

Accuracy of hyperbilirubinemia and neutrophil lymphocyte ratio as independent predictors of perforation in acute appendicitis

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Objective: To determine the accuracy of hyperbilirubinemia and neutrophil lymphocyte ratio in predicting appendicular perforation.

Methodology: This cross sectional study was conducted in surgical department of Polyclinic Hospital, Islamabad, Pakistan from July 14, 2017 to January 14, 2018. Sample size was 383 patients. A non-probability consecutive sampling technique was used. Hyperbilirubinemia was defined as total bilirubin >1mg/dl and neutrophil lymphocyte ratio (NLR) greater than 5 for predicting appendicular perforation, keeping histopathology as standard for perforation.

Results: Out 383 patients with acute appendicitis,

227(59%) were male and 156(41%) female. Mean age was 25.5±10.7 years. 35(9.14%) patients had perforated appendix on histopathology. Hyperbilirubinemia had a sensitivity of 54.3%, specificity of 87.1%, NLR >5 had a sensitivity of 74.3%, specificity of 60%.

Conclusions: Hyperbilirubinemia and high NLR should be used in combination with clinical assessment and imaging modalities to improve the diagnostic accuracy for predicting perforation in acute appendicitis. (Rawal Med J 202;45:410-413).

Keywords: Hyperbillirubinemia, Neutrophils, Lymphocytes, Perforated, Appendicitis.

INTRODUCTION

Acute appendicitis is one of the commonest surgical emergencies and appendicular perforation is one of its dreaded complications with the prevalence of approximately 16%.¹ Often, it is difficult to reach a diagnosis, especially in immunocompromised states and at extremes of age.² Different clinical signs and symptoms may mimic the diagnosis of acute appendicitis, as there are a number of causes leading to pain in right iliac fossa, particularly in female patients and children. Diagnosing acute appendicitis clinically sometimes remains a surgical problem. Diagnostic delay or late presentation often leads to perforation of appendix, which is associated with increase in the mortality and morbidity.³

Various scoring systems have been used along with different imaging modalities to predict acute appendicitis. These include Alvarado score, AIR score and RIPASA etc.⁴ Imaging including ultrasound, CT scan and MRI are used, all with different sensitivities and specificities for predicting perforation of appendix.⁵ No single score or imaging technique can predict perforation of appendix with 100% accuracy. Recently, there is a growing trend

towards the use of WBC/neutrophil counts, neutrophil percentage, neutrophil lymphocyte percentage and serological markers including CRP, total/direct/indirect bilirubin levels for predicting acute appendicitis as well as gangrenous/perforated appendix.⁶ Different studies have shown different cutoff values of total serum bilirubin to be associated with complicated appendix.⁶⁻⁸ We conducted this study to determine the accuracy of hyperbilirubinemia and neutrophil lymphocyte ratio in predicting appendicular perforation.

METHODOLOGY

This cross sectional validation study was conducted in surgical department of Polyclinic hospital, Islamabad, Pakistan from July 14, 2017 to January 14, 2018. A sample size of 383 was calculated using WHO sample size calculator. A non-probability consecutive sampling technique was used. An informed consent was taken from all patients. Patients from 12 to 60 years of age and both gender were included. Patients having positive hepatitis B or C screening test, with appendicular mass/ abscess on presentation, with pregnancy, with comorbidities

selected for conservative treatment, with known blood dyscrasia, patients on hepatotoxic drugs for any condition were excluded.

Patients presenting with sign and symptoms of acute appendicitis for less than 7 days (right lower abdominal pain, nausea, anorexia, tenderness and rebound tenderness at right iliac fossa) had their relevant baseline investigations sent, prior to surgery, including neutrophil lymphocyte ratio (derived from complete blood picture) and serum total bilirubin level were performed from the hospital lab and verified by pathologist. Appendectomy was performed after senior surgeon review and specimen of appendix was sent for histopathology. Hyperbilirubinemia was defined as total bilirubin >1mg/dl and neutrophil lymphocyte ratio as ratio of neutrophil percentage to lymphocyte percentage i.e. NLR had be greater than 5 for predicting appendicular perforation, keeping histopathology evidence as standard for perforation.

Statistical Analysis: Data were analyzed using SPSS version 17. Sensitivity, specificity, positive and negative predictive values and likelihood ratios were calculated.

RESULTS

The study included 383 patients (mean age 25.5±10.7 years). Acute appendicitis was more common in males (227 patients) 59% of study population than 41% of female patients (156 patients). 35 (9.14%) patients had perforated appendix on histopathology while 348 (90.86%) patients had inflamed but non-perforated appendix. Hyperbilirubinemia was present in 61 patients with acute appendicitis, out of which only 19 patients had histopathological evidence of perforation of appendix.

Table 1. Diagnostic accuracy of hyperbilirubinemia.

Hyper-bilirubinemia	Histopathology		Total	Statistics	p-value
	+ve	-ve			
>1mg/dl (+)	19	42	61	Sensitivity =54.3% Specificity =87.1% PPV = 26.2% NPV= 94.1% Positive LR =3.46 Negative LR=0.63	<0.001
≤1mg/dl (-)	16	306	322		
Total	35	348	383		

Table 2. Diagnostic accuracy of nlr>5.

NLR>5	Histopathology		Total	Statistics	P-value
	+ve	-ve			
Yes (+)	26	139	165	Sensitivity=74.3% Specificity = 60% PPV = 15.7% NPV= 95.9% Positive LR =1.85 Negative LR=0.43	<0.001
No (-)	9	209	218		
Total	35	348	383		

High neutrophil lymphocyte ratio was present in 165 patients with acute appendicitis, out of which only 26 patients had histopathological evidence of perforation. Both indicators were positive in 10 patients with perforation, but remaining patients with perforation had either of them positive. Mean total serum bilirubin level was 0.92±0.65 and mean NLR of study group was 6.10±5.50. Hyperbilirubinemia had a sensitivity of 54.3%, specificity of 87.1% (Table 1). NLR >5 had a sensitivity of 74.3%, specificity of 60% (Table 2).

DISCUSSION

Early diagnosis of acute appendicitis and early prediction of perforated appendix leads to early surgical management and reduction in complications rates. Patients with complicated appendicitis have a longer history of symptoms, more guarding, fever, and higher CRP values.⁹⁻¹³ Radiological diagnosis of perforation alone is uncertain. There is excellent diagnostic performance of CT in suspected appendicitis, that reduced negative appendectomy rate from 20% to less than 10% but the distinction between complicated and uncomplicated appendicitis by CT has not been reliable. The CT findings of focal defect in the appendiceal wall, abscess, extraluminal gas, ileus, periappendiceal fluid, and appendicolith have had the highest specificity, but the sensitivity of these findings has been low (28-70%).¹¹⁻¹⁶ MRI is often used to replace CT for pregnant patients after inconclusive or negative US. The reported sensitivity and specificity of MRI are 82-98% and 71-100%, respectively, depending on the expertise of the MRI reader.^{17,18} However, MRI is not accurate at detecting appendiceal perforation.¹⁸

Recent research suggests inflammatory markers measurements, as well as clinical symptoms and examination findings, have the strongest associations with appendicitis when they are combined with each other.^{19,20} There are no laboratory examinations, independent or combined with each other that have 100% positive or negative predictive values for complicated appendicitis.²¹ Several studies have recognized high CRP level as a marker for complicated appendicitis.^{9,11,13}

Isolated hyperbilirubinemia without associated elevation of ALT/AST or ALP is associated with gangrenous /perforated appendicitis. Serum bilirubin >3mg/dl showed higher sensitivity and specificity in previous studies.^{7,22,23} compared to our study in which serum bilirubin cut off was set low 1mg/dl.

Kahramanca et al have showed that neutrophil lymphocyte ratio is better predictor of perforation in acute appendicitis,¹ but Ishizuka et al showed that CRP was much better in diagnostic accuracy than NLR alone and combination of both CRP and high NLR added to their accuracy.²⁴ Sensitivity and specificity of NLR in these two studies were similar to our study. In our study, hyperbilirubinemia was more specific for predicting perforation comparable to that of high NLR while high NLR has a sensitivity of that is much higher than that of hyperbilirubinemia.

Serum bilirubin estimation, a simple economical and easily available test in every laboratory can be added to the routine investigation list of clinically suspected case of complicated acute appendicitis along with neutrophil lymphocyte ratio for the increasing the accuracy of diagnosis. Other serological markers like CRP can be combined with hyperbilirubinemia and high NLR. In addition, clinical evaluation and appropriate imaging studies should make an important contribution to the decision making process regarding treatment plan in individual patient presenting with acute appendicitis and to detect perforated appendicitis early, this will minimize the rate of complications in different groups especially those at extremes of age, immunocompromised status and with comorbid conditions.

CONCLUSION

Hyperbilirubinemia (Serum bilirubin >1mg/dl) is more specific while high neutrophil to lymphocyte ratio (NLR>5) is more sensitive in predicting perforation in acute appendicitis. These two parameters should be used in combination with clinical assessment and imaging modalities to improve the diagnostic accuracy for predicting perforation in clinical setting of acute appendicitis.

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