Evaluation of Hyperbilirubinemia in Acute Appendicitis

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ABSTRACT

Introduction: Evaluation of hyperbilirubinemia in acute appendicitis aids in diagnosing complications of acute appendicitis such as gangrenous appendix and perforation. Study aimed to evaluate increased bilirubin levels associated in acutely inflamed appendix and to compare with the diagnostic value of total leucocyte count associated in acute inflammation of appendix

Material and methods: A prospective one year study was conduced to evaluate the association of hyperbilirubinemia in acute inflammation of appendix and to compare it with diagnostic value of total leucocyte count associated in acute inflammation of appendix.

Results: Hyperbilirubinemia is seen in 65.8% of patients with acute appendicitis and its complications**.** Elevated serum bilirubin is better laboratory test (100% specificity, 65.78% sensitivity and) than total leucocyte count with 69.7% specificity and 88.3% sensitivity.

Conclusion: Hyperbilirubinemia is seen more in complications of acute appendicitis. Elevated serum bilirubin is better diagnostic test than total leucocyte count. for evaluation acute appendicitis and its complications

Keywords: Acute Appendicitis, Hyperbilirubinemia, Total Leucocyte Count, Gangrenous Appendix, Perforation.

INTRODUCTION

Acute appendicitis is a common abdominal emergency encountered in general surgery. Acute appendicitis, when presenting in a teenager and with a classical history, presents the surgeon with little by way of a diagnostic challenge. Nevertheless, unnecessary appendicectomy is not altogether without problems. There will be a small incidence of wound sepsis and the subsequent adhesive intestinal obstruction and incisional hernia. Diagnostic difficulty in patient with atypical clinical findings has resulted in unnecessary appendicectomies, which have been variably reported in the literature with an average of about 20%. In fact the rate of negative appendicectomies increases to 35 to 45% in young women of child bearing age in whom differential diagnosis from pelvic inflammatory disease may be extremely difficult. The goal of appendix removal is removal of inflamed one before impending perforation occurs with a minimal number of negative explorations. To decrease the frequency of unwanted appendicectomies, the importance of laboratory value that comprises both white blood cell (WBC) counts and C-reactive protein (CRP) values has been insisted, and the utilisation of abdominal ultra sonogram as a diagnostic equipment for appendicitis has been widely evaluated. Various scores combining clinical features and lab investigations have also been developed. These are the Alvarado score and the Modified Alvarado score. Recently, elevation in serum bilirubin, was reported, but the importance of the raised total bilirubin has not been stressed. It is well established that when microbes invade the body, leucocytes defend it. This leads to increase in the leucocyte count. Bacterial invasion in the appendix leads to transmigration of bacteria and the release of TNF-alpha, IL6, and cytokines. These reach the liver via superior mesenteric vein and may produce inflammation, abscess or dysfunction of liver either directly or indirectly by altering the hepatic blood flow. So it is important to evaluate the total serum bilirubin in the diagnosis of clinically suspected cases of appendicitis.[1-3]

Liver receives blood from abdominal organs mainly through portal venous system. Portal blood consists of nutrients and other materials absorbed from gastrointestinal tract including bacteria and its toxins. In minimal percentage, even in good healthy people, there will be bacteria in portal blood. It is usually rectified by detoxification and immune action of reticular system of liver which is the first line defence in detoxification of substances, bacteria and its products. But when bacterial load diminishes the Kupffer cell function, it may cause derangements or damage to the liver cells.

An inflammatory response causes the appendix to become more oedematous and ischaemic. Subsequently, transmigration of bacteria through the ischaemic wall happens. In early sepsis with hyperdynamic circulation bacteria, its toxin or cytokines are involved whereas in late sepsis ischemia due to decreased hepatic blood flow to the liver is the mechanism of hepatic injury.

In both above situations the hepatic injury leads to dysfunction of hepatocyte and tubule leading to mixed type of hyperbilirubinemia (hepatocellular and intra- hepatic cholestasis). It shows, increase in serum bilirubin only or in combination with hepatic parenchymal enzymes depends upon the type site and severity of injury.

Study aimed to evaluate increased bilirubin levels associated with acutely inflamed appendix and to compare the diagnostic value of total leucocyte count associated with acute inflammation of appendix.

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MATERIAL AND METHODS

The study was conducted in Thanjavur medical college and hospital (TMCH) from august 2011 to October 2013. The study included all patients more than 12 years of age who presented to emergency unit of TMCH with features of acute appendicitis and scheduled for emergency appendicectomy. Patients with history of liver disease are excluded from the study. All patients are investigated with total count, differential count, liver function test, and ultrasonogram of abdomen. Intra operative findings and post operative histopathological findings are recorded with history of liver disease patients.

Observations

Total of 100 patients were included in the study out of which 55% of patients were male, with male to female ratio of 1.22:1. Age of the patients varied from 13 to 64 and maximum number of patients were in the group of 21 to 30 years of age (39 out of 100 patients).

Peroperative appearance of appendix was noted.32% of cases had minimally inflamed appendix, 39% of patients appendix were grossly inflamed, 18% had perforated appendix with local peritonitis, 6% had gangrenous appendix and in 5% of patients appendix was sloughed off.

Histopathological diagnosis was taken into account as final diagnosis in Which 51% had acute appendicitis, 19% cases were histologically unremarkable, 19% had inflamed appendix with perforation, 6% had gangrenous appendix, and 5% of cases were reported as lymphoid hyperplasia.

Mean total bilirubin for each peroperative findings were compared. Maximum value 2.133 mg/dl in gangrenous appendix, followed by perforated appendix 1.961 mg/dl, category of sloughed off had mean of 1.880mg/dl, grossly inflamed appendix had mean of 1.418mg/dl where appendix was minimally inflamed mean bilirubin was 0.607mg/dl.

Mean bilirubinin different categories as per histopathological reports

showed maximum value in gangrenous appendicitis 2.133mg/d1, followed by appendicitis with perforation which was 2.026 mg/d1, mean bilirubin was

1.312 mg/d1 in category of acute appendicitis and mean bilirubin was 0.579 mg/d1 and 0.604 mg/d1 respectively in histologically unremarkable and lymphoid hyperplasia. In the raised categories both direct and indirect bilirubin were raised.

Mean TLC in each category of histopathological diagnosis showed maximum value in gangrenous appendicities 18,100 cells/ul, acute appendicitis 12,900 cells/ul, histologically unremarkable 9,461 cells/ul, perforated appendix 15,100 cells/ul, lymphoid hyperplasia 11,800 cells/ul.

Acute appendicitis and its complications were taken as final diagnosis. As showed by 76% as histologically positive cases and 24% of cases were not acute appendicitis. Liver enzymes, SGOT, SGPT and ALP showed marginal elevation in histologically positive cases.

All patients presented to the hospital within 72 hours of onset of symptoms and 60% within 24 hours of onset.

Total bilirubin	Histopathology		Total
	Acute appendicitis	Not Acute appendicitis	
Raised >1.2 mg/dl	50	0	50
Normal	26	24	50
Total	76	24	100

Table-1: Correlation of total bilirubin level with histopathologically positive and negative cases

TLC	Histopathology		Total
	Acute appendicitis	Not Acute appendicitis	
>11000 cells/µl	53	7	60
Normal	23	17	40
Total	76	24	100

Table-2: Correlation of tlc with histopathologically positive and negative cases

Study	Specificity	Sensitivity
Present study	100%	65.78%
Salamat Khan[3]	100%	80%
Michael Sand et a1[4]	86%	70%
K Atahan et al[6]	87.2%	77.77%
Emmanuel et a1[7]	88%	72%

Table-3: Comparison of sensitivity and specificity of hyperbilirubinemia of various studies

Study	Specificity	Sensitivity
Present study	88.3%	69.7%
Salamat Khan[3]	50%	77%
Michael Sand et a1[4]	55%	81%
K Atahan et al[6]	47.77%	82.22%

Table-4: Comparison of specificity and sensitivity of TLC with various studies:

Sensitivity 50/76 = 65.78%, Specificity = 24/24 = 100%, Positive predictive value of 100%, Negative predictive value = 24/50 =48% and Diagnostic accuracy of 74% (table-1).

Sensitivity 53/76 =69.7%, Specificity =17/74 =70%, Positive predictive value of 88.3%, Negative predictive value of 57.5% and Diagnostic accuracy of 70% (table-2).

DISCUSSION

Demography

In the study population 55% were male, male to female ratio about 1.22:1, Fashina IB et al[1] in his study on Acute appendicitis showed male to female ratio of 1.2:1, almost similar to the present study. The age group of study population varied between 13-64 years, peak incidence of acute appendicitis or its complications is seen in age group 13-30 years, mean age group of presentation of symptoms in the study population is 27.14 years. Addiss DG et a1[2] in his study on epidemiology of appendix showed peak incidence of acute appendicitis is between 10-30 years, hence this study has got similar results.

Duration of symptoms

60% of the patients reported to the hospital within 24 hours

of onset of symptoms. All patients reported within 72 hours of onset of symptoms. Salamat Khan[3] in his study on the diagnostic value of hyperbilirubinemia and total leucocyte count in the evaluation of acute appendicitis, showed only 17.81% of patients reported <24 hours from the onset of symptoms, probably the improved socio economic, transportation and accessibility to tertiary care centre in this part of the world explain this difference in the reporting time to the tertiary care centre.

Bilirubin level

Hyperbilirubinemia was seen in 65.8% of patients with acute appendicitis or its complication, the raised bilirubin ranges from 1.3 to 3.2 mg/d1. Compared to study by Michael sand et a1[4] the raised bilirubin level ranges from 1-1.4mg/d1, Khan[5] showed hyperbilirubinemia was seen in 86.6% of patients and ranged from 1.2-8.4mg/d1. There is definite elevation of bilirubin, and the elevated levels are comparable with other studies.

Mixed type (both direct and indirect) fractions of bilirubin were raised. All raised cases showed an indirect fraction above 15%. Khan[5] in his study has got similar results, without concomitant raise in liver enzymes.

Mean bilirubin level was 2.026mg/d1 (SD-0.71mg/d1) in acute appendicitis with perforation which was significantly higher than those with non perforated appendix ($p<0.001$) compared to Michael Sand et al[4] the mean bilirubin in perforated appendix was 1.5mg/d1 (SD-0.9mg/d1)which was significantly higher than those of non perforated group ($p<0.05$).

Total leucocyte count

Total leucocyte count elevation was seen in 69.7% of patients with acute appendicitis or its complications, the raised level ranges from 11,100- 26,000 cells/microlitre. Salamat Khan[3] showed elevation in 76.22% of patients.

Liver enzymes

Liver enzymes were not significantly raised in the histologically positive cases. SGPT, SOOT and ALP showed marginal elevation (< l time) in 18.4%, 38.2% and 17.1% respectively. Salamat Khan[3] in his study showed marginal elevation in 19%, 25% and 34% of patients respectively with acute appendicitis or its complication.

Diagnostic value of total bilirubin

Elevated serum bilirubin when in taken into consideration among the cases that had elevated bilirubin 65.8% had positive histology for acute appendicitis or its complications, while cases with normal total bilirubin 34.2% had positive histology. Giving the specificity, sensitivity,positive predictive value, negative predictive value and overall diagnostic accuracy of 100%, 65.78%, 100%, 48% and 74% respectively. If total bilirubin is taken into consideration to reach the diagnosis in clinically suspected cases, there will not be any false positive results, but there could be 34.2% false negative results. Which mean that none of the normal appendix will be removed, but in 34.2% cases the diagnosis will be missed. Salamat Khan[3] in his study found specificity, sensitivity, positive predictive value, negative predictive value and overall diagnostic accuracy of 100%, 80%, 100%, 14% and 81.14% respectively, here false positive result was nil and false negative was 18.5%. K Atahan et a1[6] in his study showed specificity, sensitivity, positive predictivevalue, negative predictive value of 87.21%, 77.77%, 45.16% and 96.66% respectively.

Hence in the present study the specificity of raised total bilirubin in acute appendicitis or its complications is comparable to other similar studies, but the sensitivity is decreased in comparison to other studies (table-3).

Diagnostic value of TLC

Among the cases that had elevated total leucocyte count 69.7%, had positive histology for acute appendicitis, while the remaining 29.2% had normal histology. Among 40% cases that had normal histology 57.6% had positive histology for acute appendicitis or its complications. 42.5% normal histology. Giving a specificity, sensitivity, positive predictive value, negative predictive value and overall diagnostic accuracy of 69.2%, 69.7%, 88.3%, 57.5% and 70% respectively. If total leucocyte count is taken into consideration to reach the diagnosis in clinically suspected cases of acute appendicitis, there is possibility that 11.7% cases is false positive (elevation of total leucocyte count without inflammation), and 30.3% results could be false negative (positive histology without elevation in total leucocyte count). Which means that there are chances that 11.7% normal appendix will be removed, while 30.3% cases the diagnosis will be missed.

Salmat Khan[3] in his study found out specificity, sensitivity, positive predictive value, negative predictive value and overall diagnostic accuracy of 50%, 77%, 97.8%, 7.4% and 76.22% respectively.

K Atahan et al[6] in his study showed specificity, sensitivity, positive predictive value, negative predictive value of 47.77%, 82.22%, 22.89% and 94.48% respectively.

Hence in the present study the specificity elevated TLC for acute appendicitis or its complications is more as compared to other studies, but the sensitivity is decreased in comparison to other studies (table- 4).

Limitations of this study

This study has limitation that there was no reliable way of detecting patients with Gilbert's syndrome, although a small number of patients with this condition would likely to have been distributed evenly between the histological groups.

Moreover the patients who underwent appendicectomy were only included in this study, which could result in elevated specificities for various inflammatory markers.

CONCLUSIONS

Hyperbilirubinemia is seen in 65.8% of patients with Acute appendicitis and its complications. Raised total bilirubin level ranges from 1.3 to 3.2 mg/dl. The raise in serum bilirubin was mixed type (both direct and indirect) The liver enzymes were not raised significantly in patients with Acute appendicitis and its complications. Level of Hyperbilirubinemia is seen more in complications of acute appendicitis (perforation or gangrenous appendicitis). Elevated serum bilirubin is better

laboratory test (100% specificity, 65.78% sensitivity and 74% overall diagnostic accuracy) than total leucocyte count with 69.7% specificity. 88.3% sensitivity and 70% overall diagnostic accuracy.

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