ASSESSMENT OF ACCURACY OF HYPERBILIRUBINEMIA IN EARLY DIAGNOSIS OF ACUTE APPENDICITIS IN OUR POPULATION

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ABSTRACT

Objective: To determine the assessment of accuracy of hyperbilirubinemia in the diagnosis of acute appendicitis keeping histopathology as gold standard.
Study Design: Cross-sectional validation study.
Place and Duration of Study: Combined Military Hospital Rawalpindi, form Jan 2014 to Jul 2014.
Methodology: After approval of hospital ethical committee, total number of 180 consecutive patients presenting in emergency department with suspicion of acute appendicitis were admitted in hospital. After fulfilling the inclusion and exclusion criteria and taking detailed history and examination, investigations were ordered and appendectomy was done within 24 hours and sent for histopathology examination by the consultant at armed forces institute of pathology.
Results: In our study, mean age was 35.45 ± 7.43 years, 97 (53.89%) were male and 83 (46.11%) were females, frequency of acute appendicitis on histopathology (gold standard) was recorded in 149 (82.78%). Assessment of accuracy of hyperbilirubinemia in diagnosis of acute appendicitis using histopathology as gold standard shows 119 (66.11%) were true positive, 11 (6.11%) were false positive, 20 (11.11%) were true negative and 30 (16.67%) were false negative. Sensitivity, specificity, positive predictive value, negative predictive value and accuracy rate was computed as 79.87%, 64.52%, 91.54%, 40% and 77.22% respectively.
Conclusion: The assessment of accuracy of hyperbilirubinemia in diagnosis of acute appendicitis keeping histopathology as gold standard was found a useful marker and may be used as an adjuvant diagnostic technique for acute appendicitis.

Keywords: Assessment, Acute appendicitis, Diagnosis, Hyperbilirubinemia.

INTRODUCTION

In most tertiary care hospitals surgical emergency department acute appendicitis most commonly as a surgical emergency as acute abdomen[1]. The approximated prevalence of acute appendicitisis 28.6%[1]. If the surgeon makes a decision of surgical procedure dependently only on the patient's signs and symptoms may results in white appendectomy in 14.7%[2], if there is any kind of therapeutic delay or misdiagnosis, it may results in complicated perforated appendix or peritonitis[2].

Diagnosis of acute appendicitis in emergency department is commonly made clinically. The availability of modern diagnostic tools like Modified Alvarado scoring system efficiently aids in diagnosis[3]. Conclusions of recent studies show that hyperbilirubinemia is a a good helper for diagnosis of acute appendicitis[4] having a sensitivity 82.07%[1] and specificity of 88%[4]. Hyperbilirubinemia explains an elevated serum bilirubin above physiological level in the human body blood which can be utilized as a diagnostic marker for acute appendicitis[5]. Acute appendicitis causes release of endotoxins which shifts through portal circulation in to liver resulting into raised level of bilirubin. Specificity of hyperbilirubinemia is very high[6]. Patient with signs and symptoms of acute appendicitis with hyperbilirubinemia should be considered for appendectomy[7].

The objective of my study was to suggest a simple, cheap, quick and effective marker for early appropriate diagnosis of acute appendicitis

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which is one of the commonest emergencies presenting with acute abdomen in emergency department of any setup resulting in 14.7% negative appendicectomies[2]. Our rationale of the study was to explore the accuracy of hyperbilirubinemia in diagnosing acute appendicitis. If this studyand further larger scale studies which could potentially prove hyperbilirubinemia as an accurate biomarker can aid in provision of an easier, earlier and cheaper adjuvant diagnostic tools for diagnosis of acute appendicitis and therefore help in reducing delay in diagnosis and therefore complication rate. It will also cause reduction in rate of unnecessary appendectomies.

METHODOLOGY

After approval of hospital ethical committee this cross-sectional validation study was conducted in surgical unit 1 Combined Military Hospital Rawalpindi from 1st January to 31st July 2014 with a sampling technique of non-probability consecutive. Each patient received routine medical attention for acute appendicitis including detailed medical history, complete medical examination in proper environment with due respect after taking proper consent from the patient, routine laboratory investigations (blood complete picture, urine routine examination). In addition to see patient bilirubin LFTs were done. LFTs were sent to hospital laboratory and assessed by SPECTRA-E machine by spectroscopic method. Patient was kept NPO, Intravenous Normal Saline was started, analgesia was given as patients requirements. After getting all investigation informed written consent was taken for appendectomy and Appendectomy was performed within 24 hours. Post-operatively analgesia was given to the patient on requirement. Following operation diagnosis was confirmed by histopathological examination of appendix by consultant histopathologist at Armed forces Institute of Pathology. Sample size was calculated by the following formula.

Expected sensitivity	:	82.07%[1]
Expected specificity	:	88%[4]
Prevalence	:	28.6%[6]
Prevalence	:	28.6%[6]
Desired precision	:	10%
Desired precision	:	10%
Confidence level	:	95%
Confidence Level	:	95%
Sample size (n)	=	135
Sample Size (n)	=	40
Final total sample size	=	180

The data were entered and analyzed using SPSS version 20. For quantitative variables like age, mean and standard deviation was calculated. For qualitative variables frequency and percentage was calculated. During study number of True Positive, False Positive, True Negative, False Negative, Positive Predictive Value, Negative Positive Value was measured and specificity, sensitivity, PPV, NPV was calculated. Keeping histopathology as gold standard as keeping ≤0.05 *p*-value was considered statistically significant.

RESULTS

A total of 180 cases fulfilling the inclusion/ exclusion criteria were enrolled to determine assessment of accuracy of hyperbilirubinemia in diagnosis of acute appendicitis keeping histopathology as gold standard.

Age distribution of the patients was done showing that 112 (62.22%) were between 12-35 years of age while 68 (37.78%)[8] were between 36-50 years of age, Mean ± SD was calculated as 35.45 ± 7.43 years.

Patients were distributed according to gender showing that 97 (53.89%) were males and 83 (46.11%) were females.

Frequency of acute appendicitis on histopathology (gold standard) was recorded in 149 (82.78%) while 31 (17.22%) had no findings of the morbidity.

Assessment of accuracy of hyperbilirubinemia in diagnosis of acute appendicitis using histopathology as gold standard, where 119 (66.11%) were true positive, 11 (6.11%) were false positive, 20 (11.11%) were true negative and 30

(16.67%) were false negative. Sensitivity, specificity, positive predictive value, negative predictive value and accuracy rate was computed as 79.87%, 64.52%, 91.54%, 40% and 77.22% respectively (table).

Table: Assessment of accuracy of hyperbilirubinemia in early diagnosis of acute appendicitis keeping histopathology as gold standard (n=180).

Hyperbilirubinemia	Histopathology for acute appendicitis		Total
	Appendicitis Present	Appendicitis Absent	
Present	True positive (a) 119 (66.11%)	False positive (b) 11 (6.11%)	a + b 130 (72.22%)
Absent	False negative (c) 30 (16.67%)	True negative (d) 20 (11.11%)	c + d 50 (27.78%)
Total	a + c 149 (82.78%)	b + d 31 (17.22%)	180 (100%)

Sensitivity=79.87%, Specificity=64.52%, PPV=91.54%, NPV=40%, DA=77.22%

DISCUSSION

Young adults presenting in common hospitals emergency departments with acute abdominal pain as acute abdomen commonly diagnose as acute appendicitis[1]. In these patients commonly surgeon performs emergency appendectomy as a emergency surgical procedure, if there is decision to operate on the choice of the surgeon or surgical resident on the overall clinical suspicion. It is commonly seen that a number of patients undergoing emergency appendectomy result to be found as a white on the histopathology of the surgically removed appendix, which is considered as a gold standard for the diagnosis of the appendicitis[2].

We planned this study to conclude the accuracy of hyperbilirubinemia in diagnosing acute appendicitis.

The findings of our study are in agreement with the studies showing the sensitivity of hyperbilirubinemia in acute appendicitis was 82.07%[1] and specificity of 88%[4].

A study by Silva *et al* revealed sensitivity was found to be (54.6%) and specificity was (70.0%) and his study revealed that hyperbilirubinaemia alone cannot help in diagnosis of acute appendicitis and its complications[9].

Muller *et al*[10] assessed the diagnostic accuracy of serum bilirubin in foreseeing appendicitis and its severity and revealed hyperbilirubinaemia has a low diagnostic valuein acute appendicitis in differentiating between any appendicitis versus no appendiceal inflammation and perforated versus non-perforated appendicitis and has limited value in clinical routine, which is against to our findings.

In a study[11] diagnostic value of bilirubin was compared between perforated and non-complicated simple appendicitis, and it was compared with the white blood cell count (WBC), serum C-reactive protein (CRP) and it was concluded that hyperbilirubinaemia has a high specificity for differentiating acute appendicitis, when complicated with perforation, from other reasons of RIF pain, particularly those causes not requiring surgical procedure, these findings have the same findings as our study.

A very new local study[12] revealed the role of hyperbilirubinaemia as an anticipating factor for complicated appendiceal perforation in acute appendicitis and revealed that patients presenting in emergency departments with suspicious signs and symptoms of acute appendicitis and an elevated total serum bilirubin level revealed that a complication of acute appendicitis has occurred and require an early surgical intervention to prevent peritonitis and septicaemia. A high serum bilirubin level is an excellent sign of complicated acute appendicitis, and should be used in early assessment of patients with suspected complicated acute appendicitis.

A study[13] which was carried out and which showed more reliable laboratory and clinical diagnostic markers for the diagnosis of acute

appendicitis and to assess the severity score on multiple number of patients with acute appendicitis and finalized that hyperbilirubinemia was a statistically important diagnostic marker for acute appendicitis and the chances of perforation.

According to study carried out in Italy revealed that appendix perforation is associated with increased leel of bilirubin[14].

Another study conducted in japan which also concluded that increase level of bilirubin is used as an early marker in diagnosis of acute appendicitis[15]. Another study was conducted and which was having the same result as our study[16]. In another study significance of bilirubin level was addressed in relation with diagnosis of acute appendicitis[17,18].

We are of the opinion that sensitivity and specificity of Hyperbilirubinemia is found to be in support of early diagnosis of acute appendicitis and will help us in early diagnosis of acute appendicitis and will reduce chances of post-operative complications.

CONCLUSION

Accuracy of hyperbilirubinemia in diagnosis of acute appendicitis keeping histopathology as gold standard was found as a useful marker and may provide us for an alternative diagnostic technique for acute appendicitis.

CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

REFERENCES

1. Khan S. Elevated serum bilirubin in acute appendicitis: A new diagnostic tool. Kathmandu Uni Med J 2008; 6(2): 161-65.
2. Limpawattanasiri C. Alvarado score for the acute appendicitis in a provincial hospital. J Med Assoc Thai 2011; 94(4): 441-49.
3. Kamran H, Naveed D, Asad S, Hameed M, Khan U. Evaluation of modified alvarado score for frequency of negative appendicectomies. J Ayub Med Coll Abbottabad 2010; 22(4): 46-49.
4. Emmanuel A, Murchan P, Wilson I, Balfe P. The value of hyperbilirubinemia in the diagnosis of acute appendicitis. Ann R Coll Surg Engl 2011; 93(3): 213–17.
5. Hong YR, Chung CW, Kim JW, Kwan CI, Ahn DH, Kwon SW, Hyperbilirubinemia is a significant indicator for the severity of acute appendicitis. J Korean Soc Coloproctol 2012; 28(5): 247–52.
6. Huckins DS, Simon HK, Copeland K, Spiro DM, Gogain J, Wandeli M. A novel biomarker panel to rule out acute appendicitis in pediatric patients with adominal pain. Am J Emerg Med 2013; 31(6): 1368-75.
7. Adams HL, Jaunoo SS. Hyperbilirubinaemia in appendicitis: The diagnostic value for prediction of appendicitis and appendiceal perforation. Eur J Trauma Emerg Surg 2016; 42(2): 249-52.
8. Giordano S, Paakkoneu M, Salminen P, Gronroos JM. Elevated serum bilirubin in assessing the like hood of perforation in acute appendicitis: A diagnostic meta analysis. Int J Surg 2013; 11(9); 795-800.
9. Silva FR, da Rosa Mi, Silva BR, Simon C, Alexandre MC, Medeiros LR, et al. Hyperbilirubinaemia alone cannot distinguish a perforation in acute appendicitis. Aust New Zealand J Surg 2016; 86(4): 255-59.
10. Muller S, Falch C, Axt S, Wilhelm P, Hein D, Königsrainer A, et al. Diagnostic accuracy of hyperbilirubinaemia in anticipating appendicitis and its severity. Emerg Med J 2014; 2013: 203349.
11. D'Souza N, Karim D, Sunthareswaran R. Bilirubin; A diagnostic marker for appendicitis. Int J Surg 2013; 11(10): 1114-7.
12. Jamaluddin M, Hussain SM, Ahmad H. Hyperbilirubinaemia a predictive factor for complicated acute appendicitis: A study in a tertiary care hospital. J Pak Med Assoc 2013; 63(11): 1374-8.
13. Hong YR, Chung CW, Kim JW, Kwon CI, Ahn DH, Kwon SW. Hyperbilirubinemia is a significant indicator for the severity of acute appendicitis. J Korean Soc Coloproctol 2012; 28(5): 247-52.
14. Akturk OM, Yıldırım D, Çakır M, Vardar YM. Elevated serum bilirubin levels may predict perforation of the appendix. Ann Ital Chir 2019; 90(1): 427-31.
15. Akai M, Iwakawa K, Yasui Y, Yoshida Y, Kato T, Kitada K. Hyperbilirubinemia as a predictor of severity of acute appendicitis. J Int Med Res 2019; 47(8): 3663-69.
16. Gavriilidis P, de'Angelis N, Evans J, Di Saverio S, Kang P. Hyperbilirubinemia as a Predictor of Appendiceal Perforation: A Systematic Review and Diagnostic Test Meta-Analysis. J Clin Med Res 2019; 11(3): 171-78.
17. Ramu TR, Kandhasamy SC, Andappan A, Sankar B. A Prospective study on the diagnostic value of hyperbilirubinemia as a predictive factor for appendicular perforation in acute appendicitis. Cureus 2018; 10(8): e3214.
18. Yoon HM, Kim JH, Lee JS, Ryu JM, Kim DY, Lee JY. Pediatric appendicitis with appendicolith often presents with prolonged abdominal pain and a high risk of perforation. World J Pediatr 2018; 14(2): 184-90.