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## **Serum bilirubin as a diagnostic marker in acute appendicitis- A prospective study**

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**Abstract**---Background- Acute Appendicitis is the most common cause of acute abdomen. The initial diagnosis of acute appendicitis is based on clinical history and physical examination. Objectives- To determine the relationship between hyperbilirubinemia and acute appendicitis and to evaluate the usefulness of Serum Bilirubin as a diagnostic marker for acute appendicitis. Methods-It was Prospective study. Patients admitted with clinical diagnosis of acute appendicitis under the Department of Surgery in Vinayaka Mission's KirupanandaVariyar Medical College and Hospital, Salem from January 2020 to October 2021. Convenient Sampling (Non-Probability) was used. The sample size was 100. Chi- square or Fischer exact test was used as test of significance. SPSS (Version 16.0) was used. Results-The mean Age among the subjects was 25.04 years ranging from 8 to 70 years. Among the subjects, 59 (59%) were Males and 41 (41%) were Females. Among the subjects, 81 (81%) had Acute Appendicitis and 19 (19%) had Appendicular Perforation the patients with Direct bilirubin > 0.3 mg/dl, 15 (18.75%) had Appendicular Perforation and among the patients with Direct bilirubin < 0.3 mg/dl, 4 (20%) had Appendicular Perforation. There is no difference in Appendicular Perforation among patients with Direct bilirubin > 0.3 mg/dl and <0.3 mg/dl (18.75% vs 20%). The mean

Total Bilirubin among Acute Appendicitis was 1.4 mg/dl which is lower than among Appendicular Perforation which was 1.94 mg/dl and the difference was statistically significant. Conclusion-With the absence of 100% accurate test in diagnosis and prognosis of acute appendicitis, the increased values of Total, Indirect, Direct Bilirubin, will be helpful in suspecting the appendicular perforation. Also, cut-offs for these values of bilirubin, in the situations of acute appendicitis for forecasting the complications need to be adjusted.

**Keywords**---Acute appendicitis, appendicular perforation, serum bilirubin, Hyperbilirubinemia, appendicectomy, Mortality.

## **Introduction**

Acute Appendicitis is the most common cause of acute abdomen. The initial diagnosis of acute appendicitis is based on clinical history and physical examination. The confirmation of the diagnosis with the imaging technologies are challenging especially in the early stages and in cases of retrocecal or retroileal appendix. Laboratory investigations play a key role in assessing the severity of the disease. [1-3]

Appendectomy is the most performed abdominal surgery and the 15-30% of appendicectomy specimen collected will be found to be normal. These negative findings later make a concern on the unwanted cost involved in the surgery and postoperative complications if any. Postoperative complications can occur in up to nearly 50% of these patients. Acute Appendicitis can lead to deadly complications like perforation and peritonitis and can cause increased mortality rates.[4-6]

Studies show that serum bilirubin is raised in acute appendicitis and appendicular perforations. But the significance of which is not stressed. On bacterial invasion of the appendix, there is transmigration of bacteria and release of proinflammatory cytokines like TNF  $\alpha$ , IL6. The cytokines reach the liver through the superior mesenteric vein and may lead to inflammation, abscess, and liver dysfunction. [7,8].

There are no 100% accurate tests in diagnosis and prognosis of acute appendicitis. Therefore, any contribution made by any investigation, will be useful. In view of the above context, 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, to see whether elevated bilirubin levels have a predictive potential for the diagnosis of appendicular perforation.

## **Materials and Methods**

It was Prospective study Patients admitted with clinical diagnosis of acute appendicitis under the Department of Surgery in Vinayaka Mission's Kirupananda Variyar Medical College and Hospital, Salem from January 2020 to October 2021. Convenient Sampling (Non-Probability) was used.

**Inclusion criteria:**

- \_ all patients diagnosed as acute appendicitis clinically on admission.
- \_ Patients who are willing to participate in the study.

**Exclusion criteria:**

All patients documented to have a history of

- i. Jaundice or Liver disease.
- ii. Chronic alcoholism (that is intake of alcohol of > 40 g/day for Men and > 20 g/day in Women for 10 years).
- iii. Haemolytic disease.
- iv. Acquired or congenital biliary disease.

\_\_\_\_\_All patients with positive HBsAg.

\_\_\_\_\_All patients with cholelithiasis.

\_\_\_\_\_All patients with cancer of hepato-biliary system.

**Sample size:**

According to Joaquin J Estrada et al study,[9] considering the prevalence of Prevalence of

Hyperbilirubinemia (Total bilirubin >1 mg/dl) in acute appendicitis as 38% with a precision of 9.5% and 95% confidence interval, the sample size is calculated as

**$N = Z^2$**

**$1 - \alpha/2 * p * (1 - p) / d^2$**

$Z_{1-\alpha/2}$  - two tailed probability for 95% confidence interval = 1.96

p (%) - prevalence of Prevalence of Hyperbilirubinemia (Total bilirubin >1 mg/dl) in acute

appendicitis = 0.38 d (%) - precision or allowable error for Prevalence of Hyperbilirubinemia (Total bilirubin >1 mg/dl) in acute appendicitis = 0.095

$N = 1.96^2 * 0.38 * (1 - 0.38) / 0.095^2$

$N = 100.28$

Thus, the total sample size required for the study is 100

The study was approved by Institutional ethics committee. Written informed consent taken from patients.

**Statistical Analysis**

Data was entered in MS excel sheet and analysed using SPSS software version 16. When a Numerical variable is compared with the presence of acute appendicitis, independent t test is used. When a Categorical Variable is compared with the presence of acute appendicitis, the variables are represented in both by tables and bar diagrams. For test of significance, chi-square test is used. P-values less than 0.05 were statistically significant.

**Results**

The mean Age among the subjects was 25.04 years ranging from 8 to 70 years. Among the subjects, 59 (59%) were Males and 41 (41%) were

Females. Among the subjects, 81 (81%) had Acute Appendicitis and 19 (19%) had Appendicular Perforation.

Table 1- Distribution of Total Bilirubin with the Diagnosis in the study population

Total Bilirubin	Diagnosis		Total	Fisher exact pvalue
	Acute Appendicitis	Appendicular Perforation		
>1.0mg/dl	58(78.37%)	16(21.62%)	74(100%)	0.133 (Not Significant)
<1.0mg/dl	23(88.46%)	3(11.53%)	26(100%)	
Total	81(81%)	19(19%)	100(100%)	

As per table 1 Of the patients with Total bilirubin > 1.0 mg/dl, 16 (21.62%) had Appendicular Perforation and among the patients with Total bilirubin < 1.0 mg/dl, 3(11.53%) had Appendicular Perforation. This difference of increased proportion of Appendicular Perforation among patients with > 1.0 mg/dl Total Bilirubin (21.62% vs 11.53%) is not statistically significant.

Table 2-Distribution of Direct Bilirubin with the Diagnosis in the study population

Direct Bilirubin	Diagnosis		Total	Fisher exact pvalue
	Acute Appendicitis	Appendicular Perforation		
>0.3mg/dl	65(81.25%)	15(18.75%)	80(100%)	0.243
<0.3mg/dl	16(80%)	4(20%)	20(100%)	
Total	81(81%)	19(19%)	100(100%)	

As per table 2 of the patients with Direct bilirubin > 0.3 mg/dl, 15 (18.75%) had Appendicular Perforation and among the patients with Direct bilirubin < 0.3 mg/dl, 4 (20%) had Appendicular Perforation. There is no difference in Appendicular Perforation among patients with Direct bilirubin > 0.3 mg/dl and <0.3 mg/dl (18.75% vs 20%).

Table 3- Distribution of Indirect Bilirubin with the Diagnosis in the study population

Indirect Bilirubin	Diagnoses		Total	Fisher exact pvalue
	Acute Appendicitis	Appendicular Perforation		
>0.8mg/dl	9(69.23%)	4(30.76%)	13(100%)	0.143
<0.8mg/dl	72(82.75%)	15(17.24%)	87(100%)	
Total	81(81%)	19(19%)	100(100%)	

As per table 3 Of the patients with Indirect bilirubin > 0.8 mg/dl, 4 (30.76%) had Appendicular Perforation and among the patients with Indirect bilirubin < 0.8 mg/dl,15 (17.24%) had Appendicular Perforation. These differences of increased proportion of Appendicular Perforation among patients with indirect bilirubin > 0.8 mg/dl (30.76% vs 17.24%) are not statistically significant.

Table 4- Distribution of Total Bilirubin with Diagnosis among the study population

	Diagnosis	N	Mean	Std.dev.	pvalueby' t'test
Total Bilirubin	AcuteAppendicitis	81	1.40	0.64	0.042
	Appendicular Perforation	19	1.94	1.10	

As per table 4 the mean Total Bilirubin among Acute Appendicitis was 1.4 mg/dl which is lower than among Appendicular Perforation which was 1.94 mg/dl and the difference was statistically significant.

## Discussion

The main objective of the study is to study the relationship between hyperbilirubinemia and acute appendicitis, and to evaluate its credibility as a diagnostic marker for acute appendicitis. This is a Prospective Study among 100 Patients admitted with clinical diagnosis of acute appendicitis under the Department of Surgery in Vinayaka Mission's KirupanandaVariyar Medical College and Hospital, Salem.

Advancing age adversely affects the precise clinical diagnosis, the staging of the disease and the undesirable outcome of patients.[10] The post operative morbidity and mortality is high as the age increases. Among the children, younger children were found to have higher prevalence of appendicular perforation. [11]Anna Lasek et al,observed that the Older patients are at high risk both in the preoperative diagnosis and severity, intra-operative complications, and postoperative recovery. [12]

Salvatore Giordano et al, observed that the hyperbilirubinemia (cut-off 1 mg/dl) for prediction of perforation in acute appendicitis, sensitivity of 0.49, specificity of 0.82, positive likelihood ratio of 2.51, negative likelihood ratio of 0.58, diagnostic odds ratio of 4.42.[13]KulsoomMoulaBux et al, studied all the liver function test, of which the serum bilirubin levels independent predictors of appendix perforation/gangrene. [14]

A C Chambers et al, concluded that the serum bilirubin levels were significantly higher among the gangrene/perforation, but it cannot be an independent predictor of neither the diagnosis nor the complications of the acute appendicitis. [15]Andrew Emmanuel et al, observed that the mean bilirubin levels are significantly higher among the simple appendicitis and appendicitis with gangrene/perforation compared to the non-inflamed appendix. Elevated bilirubin levels had a good specificity of 88% for diagnosis of acute appendicitis and a

positive predictive value of 91%. [16] J Burcharth et al, observed that the mean bilirubin levels are significantly higher among the appendicitis with gangrene/perforation. Elevated serum bilirubin levels had a sensitivity ranging from 38% to 77% and a specificity ranging from 70% to 87% in forecasting the perforation of the appendix. [17] Michael Sandet et al, observed that the mean bilirubin levels are significantly higher among the appendicitis with gangrene/perforation. [18] Joaquin J Estrada et al, observed that the presence of hyperbilirubinemia was significantly associated with the gangrene/perforation among the patients with acute appendicitis. [9]

## Conclusion

The mean Values of Total, Indirect, and Direct Bilirubin among Acute Appendicitis with perforation were significantly higher than the corresponding values among patients without Appendicular Perforation. But the increase of proportion of the Appendicular Perforation with the higher than cut off values (among the normal patients) were not statistically significant. With the absence of 100% accurate test in diagnosis and prognosis of acute appendicitis, the increased values of Total, Indirect, Direct Bilirubin, will be helpful in suspecting the appendicular perforation. Also, cut-offs for these values of bilirubin, in the situations of acute appendicitis for forecasting the complications need to be adjusted.

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## References

1. Burcharth J, Pommergaard HC, Rosenberg J, Gögenur I. Hyperbilirubinemia as a predictor for appendiceal perforation: a systematic review. *Scand J Surg SJS Off organ Finnish Surg Soc Scand Surg Soc.* 2013;102(2):55–60.
2. Chambers AC, Bismohun SL, Davies H, White P, Patil A V. Predictive value of abnormally raised serum bilirubin in acute appendicitis: a cohort study. *Int J Surg.* 2015 Jan;13:207–10.
3. Emmanuel A, Murchan P, Wilson I, Balfe P. The value of hyperbilirubinaemia in the diagnosis of acute appendicitis. *Ann R Coll Surg Engl.* 2011 Apr;93(3):213–7.
4. Estrada JJ, Petrosyan M, Barnhart J, Tao M, Sohn H, Towfigh S, et al. Hyperbilirubinemia in appendicitis: a new predictor of perforation. *J Gastrointest Surg Off J Soc Surg Aliment Tract.* 2007 Jun;11(6):714–8.
5. Giordano S, Pääkkönen M, Salminen P, Grönroos JM. Elevated serum bilirubin in assessing the likelihood of perforation in acute appendicitis: a diagnostic metaanalysis. *Int J Surg.* 2013;11(9):795–800.
6. Gürleyik G, Gürleyik E. Age-related clinical features in older patients with acute appendicitis. *Eur J Emerg Med Off J Eur Soc Emerg Med.* 2003 Sep;10(3):200–3.
7. Hansen JB, Smithers BM, Schache D, Wall DR, Miller BJ, MenZies BL. Laparoscopic versus open appendectomy: prospective randomized trial. *World J Surg.* 1996;20(1):17–21.

8. Heikkinen TJ, Haukipuro K, Hulkko A. Cost-effective appendectomy. *SurgEndosc.* 1998;12(10):1204–8.
9. Heinzelmann M, Simmen HP, Cummins AS, Largiader F. Is laparoscopic appendectomy the new 'gold standard'? *Arch Surg.* 1995;130(7):782–5.
10. Lasek A, Pedziwiatr M, Kenig J, Waledziak M, Wysocki M, Mavrikis J, et al. The significant impact of age on the clinical outcomes of laparoscopic appendectomy: Results from the Polish Laparoscopic Appendectomy multicenter large cohort study. *Medicine (Baltimore).* 2018;97(50).
11. Lee SL, Stark R, Yaghoubian A, Shekherdimian S, Kaji A. Does age affect the outcomes and management of pediatric appendicitis? *J Pediatr Surg.* 2011 Dec;46(12):2342–5.
12. Mazzei MA, Guerrini S, Squitieri NC, Cagini L, Macarini L, Coppolino F, et al. The role of US examination in the management of acute abdomen. *Crit Ultrasound J.* 2013;5(1):1–9.
13. MoulaBux K, Parveen S, Iqbal M, Mehboob A. The effect of acute complicated appendicitis on liver function test. *Pakistan J Med Sci.* 2021;37(2):351–4.
14. Paaajanen H, Mansikka A, Laato M, Ristamäki R, Pulkki K, Kostianen S. Novel serum inflammatory markers in acute appendicitis. *Scand J Clin Lab Invest.* 2002;62(8):579–84
15. Sand M, Bechara FG, Holland-Letz T, Sand D, Mehnert G, Mann B. Diagnostic value of hyperbilirubinemia as a predictive factor for appendiceal perforation in acute appendicitis. *Am J Surg.* 2009 Aug;198(2):193–8.
16. Siewert B, Raptopoulos V, Mueller MF, Rosen MP, Steer M. Impact of CT on diagnosis and management of acute abdomen in patients initially treated without surgery. *AJR Am J Roentgenol.* 1997;168(1):173–8.
17. Suryasa, I. W., Rodríguez-Gámez, M., & Koldoris, T. (2022). Post-pandemic health and its sustainability: Educational situation. *International Journal of Health Sciences*, 6(1), i-v. <https://doi.org/10.53730/ijhs.v6n1.5949>
18. Türkyilmaz Z, Sönmez K, Karabulut R, Elbeğ S, Moralioglu S, Demirtola A, et al. Sequential cytokine levels in the diagnosis of appendicitis. *Scand J Clin Lab Invest.* 2006;66(8):723–32.
19. Wido, A., Bajamal, A. H., Apriawan, T., Parenrengi, M. A., & Al Fauzi, A. (2022). Deep vein thrombosis prophylaxis use in traumatic brain injury patients in tropical climate. *International Journal of Health & Medical Sciences*, 5(1), 67-74. <https://doi.org/10.21744/ijhms.v5n1.1840>
20. Wray CJ, Kao LS, Millas SG, Tsao K, Ko TC. Acute appendicitis: controversies in diagnosis and management. *CurrProbl Surg.* 2013;50(2):54–86.