kathmandu University Medical J. 2008;6(2):161-5.
17. 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;198(2):193-8.
18. Estrada JJ, Petrosyan M, Krumenacker J Jr, Huang S, Moh P. Hyperbilirubinemia in Appendicitis: A New Predicator of Perforation. J Gastrointestinal Surgery. 2007;11:714-5.

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