

Preoperative Diagnostic Role of Hyperbilirubinemia as a Marker of Acute Appendicitis & Appendicular Perforation

Naveen Verma¹, Hanuman Ramkhoja², Surendra Pal Maurya³, Farukh Khan⁴, Anand Mohan⁵, Ashutosh Saini⁶

¹Resident, Department of Surgery, SawaiMan Singh Medical College and Hospital, Jaipur, Rajasthan, India (pin-302004)

²Assistant Professor, Department of Surgery, SawaiMan Singh Medical College and Hospital, Jaipur, Rajasthan, India (pin-302004)

³Medical Officer, Department of Surgery, SawaiMan Singh Medical College and Hospital, Jaipur, Rajasthan, India (pin-302004)

⁴Assistant Professor, Department of Surgery, SawaiMan Singh Medical College and Hospital, Jaipur, Rajasthan, India (pin-302004)

⁵Resident, Department of Surgery, SawaiMan Singh Medical College and Hospital, Jaipur, Rajasthan, India (pin-302004)

⁶Resident, Department of Surgery, SawaiMan Singh Medical College and Hospital, Jaipur, Rajasthan, India (pin-302004)

Abstract: *This study was done to conclude whether the 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 Appendicular perforation. A total of 100 patients with clinical diagnosis of acute appendicitis or appendicular perforation were studied. The serum bilirubin and liver function tests were carried out in all the patients. In this study, males (71%) outnumbered females (29%) and overall mean age was 27.43±10.72 years. Of the 100 patients, 87% were confirmed as acute appendicitis while 13% were diagnosed with Appendicular perforation. Of 87 patients with acute appendicitis, 62.06% had raised bilirubin levels, while 37.93% had normal levels. 13 patients were diagnosed as Appendicular perforation, 10 patients (76.92 %) had raised bilirubin levels, while the remaining 3 patients (23.07%) had normal levels. The Sensitivity and Specificity of serum bilirubin as a marker in predicting Acute appendicitis and Appendicular perforation was 62.06% and 23.07% respectively. Patients with clinical signs and symptoms of appendicitis and with hyperbilirubinemia higher than normal range 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: Appendicular perforation, Hyperbilirubinemia, Acute appendicitis, Acute surgical abdomen, Appendicectomy

1. Introduction

Acute appendicitis is the commonest cause of "Acute Surgical abdomen"[1,2]. Appendicectomy is the most frequently performed urgent abdominal operation and is often the first major procedure performed by a surgeon in training [1].

The diagnosis of Appendicitis still remains a dilemma in spite of advances in the radiological and laboratory investigations. Experienced clinicians accurately diagnose appendicitis based on a combination of history, physical examination and laboratory studies about 80% of the time[3]. Although most patients with Acute Appendicitis can be easily diagnosed, 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 appendix subsequently found to be normal varies 15-50%[4] and postoperative complications can occur in up to 50%[5] of these patients. Delay in diagnosis of Acute Appendicitis leads to perforation and peritonitis and increased mortality. Perforation ranges 50- 90% in various series [6,7].

To supplement the 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) etc values has been stressed. The use of Ultrasonography (USG) as a diagnostic tool for appendicitis has been widely known and studied. Various scores combining clinical features and laboratory investigations have also been developed and are good enough to reach the diagnosis. These are the Alvarado score [13] and the Modified Alvarado score [14].

However up to date there is no confirmatory laboratory marker for the preoperative diagnosis of acute appendicitis and appendicular perforation.

Recently, elevation in serum bilirubin was reported, but the importance of the raised total bilirubin has not been stressed in acute appendicitis and appendicular perforation [15]. It is well established that when microbes invade the body, leukocytes defend it. This leads to increase in the leukocyte count. Bacterial invasion in the appendix leads to transmigration of bacteria and the release of proinflammatory cytokines such as TNF alpha, IL6 and cytokines. These reach the liver via Superior mesenteric vein (SMV) and may produce inflammation, abscess or dysfunction of liver either directly or indirectly by altering the hepatic blood flow [16-22].

Volume 5 Issue 8, August 2016

www.ijsr.net

Licensed Under Creative Commons Attribution CC BY

In view of the above context, the present study was undertaken to assess relationship between hyperbilirubinemia and acute appendicitis and to evaluate its credibility as a diagnostic marker for acute appendicitis and also, to see whether elevated bilirubin levels have a predictive potential for the diagnosis of appendicular perforation.

2. Objectives

- To study the relationship between hyperbilirubinemia and acute appendicitis; and to evaluate its credibility as a diagnostic marker for acute appendicitis.
- To evaluate whether elevated bilirubin levels have a predictive potential for the diagnosis of Appendicular perforation.

3. Materials and Methods

This was a Hospital based observational study which included 100 patients of Acute Appendicitis admitted in the Department of General Surgery, S.M.S. Hospital, Jaipur, during the period of May 2015 to April 2016.

Inclusion

Patients fulfilling the following criteria will be considered for the study.

- Patients scheduled for appendicectomy for acute appendicitis at the Department of Surgery, SMS Medical College, Jaipur.
- Patients > 15 years of age.
- Patients with a history of alcohol intake with AST/ALT <2 or no history of hepatotoxic drug intake.
- No past history of jaundice with acute appendicitis.

Exclusion

Patients with the following features shall be excluded from the study:

- Incidental appendicectomy
- Patients younger than 15 years of age.
- History of alcohol intake with SGOT / SGPT > 2.
- History of hepatotoxic drug intake
- HBsAg positive
- Past history of jaundice and acute appendicitis
- Unwillingness for surgery.

4. Procedure

Ethical clearance has been obtained from "Ethical Clearance Committee" of the institution for the study. It is in the form of signature from Head of Dept. Surgery and Dean of S.M.S. Medical College, Jaipur. Based on the selection criteria patients admitted with clinical diagnosis of acute appendicitis or appendicular perforation were screened for eligibility. The eligible patients were briefed about the nature of the study and a written informed consent was obtained from the consented patients. Thorough history was taken and clinical examination was done for all patients and findings were recorded on predesigned and pretested proforma.

The following tests were carried out on admission.

- Routine blood investigations (Complete blood count, platelet count, reticulocyte count).
- Serum Bilirubin (Total and Direct bilirubin).
- Liver Function Tests (LFTs) which include;
 - SGPT (Alanine transaminase).
 - SGOT (Aspartate transaminase).
 - ALP (Alkaline phosphatase).
- Seropositivity for HbsAg
- Urine analysis (routine and microscopy).

The serum bilirubin and LFTs were carried out using the Auto Analyser (cobas 111) machine available in the hospital and HbsAg was tested by ELISA/Spot technique using HEPALISA or HEPACARD kit.

Reference Range of Serum Bilirubin and Liver Enzymes

Test	Normal Range
Serum Bilirubin	
Total	0.3-1 mg/dl
Direct	0.1-0.3mg/dl
Liver Enzymes	
SGOT	0-35 U/L
SGPT	0-35 U/L
ALP	30-120 U/L

The results were grouped as 'Normal' or 'Raised' (hyperbilirubinemia) as per the above reference values.

5. Results

A total of 100 patients with clinical diagnosis of acute appendicitis or appendicular perforation admitted in the Department of General Surgery, S.M.S. Medical College, Jaipur were studied.

Distribution of patients by age

Age Group (year)					
15-24	25-34	35-44	45-54	55-64	65-74
49	27	15	7	1	1

As per the study, the age group 15-24 years is most commonly affected (49%) followed by age group 25-34 (22%). The youngest patients of this study were of 15 years old while the oldest patient was a 67 year Male.

Sex Distribution

Sex	Number	Percentage
Male	71	71
Female	29	29
Total	100	100.00

Out of 100 patients enrolled for the study, 71 patients (71%) were males while the remaining 29 patients (29%) were females.

Liver Function Tests

Parameters	Mean	SD
Total bilirubin (mg/dL)	1.296	0.58
Direct bilirubin (mg/dL)	0.526	0.25 (0.2464)
Indirect bilirubin (mg/dL)	0.77	0.4 (0.3625)
SGOT (U/L)	42.88	17 (17.02)
SGPT (U/L)	30 (29.95)	17 (17.16)

The mean Total bilirubin of all 100 patients was 1.29 ± 0.58 mg/dL (range, 0.71 - 1.87 mg/dL) While the Direct bilirubin was 0.52 ± 0.25 mg/dL (range, 0.27 - 0.77 mg/dL). The mean SGOT and SGPT were 42.88 ± 17 U/L (range, 25.88 - 59.88 U/L) and 29.95 ± 17.16 U/L (range, 12.79 - 47.11).

Total bilirubin levels

Total bilirubin (mg/dL)	Number	Percentage
<1	36	36
> 1	64	64
Total	100	100.00

36 patients (36%) of all 100 patients were found to have normal bilirubin levels (<1.0 mg/dL), while 64 patients (64%) had raised bilirubin levels (>1.0 mg/dL).

Bilirubin levels in patient with uncomplicated acute appendicitis as diagnosis

Total bilirubin (mg/dL)	Distribution in Patients with uncomplicated Acute Appendicitis	
	Number	Percentage
>1.0	54	62.06
<1.0	33	37.93
Total	87	100.00

Of 87 patients diagnosed as uncomplicated acute appendicitis, 54 patients (62.06) had raised bilirubin levels (>1.0 mg/dL), while the remaining 33 patients (37.93) had normal levels (<1.0 mg/dL).

Bilirubin levels in patient with Appendicular perforation diagnosis

Total bilirubin (mg/dL)	Distribution in Patients with Appendicular perforation (n= 19/13)	
	Number	Percentage
>1.0	54	62.06
<1.0	33	37.93
Total	87	100.00

13 patients diagnosed as Appendicular perforation, 10 patients (76.92) had raised bilirubin levels (>1.0 mg/dL), while the remaining 03 patients (23.07) had normal levels (<1.0 mg/dL).

Correlation of acute appendicitis and Appendicular perforation with total serum bilirubin levels

Serum bilirubin (mg/dL)	Final diagnosis (n=100)			
	Acute appendicitis (n=87)		Appendicular perforation (n=13)	
	Number	%	Number	%
>1.0	(a) 58.54	62.06	(b) 10	76.92
<1.0	(c) 33	37.93	(d) 03	23.07
Total	87	100	13	100

54 patients (62.06%) of the total patients diagnosed with Acute appendicitis (n=87) were found to have elevated bilirubin levels (>1.0mg/dL) while 33 patients (37.93) had normal bilirubin levels (<1.0 mg/dL). Similarly, 10 patients (76.92%) of the total patient diagnosed with Appendicular perforation (n=13) were found to have elevated bilirubin levels (>1.0 mg/dL) while 3 patients (23.08%) had normal bilirubin levels (<1.0 mg/dL).

Accuracy of serum bilirubin as a marker in predicting Appendicular perforation

	Accuracy
Sensitivity	62.06%
Specificity	23.07%
Positive predictive value	84.37%
Negative predictive value	8.33%
Odds ratio	0.4909

6. Discussion

Acute appendicitis is the most common cause of 'Acute Abdomen' in young adults. Appendicectomy is 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[3].

The peak incidence of acute appendicitis is in the second and third decade of life. It is relatively rare in infants, and becomes increasingly common in childhood and early adult life. The incidence of appendicitis is equal in males and females before puberty. In teenagers and young adults, the male-female ratio increases to 3:2 at age 25[1]. The lifetime rate of appendicectomy is 12% for men and 25% for women, with approximately 7% of all people undergoing appendectomy for acute appendicitis during their lifetime.

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%[4] of cases. 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 elderly[1] as such procedures are associated with complications in 50% cases[5]. 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.

This study was taken up with this thought that is it possible to add serum bilirubin as a new laboratory marker to aid in the diagnosis of acute appendicitis and if so, does it have the credibility to help us foresee an impending complication of acute appendicitis?

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

In the present study of the 100 patients enrolled for the study 71 patients (71%) were males while the remaining 29 patients (29%) were females. The mean age in our study

population (100 patients) was 27.43 ± 10.72 years (range, 16.71-38.15 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[33,34]. The average age group in males 26.76 ± 11.10 years (range, 15.66 ± 37.86 years) was slightly lower than females 29.06 ± 9.70 years (range 19.36-38.76 years).

Hyperbilirubinemia (>1.0 mg/dL) in our study was found in 64 patients (64%) of all the 100 patients ($n=100$) enrolled in the study, while 36 patients (36%) had normal bilirubin levels (<1.0 mg/dL). Estrada et al[35] had found hyperbilirubinemia in 59 (38%) of 157 patients studied with acute appendicitis.

The mean total serum bilirubin of all 100 patients was 1.29 ± 0.58 mg/dL (range, 0.71-2.3 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 0.52 ± 0.25 mg/dL (range, 0.27-0.71 mg/dL) while that of Indirect bilirubin was 0.77 ± 0.4 mg/dL (range, 0.37-1.17 mg/dL). Our finding was consistent with hyperbilirubinemia found in a study conducted by Khan S, who found average level of serum bilirubin in his study population to be 2.38mg/dl.

Amongst the patients diagnosed with Acute appendicitis without perforation ($n=87$), 54 patients (62.06%) were found to have elevated bilirubin (>1.0 mg/dL) while only 33 patients (37.93%) had normal bilirubin levels (<1.0 mg/dL). In patients diagnosed with Appendicular perforation ($n=13$), 10 patients (76.92%) had bilirubin elevated (>1.0 mg/dL), while only 3 patients (23.07%) had normal levels (>1.0 mg/dL). Thus, Hyperbilirubinemia was found in most of the patients diagnosed with acute appendicitis (62.06%) or Appendicular perforation (76.92%).

The mean bilirubin levels in patients diagnosed with Acute appendicitis was 1.28 ± 0.61 mg/dL (range, 0.67 - 1.89 mg/dL) while in patients diagnosed with Appendicular perforation was 1.34 ± 0.29 mg/dL (range, 1.05-1.63 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 al[36] in his study found the mean bilirubin levels in patients with Appendicular perforation to be significantly higher than those with a nonperforated appendicitis.

7. Conclusion

The present study suggests -

- Serum bilirubin levels appears to be a promising new laboratory marker for diagnosing acute appendicitis, however diagnosis of appendicitis remains essentially still-clinical. 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 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.

References

- [1] O' Connel 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] Smink DS, Soybel DI. "Appendix and Appendectomy". In: Zinner MJ, Stanely W (eds) Maingot's abdominal operations. 11th ed. Ashely: McGraw Hill; 2007. p. 589-612.
- [3] 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.
- [4] 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.
- [5] Piper R, Kager E, Nasman P. Acute appendicitis a clinical study of 1018 cases of emergency appendectomy. Acta Chir Scand. 1982; 148:51-62.
- [6] Von vonTitte SN, McCabe CJ, Ottinger LW. Delayed appendectomy for appendicitis causes and consequences. Am J Emerg Med. 1996; 14:620.
- [7] Temple CL, Huchcroft SA, Temple WJS. Natural History of appendicitis in adult: A prospective study. Ann Surg. 1995; 221: 78.
- [8] Gronroos JM, Grinrous 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] Jeffrey RB, Laing FC, Lewis FR. Acute appendicitis: high-resolution real time US findings. Radiology 1987; 163: 11-4.
- [10] Puylaert JBCM, Rutgers PH, Lalisang RI, de Vries 13C, van der Werf SD, Dorr JP, et al. A prospective study of ultrasonography in the diagnosis of appendicitis. N Engl J Med 1987; 317: 666-9.
- [11] Rioux M. Sonographic detection of the normal and abnormal appendix. AJR Am J Roentgenol 1992; 158: 773-8.
- [12] Lim. HK, Lee WJ, Lee SJ, Namgung S, Lim JH. Focal appendicitis confined to the tip: diagnosis at US. Radiology 1996; 200: 799-801.
- [13] Alvarado A. A practical score for early diagnosis of acute appendicitis. Ann Emerg Med 1986; 15: 557-64.
- [14] Kalan M, Tabbot O, 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: 418-9.
- [15] Khan S. Evaluation of hyperbilirubinemia in acute inflammation of appendix: A prospective study of 45 cases. KUMJ 2006; 4(3) 15: 281-9.
- [16] Beg RB, Garlungton AW. Translocation of certain endogenous bacteria from the GI tract to mesenteric lymph node and other organ in Gonoblotic mouse model. Infect Immunol 1979; 23: 403-11.

- [17] Juric I, Primorac D, Zagar Z, Biocic M, Pavid S, Furlan D, et al. Frequency of portal and systemic bacteremia in acute appendicitis. *PediatrInt* 2001; 43(2): 152-6.
- [18] Koito Scathen WE, Desprez JD and Holden WD. A bacteriologic study in portal blood in man. *Arch Surg* 1995; 71: 404-9.
- [19] Wang P, Ayala A, Ba ZF, Zhou M, Perrin MM, Chaudry IH. Tumor necrosis factor -alpha produces hepatocellular dysfunction despite of normal cardiac output and hepatic microcirculation. *Am J PhysiolGastrointet Liver Physiol* 1993; 265(1): 126-32.
- [20] Wang P, Ba ZF, Chaudhary IH. Hepatic extraction of indo-cyanine green is depressed in early sepsis despite increase hepatic blood flow and cardiac output. *Arch Surg* 1991; 126(2):219-24.
- [21] Wang P, Chudhary IH. Mechanism of hepatocellular dysfunction during hyper dynamic sepsis. *Am J PhysiolRegulIntegr Comp Physiol* 1996; 270: 927-38 and 363-61.
- [22] Whiting JF, Green RM, Rosen AB, Gollan JL. TNF-alpha decreases hepatocyte bile salt uptake and mediated endotoxin-induced cholestasis. *Hepatology*. 1995; 22(4 Pt 1): 1273-8.
- [23] Bernard, M. Jaffe and David H. Berger. "The Appendix". In Brunickardi F, Andersen D, Billiar T, Dunn D, Hunter J, Matthews J, et al. *Schwartz's Principles of Surgery*. 9thed. New York: McGraw Hill; 2009. p.1073-1092.
- [24] Wolff H. Medical history aspects of appendicitis treatment. *ZentralblChir* 1998; 123 Suppl 4: 2-5.
- [25] Reith HB. Appendicitis and Perityphilitis: HistorischerUberblick. *ChirGastroenterol* 1993; 9: 184-96.