



## ROLE OF HYPERBILIRUBINEMIA: A NEW DIAGNOSTIC TOOL AS A PREDICTOR OF GANGRENOUS/PERFORATED APPENDICITIS

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### ABSTRACT

**Introduction-** Appendicitis is one of the commonest causes of abdominal pain which require emergency surgery. The aim of this study was to determine the role of hyperbilirubinemia as a new diagnostic tool for predictor of gangrenous/perforated appendicitis. **Methods-** Hospital based prospective study was conducted on 100 patients with perforated/gangrenous appendix. **Results-** Mean age of presentation was  $25.92 \pm 9.13$  years. Majority of the patients were male adults 58 as against 42 female adults. Total bilirubin(mg/dl) in uncomplicated cases was  $0.90 \pm 0.34$  mg/dl, in perforated appendicitis was  $2.15 \pm 0.83$  mg/dl and in perforated appendicitis was  $2.47 \pm 1.23$  mg/dl. SGOT level in uncomplicated cases was  $33.15 \pm 9.06$  IU/L, in perforated appendicitis was  $58.33 \pm 17.62$  IU/L and in perforated appendicitis was  $51.33 \pm 25.40$  IU/L. SGPT level in uncomplicated cases was  $29.75 \pm 7.12$  IU/L, in perforated appendicitis was  $50.17 \pm 13.06$  IU/L and in perforated appendicitis was  $63.67 \pm 24.80$  IU/L. ALP level in uncomplicated cases was  $64.20 \pm 18.74$  IU/L, in perforated appendicitis was  $143.58 \pm 43.59$  IU/L and in perforated appendicitis was  $131.33 \pm 42.72$  IU/L. Mean total leucocyte count was  $11764.00 \pm 4236.76/\text{mm}^2$ . 8 cases were diagnosis pre-operative perforated/ gangrenous appendicitis. In USG finding 76 cases were acute appendicitis and 8 cases were diagnosed perforated /gangrenous appendicitis. Histopathologically, 85 patients were confirmed as acute appendicitis, 3 patients as gangrenous appendicitis and 12 patients as perforated appendicitis. In acute appendicitis case out of 85 cases 26 cases bilirubin level was more than 1mg/dl, in gangrenous appendicitis out of 3 cases all cases bilirubin level was more than 1mg/dl and in perforated appendicitis out of 12 cases 11 cases bilirubin level was more than 1mg/dl. **Conclusion-** It is concluded from present study that elevated total serum bilirubin without elevation of liver enzymes is a good indicator of appendicular perforation. Total serum bilirubin appears to be a new promising laboratory marker for diagnosing appendicular perforation. The patients with clinical signs and symptoms of appendicitis and with hyperbilirubinemia should be identified as having a higher probability of appendicular perforation suggesting, total serum bilirubin levels have a predictive potential for the diagnosis of appendicular perforation.

**KEYWORDS :** USG, Appendicitis, Bilirubin

### INTRODUCTION

The appendix was first described in 1521 and inflammation of the appendix has been known to be a clinical problem since 1759. The term 'appendicitis', however, was not used until Reginald Fitz described this condition in 1886. Appendicitis is one of the commonest causes of abdominal pain which require emergency surgery. It is rare in infancy and amongst the elderly, but is common in children, teenagers and young adults. The classical signs and symptoms of acute appendicitis were first reported by Fitz in 1886.<sup>1</sup>

Obstruction of the lumen is believed to be the major cause of acute appendicitis. Faecoliths are the usual cause of obstruction. Less- common causes are hypertrophy of lymphoid tissue, tumors, intestinal parasites. The bacteriology of normal appendix is similar to that of normal colon. The principal organism seen in normal appendix, acute appendicitis and perforated appendicitis are *Escherichia Coli* and *Bacteroids fragilis*. However a wide variety of both facultative and anaerobic bacteria may be present.<sup>2</sup>

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. Whereas non-perforated acute appendicitis can be cured by an appendectomy without a long recovery period, perforated appendicitis or suppurative appendicitis can cause various complications that can result in life-threatening conditions. Hyperbilirubinemia is the result of imbalance between synthesis and excretion of bilirubin by the liver. Portal blood carries nutrients and other substances absorbed from gut including bacteria and its product (toxins). It is commonly cleared by detoxification and immunological action of the reticuloendothelial system of the liver that acts as

first-line defense in clearing toxic substances, bacteria and its products. But when bacterial load overwhelms the Kupffer cell function, it may cause dysfunction or damage to hepatocytes (liver parenchyma). It reflects a rise in serum bilirubin (SB) alone or in combination with liver enzymes depending upon the type, severity and site of the lesion.<sup>3-5</sup>

Due to limited study in Rajasthan on role of hyperbilirubinemia in gangrenous/ perforated appendicitis. So we conducted study on role of hyperbilirubinemia as a new diagnostic tool for predictor of gangrenous/perforated appendicitis.

### MATERIALS AND METHODS

The prospective study was conducted by the Department of surgery Sardar Patel Medical College & A.G. Hospitals, Bikaner from May 2018 to April 2021. Cases of acute appendicitis in general surgery department were recruited in the study.

1. STUDY DESIGN: Cross sectional Hospital based study
2. STUDY PLACE: Department of General Surgery, PBM Hospital, Bikaner
3. STUDY DURATION: one year
4. STUDY POPULATION: All patients with perforated/ gangrenous appendix admitted in ward of department of surgery
5. SAMPLING TECHNIQUE: Consecutive sampling
6. SAMPLE SIZE: all eligible patients admitted in surgery ward were included in study
7. INCLUSION CRITERIA : All patients with right iliac fossa pain clinically suggestive of appendicitis or appendicular perforation.
8. EXCLUSION CRITERIA : All patients documented to have a past history of Jaundice or liver disease, positive HbsAg, cholelithiasis, cancer of hepatobiliary system.

**METHOD:**

Clinical signs of acute appendicitis determined by the surgeons and the duration of the symptoms were documented on admission. An informed consent were obtained from all registered cases. In all patients with pain in right iliac fossa the provisional diagnosis of acute appendicitis will be made on the basis of history, clinical signs and relevant clinical data. Routine laboratory investigations were carried out like Haemoglobin, TLC count, Neutrophil count, Serum Bilirubin, Liver enzymes, which include SGPT (Alanine transaminase), SGOT (Aspartate transaminase), ALP (Alkaline phosphatase), Urine routine microscopy, Chest X-ray PA, X-Ray abdomen erect, Ultrasonography abdomen and pelvis, Urine pregnancy test in suspected pregnancy. Serum Bilirubin level measurement was done in all patients by fully automatic analyzer machine.

**Statistical Analysis:** Statistical analysis were performed using ANNOVA and P value < 0.05 will be checked for statistical significance of the obtained data.

**OBSERVATIONS**

22.00% patients in our study was found to between 13 to 20 age group. 56.00 % of patients are from 21-30 years age group. Mean age of presentation was 25.92±9.13 years. Majority of the patients were male adults 58 as against 42 female adults.

**TABLE 1. LIVER FUNCTION TESTS**

Parameters	Un-complicated (n=85)	Perforated appendicitis	Gangrenous appendicitis	p-value
Total bilirubin(mg/dl)	0.90±0.34	2.15±0.83	2.47±1.27	0.001
Direct bilirubin(mg/dl)	0.58±0.31	1.71±0.73	2.00±1.38	0.001
Indirect bilirubin(mg/dl)	0.32±0.17	0.51±0.18	0.44±0.12	0.001
SGOT (IU/L)	33.15±9.06	58.33±17.62	51.33±25.40	0.001
SGPT (IU/L)	29.75±7.12	50.17±13.06	63.67±24.80	0.001
ALP (IU/L)	64.20±18.74	143.58±43.59	131.33±42.72	0.001

Total bilirubin(mg/dl) in uncomplicated cases was 0.90±0.34 mg/dl, in perforated appendicitis was 2.15±0.83 mg/dl and in perforated appendicitis was 2.47±1.23 mg/dl. SGOT level in uncomplicated cases was 33.15±9.06 IU/L, in perforated appendicitis was 58.33±17.62 IU/L and in perforated appendicitis was 51.33±25.40 IU/L. SGPT level in uncomplicated cases was 29.75±7.12 IU/L, in perforated appendicitis was 50.17±13.06 IU/L and in perforated appendicitis was 63.67±24.80 IU/L. ALP level in uncomplicated cases was 64.20±18.74 IU/L, in perforated appendicitis was 143.58±43.59 IU/L and in perforated appendicitis was 131.33±42.72 IU/L.

**TABLE 2. DIFFERENTIAL LEUCOCYTE COUNT (DLC)**

Differential leucocyte count (DLC)		Mean value	
		Mean	SD
Total count (/mm <sup>3</sup> )		11764.00	4236.76
Differential count	Neutrophils	76.15	9.60
	Lymphocytes	16.50	6.73
	Monocytes	1.77	1.99
	Eosinophils	5.73	4.11

Mean total leucocyte count was 11764.00±4236.76/mm<sup>2</sup>

**TABLE 3. PRE-OPERATIVE DIAGNOSIS:**

Pre-operative diagnosis	Distribution (n=100)	
	Number	Percentage
Acute appendicitis	92	92%
Perforated/ gangrenous appendicitis	8	8%

8 cases were diagnosis pre-operative perforated/ gangrenous appendicitis.

**TABLE 4. ULTRASONOGRAM FINDING**

Ultra sonogram finding	Distribution (n=100)	
	Number	Percentage
Normal appendix	16	16.00%
Acute appendicitis	76	76.00%
Perforated /gangrenous appendicitis	8	8.00%

In USG finding 76 cases were acute appendicitis and 8 cases were diagnosed perforated /gangrenous appendicitis.

**TABLE 5. PER OPERATIVE DIAGNOSIS**

Per operative diagnosis	Distribution (n=100)	
	Number	Percentage
Acute appendicitis	85	85.00%
Perforated appendicitis	12	12.00%
gangrenous appendicitis	3	3.00%

Per operatively, of 100 patients 85 of appendix showed gross features of acute appendicitis, 12 showed perforated appendix and 3 showed gangrenous appendix.

**TABLE 6. HISTOPATHOLOGICAL DIAGNOSIS**

HPE diagnosis	Distribution	
	Number	Percentage
Acute appendicitis	85	85.00%
Gangrenous appendicitis	3	3.00%
Perforated appendicitis	12	12.00%

Histopathologically, 85 patients were confirmed as acute appendicitis, 3 patients as gangrenous appendicitis and 12 patients as perforated appendicitis.

**TABLE 7. ASSOCIATION BETWEEN HISTOPATHOLOGICAL DIAGNOSIS AND TOTAL BILIRUBIN**

HPE diagnosis	Total bilirubin		Total
	< 1mg/dl	> 1mg/dl	
Acute appendicitis	59	26	85
Gangrenous appendicitis	0	3	3
Perforated appendicitis	1	11	12

p-value=0.001

In acute appendicitis case out of 85 cases 26 cases bilirubin level was more than 1mg/dl, in gangrenous appendicitis out of 3 cases all cases bilirubin level was more than 1mg/dl and in perforated appendicitis out of 12 cases 11 cases bilirubin level was more than 1mg/dl.

**DISCUSSIONS**

Acute appendicitis remains the most common acute surgical condition of the abdomen, it is also the most commonly misdiagnosed condition. Appendectomy is the most commonly performed emergency procedure for acute appendicitis in the world. The life time risk of developing acute appendicitis is 8% for people in western countries.<sup>6</sup>

Majority of appendicitis is believed to be caused by appendicular lumen obstruction. These luminal obstruction is usually caused by faecolith. Less common causes are lymphoid tissue hypertrophy, intestinal parasites, and tumors. Normally appendix contains bacterial flora similar to that present in normal large intestine. Escherichia coli and Bacteroids fragilis are the most common organism observed in normal appendix, acute appendicitis, perforated appendicitis and gangrenous appendicitis. However a broad variety of both anaerobic and facultative bacteria may be present.<sup>7</sup>

Acute appendicitis is diagnosed essentially by clinical examination. It is often difficult to reach a proper diagnosis as classical signs and symptoms suggesting acute appendicitis may not be present in all. Different presenting symptoms and clinical signs always mimic the diagnosis of acute appendicitis, especially in women. The decision to operate

based purely on clinical suspicion alone can lead to removal of normal appendix in 15-50% of cases. Precise diagnosis can be assisted by additional tests and expectant management or both. The above delay in diagnosis may lead to appendiceal perforation or gangrene leading to increased morbidity. Safe alternative considered is to do appendectomy as soon as condition is suspected, this strategy leads to unnecessary appendectomy. There is still ongoing debate regarding optimal management of acute appendicitis with several studies proposing that conservative, non-operative management may be feasible.<sup>8</sup>

To make the diagnosis of AA, anticipate its extent and severity, and to decide appropriate management; a cheap, simple and readily available test having acceptable sensitivity, specificity for AA and its complications, is needed in conjunction with clinical findings.<sup>9</sup> The lack of available resources such as a CT scan or a reliable ultrasonologist to be present in the emergency setup around the clock for every suspected case of acute appendicitis demands the aide of other cheaper and noninvasive investigations to steer the diagnostic machinery. This also holds for other low resource regions where clinical tools such as the Alvarado score may dictate the decision to operate.<sup>10</sup> Where CT may be the best modality in assessing appendicitis, patients deemed high risk may demerit from the delay CT scan may cause in their surgical management. Hence however helpful, it does not alter the clinical management of such patients. In former studies, however, the diagnostic and discriminatory value of some blood markers, such as C-reactive protein (CRP) and white blood cell (WBC) count, had been explored<sup>11-14</sup> and currently are applicable in scoring systems. Still, newer biomarkers such as procalcitonin, platelet indices and red cell distribution indices<sup>15</sup> are being looked into for the diagnosis of acute appendicitis. A combination of platelet distribution width with elevated white cell count has been proven fruitful in diagnosing AA. However, mean platelet volume and red cell distribution width have not been found successful.<sup>16</sup>

Studies emerged in recent years; show that serum bilirubin levels can help indicate patients with acute appendicitis. According to some studies, hyperbilirubinemia can also be associated with perforation and the severity of appendicitis. The invasion of the Gram-negative bacteria to the appendix explains the elevated serum bilirubin levels, which leads to the direct invasion or translocation of the toxins in the portal system and the liver; these, in turn, interfere with bilirubin excretion through bile ducts by endotoxin action. Therefore, these markers along with clinical presentation can be used as a prediction of its perforated or gangrenous forms and act as a marker of severity to improve preoperative diagnosis of AA. Overall sensitivity, specificity, of Hyperbilirubinemia in diagnosing complicated appendicitis in the index study is comparable with that of literature. Hence patients with hyperbilirubinemia combined with symptoms and signs consistent with severe AA should be considered for an early appendectomy.<sup>17</sup>

## CONCLUSION

It is concluded from present study that elevated total serum bilirubin without elevation of liver enzymes is a good indicator of appendicular perforation. Total serum bilirubin appears to be a new promising laboratory marker for diagnosing appendicular perforation. The patients with clinical signs and symptoms of appendicitis and with hyperbilirubinemia should be identified as having a higher probability of appendicular perforation suggesting, total serum bilirubin levels have a predictive potential for the diagnosis of appendicular perforation.

## REFERENCES

1. Hyperbilirubinemia a predictive factor for complicated acute appendicitis: a study in a tertiary care hospital, Jamaluddin M, Hussain SM, Ahmad H, J Pak

- Med Assoc. 2013 Nov;63(11):1374-8.
2. Hyperbilirubinemia as a predictor of gangrenous/perforated appendicitis: a prospective study, Paras Chaudhary, Ajay Kumar, Neeraj Saxena, Upendra C. Biswal Postgraduate Institute of Medical Education and Research, Dr Ram Manohar Lohia Hospital (Dr RMLH and PGIMER), New Delhi, India, Ann Gastroenterol 2013; 26 (4): 1-7.
3. Addiss DG, Shaffer N, Fowler BS, et al: The epidemiology of appendicitis and appendectomy in the United States. Am J Epidemiol 132:910, 1990.
4. 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.
5. Khan S. Evaluation of hyperbilirubinemia in acute inflammation of appendix: A prospective study of 45 cases. KUMJ 2006; 4(3) 15: 281-9
6. Muzna I, Itikhar. Hyperbilirubinemia as an indicator of complicated appendicitis. International Journal of Surgery and Medicine (2019) 5(2):58-65
7. Flum DR, Morris A, Koepsell T, Dellinger EP Has misdiagnosis of appendicitis decreased over time? a populationbased analysis. Jama. 2001;286 (14):1748-53.
8. Bickell NA, Aufses AH, Rojas M, Bodian C. How time affects the risk of rupture in appendicitis. J Am Coll Surg. 2006;202(3):401-6.
9. Fike FB, Mortellaro VE, Juang D, Sharp SW, Ostlie DJ, St Peter SD. The impact of postoperative abscess formation in perforated appendicitis. J Surg Res. 2011; 170(1):24-6.
10. Farooqui W, Pommergaard HC, Burcharth J, Eriksen JR. The diagnostic value of a panel of serological markers in acute appendicitis. Scand J Surg. 2015;104(2):72-8.
11. 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.
12. Ohle, Robert et al. "The Alvarado Score for Predicting Acute Appendicitis: A Systematic Review." BMC Medicine 9 (2011): 139. PMC. Web. 18 Oct. 2018.
13. Andersson RE. Meta-analysis of the clinical and laboratory diagnosis of appendicitis. Br J Surg. 2004;91(1):28-37.
14. Birchley D. Patients with clinical acute appendicitis should have preoperative full blood count and C-reactive protein assays. Ann R Coll Surg Engl. 2006;88(1):27-32.
15. Körner H, Söreide JA, Söndena K. Diagnostic accuracy of inflammatory markers in patients operated on for suspected acute appendicitis: a receiver operating characteristic curve analysis. Eur J Surg. 1999;165(7):679-85.
16. Vaughan-Shaw PG, Rees JR, Bell E, Hamdan M, Platt T. Normal inflammatory markers in appendicitis: evidence from two independent cohort studies. JRSM Short Rep. 2011;2(5):43.
17. N Boshnak, M Boshnaq, H Elgohary, Evaluation of platelet indices and red cell distribution width as new biomarkers for the diagnosis of acute appendicitis. J Invest Surg. 2018 Apr;31 (2):121-129