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Diagnostic Value of Hyperbilirubinemia as a Predictor for Appendiceal Perforation in Acute Appendicitis

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ABSTRACT

Objectives: To determine the diagnostic accuracy of hyperbilirubinemia as a predictor for "appendiceal perforation" in acute appendicitis.

Study Design: validation study.

Place and Duration of Study: Department of General Surgery, Combined Military Hospital, Rawalpindi Pakistan, from Sep to Feb 2022.

Methodology: A total of 96 patients having acute appendicitis were included Serum bilirubin levels were documented. Patients then underwent appendectomy and based on operative finding diagnosis of simple/perforated appendicitis was made. 2x2 table was drawn for sensitivity, specificity, PPV and NPV.

Results: In our study, mean age of study population was 20.86±3.26 years. There 46(47.90%) male participants while remaining 50(52.10%) participants were female. Mean duration of symptoms was 10.79±2.56 hours. Mean serum bilirubin was 1.28±0.74 mg/dl. Sensitivity, specificity, positive predictive value and negative predictive value of "hyperbilirubinemia" as a predictor for "appendiceal perforation" in acute appendicitis was 63.64%, 76.92%, 70.00% and 71.43%, respectively.

Conclusion: Raised serum levels of bilirubin can serve as a potentially useful laboratory test for predicting "appendiceal perforation".

Keywords: Appendicitis, Appendectomy, Bilirubin, Diagnostic Accuracy, Perforation.

How to Cite This Article: *Ashraf S, Khan MS, Ali PI, Ali S, Khan RI, Rashid AR. Diagnostic Value of Hyperbilirubinemia as a Predictor for Appendiceal Perforation in Acute Appendicitis. Pak Armed Forces Med J 2025; 75(Suppl-4): S574-S577. DOI: https://doi.org/10.51253/pafmj.v75iSUPPL-4.10166*

INTRODUCTION

Appendix is a part of human gastrointestinal system that is typically found just below the cecum but is known to show a significant degree of anatomical variability in terms of its location as well as length which is commonly reported by surgeons post-operatively.[1] From evolutionary point-of-view, appendix was believed to be vestigial organ but extensive research has revealed that it contains a large quantity of microbiota as well as immune cells which has significant effect on gut functions, immune system and development of various conditions.[2,3] Under normal circumstances, lumen of the appendix is empty but in cases where there is luminal obstruction, process of acute inflammation ensues which can result in the acute presentation of "appendicitis". This obstruction can occur secondary to a wide variety of reasons including parasites, enlargement of the lymph nodes, fecolith and malignancy.[4]

The majority of young children brought to the emergency rooms with complaint of acute pain in the abdomen are diagnosed with "Acute Appendicitis", making it one of the most prevalent reasons for individuals to seek emergency care for lower abdominal pain. It most commonly effects the younger population aged between ten to thirty years and has a reported incidence of "1.9%".[5] Patients who are diagnosed with acute appendicitis have a wide range of possible presentations, depending on the severity of their condition, as well as varying degrees of surgical intervention depending upon geographical regions.[6] Diagnosing acute appendicitis clinically is complicated and requires combining information from multiple sources (such as patient history, laboratory tests and imaging studies). In an effort to help predict the risk of acute appendicitis, several easy-to-use scores have been utilized, but none has been widely adopted as a definitive tool.[7] However, CT abdomen has been most widely used investigation to make definitive diagnosis of this condition.[8]

Despite these advances in the medical field, the diagnosis of acute appendicitis still gets delayed in this day and age which may complicate the outcome of the patients as it may result in perforation of the already inflamed appendix that may require highly invasive laparotomy instead of a simple

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Received: 03 Apr 2023; revision received: 31 Oct 2023; accepted: 12 Mar 2024

appendectomy procedure.[9] Therefore, it is very important to search for such a tool which is not only easily accessible, financially feasible and quicker to get results from, to predict the occurrence of appendiceal perforation. One such method that has recently been undergoing research is "Hyperbilirubinemia" or raised serum bilirubin levels.[10] It has been hypothesized that appendicular tissue gangrene/ perforation can occur in appendicitis as a result of high intraluminal pressure and necrosis from ischemia of the mucosa. As a result, the cytotoxins helps the bacteria invade or translocate further into the parenchyma of the liver through the portal system which causes a disruption in excretion of bilirubin into the bile canaliculi leading to "hyperbilirubinemia".[10]

Based on this we conducted this study to determine whether presence of "hyperbilirubinemia" can serve as a useful laboratory parameter for predicting the presence of perforation of the appendix as well as a facilitating tool for making decision of performing early invasive intervention for improving the surgical outcome of the patients.

METHODOLOGY

This validation study on the patients admitted at the indoor surgical department of "Combined Military Hospital, Rawalpindi Pakistan" starting from September 2022 to February 2022 after taking approval from the ethical research committee of the institute (ERC#: 361). Sample size was calculated by utilizing WHO sample size calculator by assuming confidence level of 95%, precision of 9.05% and prevalence of "appendiceal perforation" of 28.5%,[11] Calculation gave a sample size of 96.

Inclusion Criteria: Patients who had age of 14 years or above, either male or female, and had been admitted with diagnosis of acute appendicitis were included in the study.

Exclusion Criteria: We excluded all those patients who presented with a history of pre-existing liver disease, had visually visible jaundice, had history of hemolytic anemia or had history of use of hepatotoxic medications (like hakeem medications/ anti-tuberculosis drugs).

Once selected, all the baseline characteristics of our included participants including their age, gender, duration of symptoms (hours) and serum bilirubin levels were documented. "Hyperbilirubinemia" was defined as having a total serum bilirubin levels more than 1mg/dl.[12] All the patients then underwent appendectomy by single team of skilled surgeons and the operative findings were documented to determine whether patent had "perforated appendicitis" or had "simple appendicitis". After that, based on the operative findings, true positive, false positive, true negative and false negative cases were identified. This was followed by drawing 2x2 contingency table. This was then used to calculate sensitivity (SN), specificity (SP), positive predictive value (PPV) and negative predictive value (NPV) of hyperbilirubinemia as a predictor for appendiceal perforation in acute appendicitis.

Data was analyzed by using Statistical Package for Social Sciences (SPSS) 22.00. Quantitative data (age, duration of symptoms and serum bilirubin levels) was represented using mean with standard deviation and the median (IQR). Qualitative data (gender, presence of hyperbilirubinemia and presence of appendiceal perforation) was represented by using percentage and frequency. A $p \leq 0.05$ was taken as significant.

RESULTS

Our study sample was 96 patients. In our study we found out that value of mean age of our study pool was 20.86±3.26 years. In our study, there were 46(47.90%) male participants while remaining 50(52.10%) participants were female. In our study mean value of duration of symptoms was 10.79±2.56 hours. Mean value of total serum bilirubin was 1.28±0.74 mg/dl. These baseline parameters are summarized in tabulated form below in Table-I.

Table-I: Baseline Parameters of Study Population (n=96)

Parameters		values
Mean age		20.86±3.26 years
Gender	Male	46(47.90%)
	Female	50(52.10%)
Duration of symptoms		10.79±2.56 hours
Mean serum bilirubin		0.74 mg/dl

After assessing this we found that composite frequency of patients who were found to have "hyperbilirubinemia" was 40(41.70%) while total number of patients who were found to have "appendiceal perforation" was 44(45.80%). Number of patients who had both hyperbilirubinemia as well as appendiceal perforation was 28(29.16%) while those who had "hyperbilirubinemia" but simple appendicitis were 12(12.50%). Similarly, patients who did not have "hyperbilirubinemia" but had "appendiceal perforation" were 16(16.67%) while those who nether had "hyperbilirubinemia" nor "appendiceal

perforation" were 40(41.67%). Based on these following 2x2 contingency table was drawn (Table-II).

Table-II: 2x2 Table of True Positives, True Negatives, False Positives and False Negatives (n=96)

	Perforated appendicitis	Simple appendicitis
Hyperbilirubinemia	28(29.16%) - (a)	12(12.50%) - (b)
No Hyperbilirubinemia	16(16.67%) - (c)	40(41.67%) - (d)

Based on the formulas mentioned above it was found that sensitivity (SN), specificity (SP), positive predictive value (PPV) and negative predictive value (NPV) of "hyperbilirubinemia" as a predictor for appendiceal perforation in acute appendicitis was 63.64%, 76.92%, 70.00% and 71.43%, respectively. This is tabulated below in Table-III.

Table-III: Diagnosis Parameters of Hyperbilirubinemia to predict Appendiceal Perforation (n=96)

Parameters	values
Sensitivity	63.64%
Specificity	76.92%
Positive predictive value	70.00%
Negative predictive value	71.43%

DISCUSSION

One of the most challenging conditions that surgeons face is making a definitive and early diagnosis of "acute appendicitis" which may lead to complications related to delay in the diagnosis and subsequent essential intervention for acutely inflamed appendix. Perforation of appendix is one such serious and life threatening complication that necessitates (a potentially avoidable) laparotomy and can even lead to even more dire consequence of development of (although rare) "necrotizing fasciitis".[13] Acute appendicitis that does not require emergency surgery has a relatively quick recovery time, but emergency appendectomy for gangrenous or perforated appendicitis can be dangerous. Early diagnosis is the most important aspect in preventing morbidities. However, one such measure, that is easy and quick is estimation of serum levels of bilirubin, is usually ignored to be performed in emergency room settings in patients with acute appendicitis.

In our study we found that the sensitivity of "hyperbilirubinemia" as a predictor for appendiceal perforation in acute appendicitis was quite low. Similar to our study, Vineed *et al.*,[14] Emmanuel *et al.*,[15] Hong *et al.*,[16] and McGowan *et al.*,[17] also reported that raised levels of serum bilirubin have relatively low sensitivity to predict occurrence of appendiceal perforation. Contrary to what we found and what was reported by aforementioned studies, Bakshi *et al.*,[10] and Atahan *et al.*,[18] reported a much higher value of sensitivity of "hyperbilirubinemia" as a predictor for "appendiceal perforation" in acute appendicitis making it a highly useful investigation in this regard.

Contrarily, in terms of specificity, our findings showed that "hyperbilirubinemia" is highly specific investigation to predict "appendiceal perforation". This finding of our study was congruent with what was reported by studies conducted by McGowen *et al.*,[17] Atahan *et al.*,[18] and Ramasamy Ramu *et al.*,[19] all of which stated that serum bilirubin levels are highly specific to predict "appendiceal perforation". Contrarily, opposite to the results of our study, Khan *et al.*,[20] reported significantly lower specificity of "hyperbilirubinemia" as a predictor for appendiceal perforation in acute appendicitis.

Based on findings of our study, "hyperbilirubinemia" can be considered a relatively useful tool to be used as a predictor for "appendiceal perforation" in acute appendicitis. Therefore, this can be included in the standard examination list of subjectively probable cases of acute appendicitis and additionally, in predicting the perforation of the already inflamed appendix. However, due to discrepancy between the findings of our study and previous studies we recommend that further researches should be conducted in this regard to help improving the management of this commonly encountered surgical morbidity.

CONCLUSION

In conclusion, raised serum levels of bilirubin can serve as a potentially useful, easily accessible and quick laboratory test for predicting appendiceal perforation.

Conflict of Interest: None.

Funding Source: None.

Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

SA & MSK: Data acquisition, data analysis, critical review, approval of the final version to be published.

PIA & SA: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

RIK & ARR: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity

of any part of the work are appropriately investigated and resolved.

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