

"Hyperbilirubinemia as A Marker for Predicting Appendicular Perforation in Cases of Acute Appendicitis "

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Abstract:

Introduction: Acute appendicitis is the most common cause of 'acute abdomen' in young adults.

Aims and Objectives: To evaluate whether hyperbilirubinemia have a predictive potential for the diagnosis of Appendicular perforation in cases of acute appendicitis.

Materials and methods: The present study is a prospective non-randomised study carried out in the Department of Surgery, Gauhati Medical College and Hospital with 110 patients, admitted with the clinical and radiological diagnosis of Acute appendicitis and Appendicular perforation, from 1st June, 2019 to 30th May, 2020. Patients with pre-existing jaundice, liver cirrhosis and chronic alcohol consumption were excluded.

Results and Observations: Bilirubin values were normal in 49.09% patients while 50.91% had hyperbilirubinemia. Based on CECT whole abdomen, intraoperative and histopathological findings, 74 patients (67.3%) were confirmed as acute appendicitis and 36 (32.7%) as appendicular perforation. The "Mean total bilirubin level" in patients of acute appendicitis was 0.99 +/- 0.39 mg/dl while in patients of appendicular perforation; it was 1.99 +/- 0.99 mg/dl. The Direct and indirect bilirubin levels in patients of acute appendicitis were 0.54 +/- 0.38 mg/dl and 0.45 +/- 0.2 mg/dl respectively. The Direct and indirect bilirubin levels in patients of appendicular perforation were 1.36 +/- 0.88 mg/dl and 0.63 +/- 0.26 mg/dl respectively. Only 27 (36.5%) patients of acute appendicitis had hyperbilirubinemia, while 47 (63.5%) had normal bilirubin levels. Whereas, 29 (80.55%) patients of appendicular perforation had hyperbilirubinemia while only 7 of them (19.45%) had normal bilirubin levels. Thus, Sensitivity and Specificity rates of "serum bilirubin" as a marker in predicting appendicular perforation were 80.5% and 63.5% respectively. Similarly, Positive and Negative predictive values were 51.7% and 87% respectively with Odds ratio of 7.2.

Conclusion: Patients of acute appendicitis with hyperbilirubinemia, have a higher possibility of appendicular perforation.

Key Words: appendicitis, hyperbilirubinemia, appendicular perforation, sensitivity, specificity, histopathological, intraoperative, acute, complications.

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I. Introduction:

Acute appendicitis is the most common cause of an 'acute abdomen' in young adults. It remains one of the most common diseases faced by the surgeon in his/ her practice. Appendicitis is sufficiently common, that Appendectomy is the most frequently performed urgent abdominal operation world wide. In the United States it is responsible for as many as 30,000 hospitalizations annually. 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. Despite its high prevalence in the Western countries, the diagnosis of acute appendicitis can be challenging and requires a high index of suspicion on the part of the examining surgeon to facilitate prompt treatment of this condition, thereby avoiding the substantial morbidity (and even mortality) associated with perforation. Appendicitis is much less common in the underdeveloped countries, suggesting that elements of the Western diet, specifically a low fibre, high-fat intake, may play a role in the disease process. Aside from its tendency to cause surgical pathology, the Appendix, long thought to be a vestigial organ, may also have important roles in both immune function and maintaining the gut microbiota. The putative role of the appendix in the pathogenesis of Ulcerative Colitis (appendectomy seems to be protective) for example, may be explained by its interaction with the intestinal flora and gut immune function. The diagnosis of any form of appendicular pathology is primarily clinical. The currently available blood tests and radiological imaging can

aid in diagnosis, but are not very specific and not pertinent to the pathology involved. Despite the increased use of ultrasonography, computed tomography (CT), and laparoscopy, the rate of misdiagnosis of appendicitis has remained constant (15.3%), as has the rate of appendiceal rupture. The percentage of misdiagnosed cases of appendicitis is significantly higher among women than among men (22.2 vs. 9.3%). The negative appendectomy rate for women of reproductive age is 23.2%, with the highest rates in women aged 40 to 49 years. The highest negative appendectomy rate is reported for women >80 years of age. Recent studies have shown that elevated bilirubin levels are associated with acute appendicitis & appendicular perforation. These studies emphasized that hyperbilirubinemia can be used as a marker for both acute appendicitis and appendicular perforation. Most of the studies conducted were retrospective on a large scale, few were prospective and were conducted on a small scale.

Taking the challenge to conduct a prospective study on this subject on a large scale basis & eliminating the bias, and to see whether the elevated bilirubin levels have a role in diagnosis of acute appendicitis and its predictive potential for appendicular perforation, this study was carried out. The main aim was of differentiating between acute appendicitis and appendicular perforation, and predict the pre-operative diagnosis to precision, thereby creating scope for proper planning and reducing the morbidity involved. With this aim, the following study was carried out in the Department of Surgery, Gauhati Medical College.

AIM:

1. To assess the relationship between Hyperbilirubinemia and Acute appendicitis and to evaluate its credibility as a diagnostic marker for Acute appendicitis.
2. To evaluate whether elevated bilirubin levels have a predictive potential for the diagnosis of Appendicular perforation.

II. Material & Methods:

The study was conducted in the Department of Surgery, Gauhati Medical College during the period June 2019 to May 2020.

STUDY TYPE: Prospective non randomised study

STUDY PERIOD: 1st June 2019 to 30th May 2020

SOURCE OF DATA: Patients admitted with clinical and radiological diagnosis of acute appendicitis or appendicular perforation, under the Department of Surgery, Gauhati Medical College and Hospital during the study period.

SAMPLE SIZE: A total of 110 patients were included in the study.

7.1 SELECTION CRITERIA:

Inclusion criteria :

All patients admitted with the clinical and radiological diagnosis of Acute appendicitis and Appendicular perforation, under the Department of General Surgery , Gauhati Medical College and Hospital are included in this study.

Exclusion criteria :

1. All patients with pre-existing medical or surgical cases of jaundice.
2. Known cases of Liver cirrhosis or Chronic Alcohol consumption (i.e > 40gm/day for men, and >20 gm/day for women for 10 years)

III. Results And Observations:

1. As per the study, the age group 11 – 20 years is most commonly affected (36.3 %) followed by age group 21-30 years (30.9 %). The youngest patients of this study was of 7 year old boy while the oldest patient was a 68yr old lady.
2. Out of the 110 patients enrolled for the study, 61 patients were male (55.45%), while the remaining 49 patients were females (44.55%).
3. The mean Total Bilirubin of all 110 patients was 1.318±0.801 mg/dl (range 0.517 – 119 mg/dl), while the Direct Bilirubin was 0.81±0.707 mg/dl (range 0.103 – 1.51mg/dl). The mean SGOT and SGPT values were 27.88 ± 12.06 U/L (range: 15.82 – 39.94 U/L) and 27.35 ± 10.88 U/L (range : 16.47 – 38.23 U/L). The mean ALP values were 79.7 ± 24.2 U/L (range 55.5 – 103.9 U/L).

PARAMETERS	MEAN	Standard Deviation
Total Bilirubin (mg/dl)	1.318	0.801
Direct Bilirubin (mg/dl)	0.81	0.707
Indirect Bilirubin (mg/dl)	0.508	0.243
SGOT (U/L)	27.88	12.06
SGPT (U/L)	27.35	10.88
ALP (U/L)	79.7	24.2

4. 54 patients (49.09%) of all 110 patients were found to have normal bilirubin levels (< 1.0 mg/dl), while 56 patients (50.91%) had raised bilirubin levels (>1 mg/dl).

5. 36 patients were diagnosed as Appendicular perforation, 29 patients (80.55%) had elevated bilirubin levels (>1 mg/dl), while 7 patients (19.45%) had normal bilirubin levels (< 1 mg/dl).

Total Bilirubin (mg/dl)	Distribution in patients with Appendicular perforation (n1 = 36)	
	Number	Percentage
> 1.0	29	80.55 %
≤ 1.0	7	19.45%
Total	36	100%

6. The mean Bilirubin levels in patients diagnosed with Acute appendicitis was 0.99 + 0.39 mg/dl (range: 0.6 – 1.38 mg/dl) while in patients diagnosed with Appendicular perforation was 1.99 + 0.99 mg/dl (range: 1 – 2.98 mg/dl). The Direct Bilirubin and Indirect Bilirubin of patients diagnosed with Acute appendicitis were 0.54 + 0.38mg/dl and 0.45 + 0.2 mg/dl respectively. The Direct Bilirubin and Indirect Bilirubin in patients diagnosed with Appendicular perforation were 1.36 + 0.88 mg/dl and 0.63 + 0.26mg/dl respectively.

Bilirubin levels (mg/dl)	Diagnosis			
	Acute Appendicitis		Appendicular perforation	
	MEAN	SD	MEAN	SD
Total Bilirubin	0.99	0.39	1.99	0.99
Direct Bilirubin	0.54	0.38	1.36	0.88
Indirect Bilirubin	0.45	0.2	0.63	0.26

7. 27 patients (36.5%) of the total patients diagnosed with Acute appendicitis (n2=74) were found to have elevated bilirubin levels (>1.0 mg/dl), while 47 (63.5%) patients had normal bilirubin levels (<1.0 mg/dl). Similarly, 29 patients (80.55%) of the total patients diagnosed with Appendicular perforation (n1=36) were found to have elevated bilirubin levels (>1.0 mg/dl) while 7 patients (19.45%) had normal bilirubin levels (< 1.0 mg/dl).

Serum Bilirubin (mg/dl)	Final diagnosis (n=110)			
	Appendicular perforation (n1=36)		Acute appendicitis (n2=74)	
	Number	Percentage	Number	Percentage
> 1.0	29	80.55 %	27	36.5 %
≤ 1.0	7	19.45 %	47	63.5 %
Total	36	100	74	100

8. Accuracy of Serum Bilirubin as a marker in predicting Appendicular perforation:

PARAMETER	ACCURACY
Sensitivity	80.5 %
Specificity	63.5 %
Positive Predictive value	51.7 %
Negative Predictive value	87 %
Odd's ratio	7.2
P value	0.001

IV. Summary:

Acute appendicitis is the most common cause of “acute abdomen” 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 has been postulated recently. It is hypothesized that an association exists between hyperbilirubinemia and acute appendicitis and its complications. The present study was undertaken to assess the 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. The present study was conducted in the Department of Surgery, Gauhati Medical College, Guwahati during the period of June 2019 to May 2020. A total of 110 patients with clinical diagnosis of Acute appendicitis or Appendicular perforation were studied. The serum bilirubin and LFTs were carried out in all the patients. In this study, males (55.45%) outnumbered females (44.55%) and overall the mean age was 27.5 + 13.02 years. The total leukocyte count was elevated in 32.7% patients, while 67.3% patients had the counts in the normal range. Mean total serum bilirubin was noted as 1.318+0.801 mg/dl while Direct bilirubin was 0.81+0.707 mg/dl. The mean SGOT and SGPT were 27.88 + 12.06 U/L and 27.35 + 10.88 U/L. The mean ALP values were 79.7 + 24.2 U/L. Normal bilirubin values were seen in 49.09% patients while, 50.91% had raised bilirubin levels (Hyperbilirubinemia). Of the 110 patients, 95 (86.4%) were diagnosed as acute appendicitis clinically while 15 (13.6%) were diagnosed with Appendicular perforation. On final diagnosis based on the CECT findings, intraoperative findings and histopathological diagnosis, 74 patients (67.3%) were confirmed as Acute appendicitis, while 36 patients (32.7%) were diagnosed as Appendicular perforation. The Mean Bilirubin levels in patients diagnosed with acute appendicitis was 0.99 + 0.39 mg/dl while in patients diagnosed with Appendicular perforation was 1.99 + 0.99 mg/dl. The Direct bilirubin and Indirect bilirubin in patients diagnosed with acute appendicitis was 0.54 + 0.38 mg/dl and 0.45 + 0.2 mg/dl respectively. The Direct bilirubin and Indirect bilirubin in patients diagnosed with Appendicular perforation were 1.36 + 0.88 mg/dl and 0.63 + 0.26 mg/dl respectively. 27 patients (36.5%) of the total patients diagnosed with acute appendicitis (n=74) were found to have elevated bilirubin levels while 47 patients (63.5%) had normal bilirubin levels. Similarly, 29 patients (80.55%) of the total patients diagnosed with Appendicular perforation (n1=36) were found to have elevated bilirubin levels while 7 patients (19.45%) had normal bilirubin levels. The Sensitivity and Specificity of serum bilirubin as a marker in predicting Appendicular perforation was 80.5% and 63.5% respectively. Similarly the Positive predictive value and Negative predictive value for the same was 51.7% and 87% respectively with odds ratio 7.2.

V. 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. About 8% of people in Western countries have appendicitis at some time in their lifetime. 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 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. 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. 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, tumours, intestinal parasites. 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 Bacteroides fragilis. However a wide variety of both facultative and anaerobic bacteria may be present.

The present study was undertaken to assess the 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. The present study was conducted in the Department of Surgery, Gauhati Medical College, Guwahati during the period of June 2019 to May 2020. A total of 110 patients with clinical diagnosis of Acute appendicitis or Appendicular perforation were studied. The serum bilirubin and LFTs were carried out in all the patients. In this study, males (55.45%) outnumbered females (44.55%) and overall the mean age was 27.5 + 13.02 years. The total leukocyte count was elevated in 32.7% patients, while 67.3% patients had the counts in the normal range. Mean total serum bilirubin was noted as 1.318+0.801 mg/dl while Direct bilirubin was 0.81+0.707 mg/dl. The mean SGOT and SGPT were 27.88 + 12.06 U/L and 27.35 + 10.88 U/L. The mean ALP values were 79.7 + 24.2 U/L. Normal bilirubin values were seen in 49.09% patients while, 50.91% had raised bilirubin levels (Hyperbilirubinemia). Of the 110 patients, 95 (86.4%) were diagnosed as acute appendicitis clinically while 15 (13.6%) were diagnosed with Appendicular perforation. On final diagnosis based on the CECT findings, intraoperative findings and histopathological diagnosis, 74 patients (67.3%) were confirmed as Acute appendicitis, while 36 patients (32.7%) were diagnosed as Appendicular perforation. The Mean Bilirubin levels in patients diagnosed with acute appendicitis was 0.99 + 0.39 mg/dl while in patients diagnosed with Appendicular perforation was 1.99 + 0.99 mg/dl. The Direct bilirubin and Indirect bilirubin in patients diagnosed with acute appendicitis was 0.54 + 0.38 mg/dl and 0.45 + 0.2 mg/dl respectively. The Direct bilirubin and Indirect bilirubin in patients diagnosed with Appendicular perforation were 1.36 + 0.88 mg/dl and 0.63 + 0.26 mg/dl respectively. 27 patients (36.5%) of the total patients diagnosed with acute appendicitis (n=74) were found to have elevated bilirubin levels while 47 patients (63.5%) had normal bilirubin levels. Similarly, 29 patients (80.55%) of the total patients diagnosed with Appendicular perforation (n=36) were found to have elevated bilirubin levels while 7 patients (19.45%) had normal bilirubin levels. The Sensitivity and Specificity of serum bilirubin as a marker in predicting Appendicular perforation was 80.5% and 63.5% respectively. Similarly the Positive predictive value and Negative predicative value for the same was 51.7% and 87% respectively with odds ratio 7.2.

VI. Conclusion:

The present study suggests Serum bilirubin levels to be a promising new laboratory marker for diagnosing acute appendicitis and its complications like appendicular perforation. However diagnosis of appendicitis remains essentially still - clinical. Its level has come out to be a credible aid in diagnosis of acute appendicitis and its complications, and would be a helpful investigation in coming to a definitive diagnosis. In the present study we conclude that 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.

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