



## Efficacy of Combined Serum Bilirubin and Serum C-Reactive Protein Preoperatively in Predicting the Diagnosis of Acute Appendicitis

Authors

**Prof Sreeramulu P N<sup>1</sup>, Dr Md Kashif Imran\*<sup>2</sup>, Dr Mohan Kumar K<sup>3</sup>,  
Dr Sandeep Vogu<sup>4</sup>, Dr Silar<sup>5</sup>**

<sup>1</sup>Professor and Head Dept. of General Surgery SDUMC Kolar

<sup>2</sup>\*Postgraduate Student in Dept. of General Surgery SDUMC Kolar

<sup>3</sup>Professor Dept. of General Surgery SDUMC Kolar

<sup>4</sup>Postgraduate Student Dept. of General Surgery SDUMC Kolar

<sup>5</sup>House Surgeon Department of Surgery SDUMC Kolar

### Introduction

Acute appendicitis is one of the most common cause of acute abdomen in young adults and about 7% of the population suffers from acute appendicitis in their lifetime, and appendectomy is the most commonly done emergency abdominal surgery worldwide<sup>1</sup>. Even though surgeons have been dealing with acute appendicitis for more than 100 years, its diagnosis remains complicated. Appendicitis can be detected by the experienced surgeons in 80% of the cases, but as acute acuteappendicitis being always a surgical emergency and the decision for proceeding with surgery (appendectomy) will be on junior surgeons with less experience. Their decision have an accuracy rate which can go down up to 50%, so it can go wrong in about 50% of time. The negative appendectomy rates are high inspite of careful clinical, laboratory and ultrasound examinations. the negative appendectomy rate is around 20-30% in patients on whom appendectomy was performed based on clinical diagnosis alone<sup>2</sup>. Computed tomography,

laparoscopy has revolutionized the diagnosis of acute appendicitis with good results, but the availability of such facility and the high cost for performing the same will not be present all the times especially in rural places.

Additional tests done will increase the specificity by decreasing the number of unnecessary operations but at the expense of high costs, which almost all population suffers in rural set up will not be able to pay. This is very important in these days when health system is driven by cost parameters. CRP is a non-specific inflammatory marker, and studies also says that serum bilirubin will be elevated in 30-40% of patients with acute appendicitis, hence this study is being done to evaluate signicance of both of the above mentioned lab tests in predicting the diagnosis of acute appendicitis<sup>3,4</sup>.

### AIM of the Study

This study aims to correlate the serum levels of bilirubin, C - reactive protein (CRP) and to evaluate their significance in acute appendicitis.

**Materials and Methods**

It is a retrospective cohort study, in which 120 patients with suspected acute appendicitis clinically and who underwent open appendectomy and admitted under department of general surgery R.L Jalappa hospital attached to SDUMC, tamakakolar between sept 2014 and july 2017 were included in the study.

**Inclusion criteria**

- All patients above the age of 15 years and below 50 years diagnosed clinically to have Acute Appendicitis, and appendectomy was performed.

**Exclusion criteria**

- All patients documented to have a past history of Jaundice or Liver disease Hemolytic disease
- Acquired or Congenital biliary disease.
- All patients with positive HBsAg /HIV
- All patients with cholelithiasis
- All patients with malignancy of hepatobiliary system.

Total Bilirubin levels. Serum CRP concentrations and Total Bilirubin levels were measured before the surgery. Normal CRP levels range from 0 to 6 mg/l and Normal serum bilirubin levels ranges from 0.3 - 1.0 mg/dl.

Operative finding and histopathological examination of appendectomy specimen and serum CRP, and Serum Total bilirubin results was documented and studied. The results of Serum CRP and Serum Total bilirubin were correlated with the operative and histopathological examination using chisquare test. Collected data was analysed by frequency, percentage, mean, standard deviation and by sensitivity, specificity, positive predictive value, negative predictive value.

**Results**

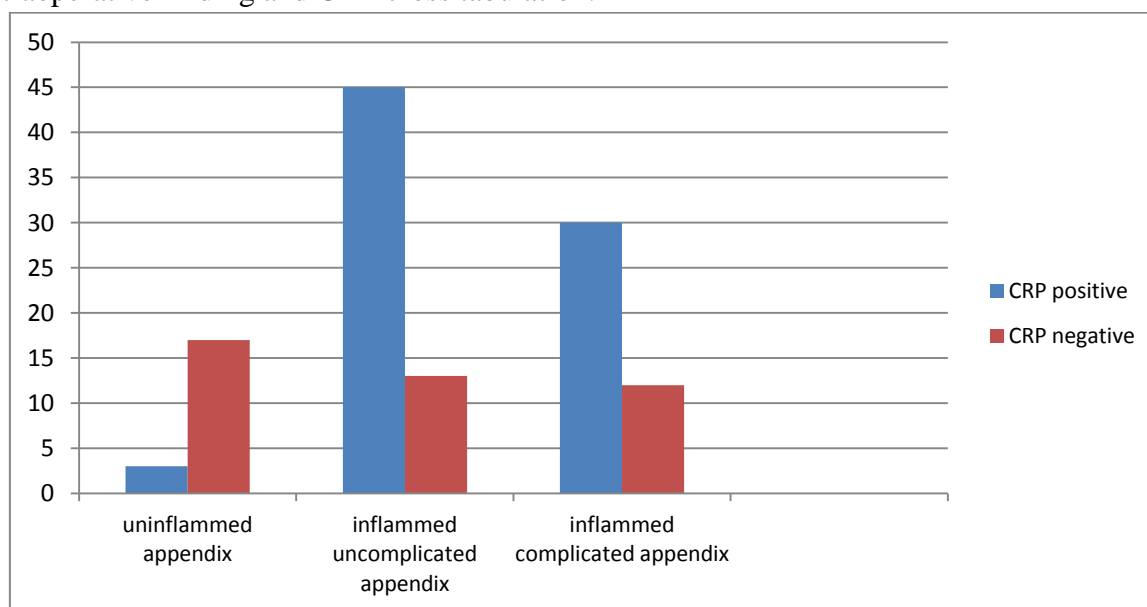
Age incidence: table 1

Age	frequency	%
<20	10	8.33%
21-30	74	61.67%
31-40	21	17.5%
41-50	15	12.5%
Total	120	100%

Intraoperative finding and CRP cross tabulation:

	CRP Positive	CRP Negative	Total
Uninflamed appendix	03	17	20
Inflamed uncomplicated appendix	45	13	58
Complicated inflamed appendix	30	12	42
Total	78	42	120

**Fig 1:** Intraoperative finding and CRP cross tabulation:



Chi square statistic is 26.39, the P value is 0. This result is significant. P<0.05

**Table 3** Sensitivity, specificity, positive predictive value and negative predictive value of CRP.

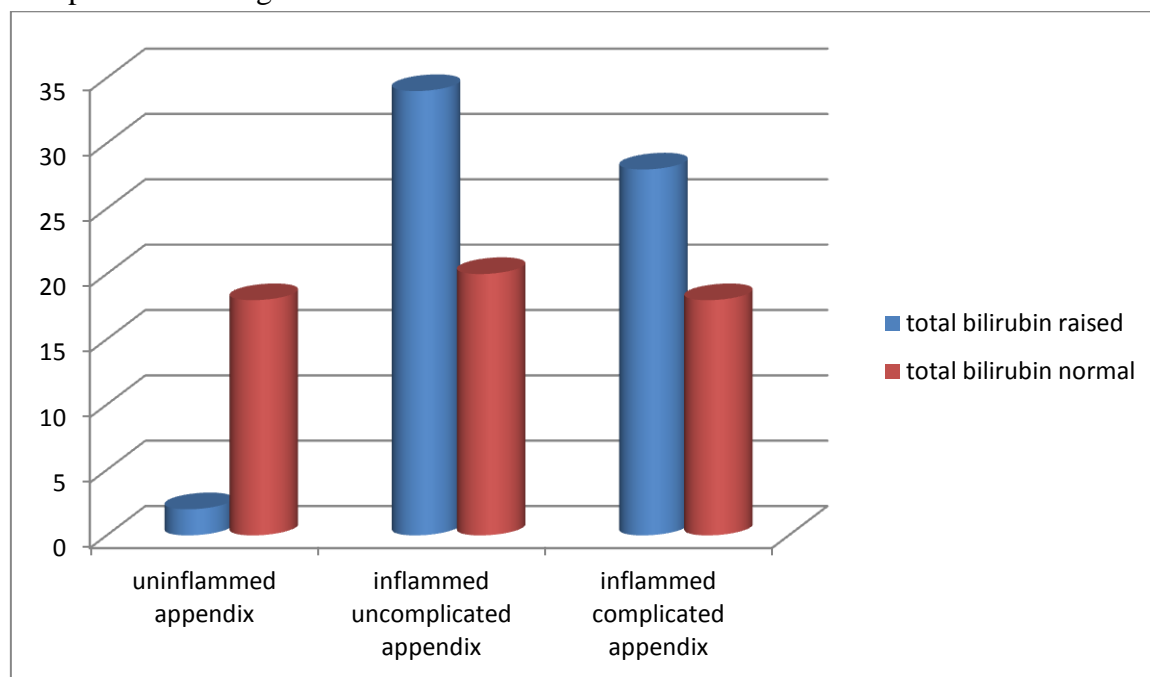
	Appendicitis positive	Appendicitis negative	total
CRP Positive	75(a)	03(b)	78
CRP Negative	25(c)	17(d)	42
Total	100	20	120

a= True positive b= False positive c= False negative d= True negative • Sensitivity( a / a+c) = 75 /100= 75.00% , Specificity ( d / b+d)= 15/16 = 85.73% • Positive predictive value ( a / a+b) = 75/ 78= 96.43% • Negative predictive value ( d / c+d)= 17/ 20 = 40.%

**Table 4:** Intraoperative finding and total bilirubin cross tabulation

	Total bilirubin raised	Total bilirubin normal	Total
Uninflamed appendix	02	18	20
Inflamed uncomplicated appendix	34	20	54
Inflamed complicated appendix	28	18	46
Total	64	56	120

**Fig 2. :** Intraoperative finding and total bilirubin cross tabulation



P=<0.05(significant)Chi-square statistics is 13.8793. The P value is 0.000195. The result is significant

**Table 5** Sensitivity, specificity, positive predictive value and negative predictive value of total bilirubin

	Appendicitis positive	Appendicitis negative	Total
Total bilirubin raised	62(a)	02(b)	64
Total bilirubin normal	38(c)	18(d)	56
Total	100	20	100

a= True positive b= False positive c= False negative d= True negative • Sensitivity ( a / a+c) = 62 /100= 62.03%, Specificity ( d / b+d)= 18/20 = 90.00% • Positive predictive value ( a / a+b) = 62/ 64= 96.87% • Negative predictive value ( d / c+d)= 18/ 56= 32.14%

In 100 patients of acute appendicitis serum CRP was elevated in 75 and normal in 25 patients. Serum Total bilirubin was elevated in 62 and normal in 38 patients. Of the 20 patients with normal appendix, serum CRP was normal in 15 patients and elevated in 03 patients. And similarly serum Total bilirubin was normal in 18 patients and elevated in 2 patients. Preoperative CRP values were false negative in 25 patients with appendicitis and false positive in 03 patients with normal appendix. Preoperative serum Total bilirubin was false negative in 38 patients with appendicitis and false positive in 2 patients with normal appendix. The difference of true and false results between CRP's test and surgeon's

diagnosis was statistically significant. Similarly, The difference of true and false results between serum Total bilirubin value and surgeon's diagnosis was statistically significant.

### Discussion

Vermiform appendix though described anatomically to be vestigial, but is one of the most important surgically concerned organs in the human body<sup>5</sup>. Acute appendicitis also known as ptyphilitis remains a common abdominal emergency throughout the world. Early and accurate diagnosis of acute appendicitis is required to reduce the morbidity and mortality associated with delayed diagnosis and its complications. Appendicitis still poses diagnostic challenge and many methods have been investigated to reduce negative appendectomy rates without increasing the perforation rate. Ultrasonography and computed tomography are the radiological methods most commonly being performed in urban population nowadays. In an attempt to increase the diagnostic accuracy, several scoring systems have been devised. The present study was undertaken to reach an accurate diagnosis in the fastest and cheapest way.

In this study the diagnostic value of the serum CRP levels and Total bilirubin levels in patients with clinical suspicion of acute appendicitis was investigated.

Following the onset of the infection, an increase occurs in the synthesis of some hepatic proteins as an acute phase response. Serum concentrations of acute phase proteins augment in 8-12 hours after the onset of infection. One of these, CRP, is a marker of acute phase response, which can be used as an indicator of disease. Elevation of serum concentrations of CRP indicates the presence of acute appendicitis<sup>6</sup>.

Recently, elevation in serum bilirubin was reported, but the importance of the raised total bilirubin has not been stressed in appendicitis. Bacterial invasion in the appendix leads to transmigration of bacteria and the release of proinflammatory cytokines such as TNF-alpha,

IL6 and cytokines<sup>7</sup>. 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.

Thus the present study was undertaken to evaluate the credibility of Hyperbilirubinaemia and elevated CRP levels as a diagnostic marker for acute uncomplicated appendicitis and complicated appendicitis.

In our study of 120 patients (63 male, 57 female), on histopathological examination 100 patients had acute appendicitis, with a negative appendectomy rate of 20%. In similar studies done by DLH Baird, JG Mariadason, Ohmann C<sup>7</sup>, and Arian GM<sup>8</sup>, negative appendectomy rates of 15%, 14.6%, 14.3% and 16.1% respectively were observed<sup>8</sup>. The mean age in our study population (100 patients) was 29.19. Majority of the patients in present study were in 2nd and 3rd decades of life.

In our study, serum CRP estimation in diagnosis of acute appendicitis yielded a sensitivity of 75.29% and specificity of 93.33%. This is comparable to the results of study done by S Yokoyama -sensitivity = 84.3%, specificity = 75.8%, S Buyukbese Sarsu sensitivity, 73.4%; specificity, 80.0%.<sup>6,7</sup> CRP is elevated in any cause of acute inflammation. But if clinical suspicion of appendicitis is not confirmed, CRP estimation provides the clue for acute appendicitis. In this study CRP and acute appendicitis were highly associated and statistically significant ( $p$  value < 0.005). This study proves the adjunct value of serum CRP estimation in suspected cases of acute appendicitis.

The development of jaundice in acute appendicitis is being explained by the fact that sepsis which is caused by variety of causative bacteria especially the gram negative bacterial infection is the one which is most commonly implicated<sup>9</sup>. The various mechanisms leading to hyperbilirubinaemia in systemic infections (appendicitis) include 1) bacterial infection associated with several bacteria including e.coli causes Hemolysis and hence

raises serum bilirubin load. 2) Bacterial infection especially with gram negative bacteria like e.coli sets endotoxemia which reduces the hepatic uptake and canalicular excretion of bilirubin causing hyperbilirubinemia. Hyperbilirubinaemia presumably occurs in appendicitis as a result of bacteraemia or endotoxaemia, which could occur both in simple appendicitis and perforated or gangrenous appendicitis<sup>10,11</sup>. In our study on evaluating Serum Total bilirubin in suspected cases of appendicitis, it was found to have elevated bilirubin in 53 patients and normal in 32 patients out of 85 patients with histopathologically proven appendicitis. In our study, serum Total bilirubin estimation in diagnosis of acute appendicitis yielded a sensitivity of 62.82% and specificity of 86.33%. In this study, no case with complicated appendicitis (appendicular perforation or abscess formation) had normal serum total bilirubin. Patients with hyperbilirubinaemia were significantly more likely to have acute appendicitis than those with a normal bilirubin. The sensitivity of hyperbilirubinaemia for appendicitis was 62.82%, which was lower than in other studies. However, we found that hyperbilirubinaemia had a high specificity of 86.33% and positive predictive value of 96.03%. In our study, serum Total bilirubin and acute appendicitis were associated and were statistically significant (p value <0.05)

Therefore, in suspected cases of appendicitis elevation of Serum bilirubin or CRP can be used as a criterion to diagnose and manage acute appendicitis. Both sensitivity and specificity of elevated total Serum bilirubin level and CRP in acute appendicitis with perforation and/or gangrene is higher. Serum CRP levels and Total bilirubin can be used with clinical examination and other laboratory investigations in the assessment of patients with suspected acute appendicitis for accurate diagnosis. Negative appendectomy rate can be decreased, if appendectomy is avoided in cases where serum CRP or Total bilirubin is negative. Bilirubin is a marker for acute appendicitis with a good positive

predictive value. It is also a valuable indicator of patients more likely to have appendiceal perforation or gangrene. Serum CRP levels are reliable inflammatory markers that could be used to support the clinical diagnosis of appendicitis

### Conclusion

No single clinical or laboratory test is able to reliably predict acute appendicitis. Rather, a combination of history, clinical examination and laboratory and radiological investigations is used to make the diagnosis and decide appropriate management. Serum bilirubin and serum CRP if estimated preoperatively would help in predicting acute appendicitis and also if checked along with total leucocyte counts, modified Alvarado helps in strongly predicting diagnosis of acute appendicitis, and can prevent unwanted negative appendectomies and also prevents unnecessary delay in performing needed appendectomy.

### References

1. Williams NS, Bulstrode CJK, O'Connell PR. Bailey & Love's SHORT PRACTICE of SURGERY. 26th ed. Boca Raton, FL: CRC Press; 2013.
2. Maingot R, Zinner M, Ashley S. Maingot's abdominal operations. New York: McGraw-Hill Medical; 2007.
3. Körner H. et al. Incidence of acute nonperforated and perforated appendicitis: Age-specific and sex-specific analysis. *World J Surg.* 1997; 21:313-317.
4. Wagner JM, McKinney WP, Carpenter JL. Does this patient have appendicitis? *JAMA.* 1996; 276:1589-1594.
5. Hardin DM Jr. Acute appendicitis: review and update. *Am Fam Physician.* 1999 Nov 1;60(7):2027-34.
6. Shozo Yokoyama C-Reactive protein is an independent surgical indication marker for appendicitis: a retrospective study. *World Journal of Emergency Surgery* 2009
7. Sevgi Buyukbese Sarsu, Fatma Sarac. Diagnostic Value of White Blood Cell and

C-Reactive Protein in Pediatric Appendicitis. BioMed Research International Vol. 2016 (2016).

8. Arian GM, Sohu KM, Ahmad E, Haider W, Naqi SA. Role of Alvarado score in diagnosis of acute appendicitis. Pak J Surg 2001;17:41-6.
9. Asfar S, Safar H, Khoursheed M, Dashti H, al-Bader A. Would measurement of Creactive protein reduce the rate of negative exploration for acute appendicitis? J R CollSurgEdinb. 2000 Feb;45(1):21-4.
10. Shakhathreh HS. The accuracy of Creactive protein in the diagnosis of acute appendicitis compared with that of clinical diagnosis. Med Arh. 2000;54(2):109-10.
11. Roelofsen H, van der Veere CN, Ottenhoff R et al. Decreased bilirubin transport in the perfused liver of endotoxemic rats. Gastroenterology 1994;107(4):1,075–1,084.