International Journal of Research in Medical Sciences
Bali RS et al. Int J Res Med Sci. 2020 Mar;8(3):859-862
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012
DOI: http://dx.doi.org/10.18203/2320-6012.ijrms20200559

Original Research Article

Evaluating serum bilirubin levels in acute appendicitis and appendiceal perforation

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Received: 25 January 2020
Accepted: 07 February 2020

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ABSTRACT

Background: Acute appendicitis is one of the commonest surgical emergencies. Authors undertook this study to evaluate serum bilirubin levels in acute appendicitis and appendiceal perforation.
Methods: A retrospective study evaluating the serum bilirubin levels in acute appendicitis and appendiceal perforation was carried out for 6 years at three tertiary care hospitals at India from 2014 to 2019. Patients having acute appendicitis and appendiceal perforation, confirmed on histopathology, with no other medical or surgical comorbidity were included in the study.
Results: The total number of our study subjects was 927. 306 patients had appendiceal perforation, amongst these, 226 (74%) had hyperbilirubinemia. Out of the 621 patients having acute appendicitis only 186 (30%) had hyperbilirubinemia. The lowest and the highest serum bilirubin levels of this study group were 0.6 and 3.1 mg/dl, respectively, with an average of 1.6 mg/dl. In patients diagnosed to be having acute appendicitis, the lowest and highest serum bilirubin levels were 0.6 and 2.4 mg/dl, respectively, with an average of 1.3 mg/dl. As for the patients having appendiceal perforation the lowest and highest serum bilirubin levels were 0.8 and 3.1 mg/dl, respectively, with an average of 1.8 mg/dl.
Conclusions: Hyperbilirubinemia is seen in acute appendicitis but predominantly in appendiceal perforation, so serum bilirubin estimation may help us in diagnosing appendiceal perforation pre-operatively if and when used in conjunction with other available diagnostic modalities.

Keywords: Appendicitis, Appendiceal, Hyperbilirubinemia, Perforation

INTRODUCTION

The disease characteristics and management of appendicitis has evolved a lot since the first historical report of appendectomy from Europe over the past years.[1,2] Acute appendicitis is one of the commonest surgical emergency and appendectomy is a commonly performed surgical procedure. Despite being a common surgical emergency, achieving an accurate clinical diagnosis is problematic due to the fact that many an acute abdomen pathology have similar clinical signs and symptoms.[3]

Delay in diagnosing acute appendicitis may be detrimental to the patient as it may lead to complications such as intra-abdominal abscess, perforation, generalized peritonitis, etc. Nowadays, due to the availability of ultrasonography and computerized tomography, having accuracies of 85-90% for diagnosing acute appendicitis, the diagnosis of appendicitis can be made readily and accurately but the fact that these diagnostic modalities are

time consuming, costly and may not be available all the while, there arises a need to find cost effective and fairly accurate investigations to diagnose acute appendicitis and it's complications in time.[4-6]

The currently available blood tests and imaging studies do help in diagnosing acute appendicitis but are not very specific about its sequelae or the pathology involved.[7] The common consensus world over as to the best diagnostic tool for diagnosing any appendiceal pathology is clinical evaluation.[8]

A search of the literature reveals that many a study have been conducted in the recent past for assessing hyperbilirubinemia as a marker for acute appendicitis and appendicular perforation.[9-11]

Aim of the study was to evaluate serum bilirubin levels in acute appendicitis and appendiceal perforation.

METHODS

Authors conducted a retrospective study for evaluating serum bilirubin levels in acute appendicitis and appendiceal perforation. It was conducted at three tertiary care hospitals at India, namely Maulana Azad Medical College-Delhi, Government Medical College-Jammu and Government Medical College-Srinagar over a period of six years from January 2014 to December 2019. Authors included a total 927 subjects who came to surgery emergency, these had no other medical or surgical comorbidity and were confirmed to have acute appendicitis or appendiceal perforation by histopathology examination of the specimen [inclusion criteria]. All the routine investigations, namely, complete blood counts, serum electrolytes (sodium and potassium), serum urea, serum creatinine, electrocardiogram, chest skiagram, blood sugar levels and liver function tests were sent at the time of admission in the pre-operative period before any surgical or anesthetic intervention was done. Patients 12 years of age and younger were not included in the present study.

Serum bilirubin levels were ascertained by photometric testing using 2,4-dichloroaniline, based on the principle that direct bilirubin forms a red colored azo compound with diazotised 2,4- dichloroaniline in an acidic solution. Total serum bilirubin levels below 1.2 mg/dl were taken as normal. Statistical analysis was done using SPSS version 17.0. At the time of admission patients were started on intravenous fluids, antibiotics (ceftriaxone and metronidazole), opioid analgesics and antipyretics (where-ever required). All the patients gave an informed consent for the surgery beforehand. The patients were then operated upon under general anaesthesia and after an appendectomy was done the patients were managed as per their specific needs and condition in the post-operative period.

RESULTS

A total of 927 patients were enrolled as study subjects in this present study. There were 614 (66%) male and 313 (34%) females in this study group. The youngest and the eldest patients were 13 and 72 years old, respectively, with an average age of 29 years.

Six hundred and twenty-one patients had acute appendicitis and three hundred and six had appendiceal perforation. The diagnosis was confirmed on the histopathological examination.

Hyperbilirubinemia was present in 412 (44%) patients amongst the total 927, out of these 186 (20%) had acute appendicitis and 226 (24%) had appendiceal perforation. On analyzing the data further, out of the 306 patients diagnosed to have appendiceal perforation 226 (74%) had hyperbilirubinemia and out of the 621 patients having acute appendicitis only 186 (30%) had hyperbilirubinemia. The lowest and the highest serum bilirubin levels of this study group were 0.6 and 3.1 mg/dl, respectively, with an average of 1.6 (SD±0.26) mg/dl. In this study group, the lowest serum bilirubin level of 0.6 mg/dl was found in a female patient having acute appendicitis and the highest was 3.1 mg/dl in a female patient having appendiceal perforation. In patients diagnosed to be having acute appendicitis, the lowest and highest serum bilirubin levels were 0.6 and 2.4 mg/dl, respectively, with an average of 1.3 (SD±0.2) mg/dl. As for the patients having appendiceal perforation the lowest and highest serum bilirubin levels were 0.8 and 3.1 mg/dl, respectively, with an average of 1.8 (SD±0.34) mg/dl. On further analysis the p-value (<0.0001) was found to be statistically significant (Table 1) implying that hyperbilirubinemia was statistically significant in appendiceal perforation.

630 (68%) of this study subjects belonged to a rural region whilst 297 (32%) were from an urban region. The commonest pathogen isolated from the intra-peritoneal cultures of 313 of this study group was *E. coli.*

Table 1: Serum bilirubin levels in acute appendicitis and appendiceal perforation patients.

	Number of patients	Hyperbilirubinemia present in	Average serum bilirubin [mg/dl]
Appendiceal perforation	306	226	1.8
Acute appendicitis	621	186	1.3
Total	927	412	1.5

DISCUSSION

Numerous research articles in the literature have concluded that there is a significant association between hyperbilirubinemia and appendiceal perforation.[3,10,11] Also, many authors have suggested that pre-operative serum bilirubin levels attained at the time of admission, if used in conjunction with other diagnostic modalities like ultrasonography and computerized tomography scans can better aid us in diagnosing appendiceal perforation pre-operatively.[11,12]

Authors conducted this study to assess the pre-operative serum bilirubin levels in acute appendicitis and appendiceal perforation. The total number of study subjects was 927, out of which 614 (66%) were males and 313 (34%) were females. Poras C et al, had 80% males and 20% females in their study.[12] Hong YR, in their study of 1195 subjects had 51% males and 49% females.[4] These differences in the gender distribution of this study and the studies quoted above may be due to the different number of study subjects in the sample size.

The average age of this study sample was 29 years, with the youngest and the eldest patient being 13 and 72 years old, respectively. Khan S has reported an average age of 27.2 years of their study sample.[10] As authors did not include pediatric age group in this study and the fact that sample size of 927 was much more than the 45 study subjects of Khan S study can be the reason for the differences in the average ages of this study and that of Khan S. Addis DG et al, reported peak age of appendicitis between 10 and 30 years of age in American population.[13]

In these 927 study subjects, 621 (67%) had acute appendicitis and 306 (33%) had appendiceal perforation. Estrada JJ et al, in their study of 157 subjects had 116 (74%) patients of acute appendicitis and 41 (26%) patients of gangrenous or perforated appendicitis on final histopathological analysis.[11] Poras C et al, in their study of 50 patients had 84% patients of acute appendicitis and 16% patients of appendiceal gangrene/perforation, confirmed on histopathological analysis.[12] This difference can be due to the larger sample size of this study as compared to studies of Estrada JJ and Poras C.

Hyperbilirubinemia was found in 412 (44%) of this study group patients. Sand et al, found hyperbilirubinemia in 24.9% patients of their study group of 538 patients, out if which 50.7% were confirmed as having appendiceal perforation.[14]

Amongst 621 patients having acute appendicitis, 186 (30%) had hyperbilirubinemia with an average of 1.3 (SD ±0.2) mg/dl. The highest and the lowest levels were 2.4 mg/dl and 0.6 mg/dl, respectively. On the other hand, out of 306 patients of appendiceal perforation, 226 (74%) had hyperbilirubinemia with an average of 1.8 (SD±0.34) mg/dl. The highest and the lowest levels were 3.1 and 1.8 mg/dl, respectively. The average serum bilirubin level of this study subjects was 1.5 (SD±0.26) mg/dl. Majority (98%) of this study subjects had normal liver enzymes (AST, ALT, ALP). This observation suggests that there may be a dysfunction of the hepatocytes rather than them being damaged. Khan S had also reported similar findings in their research and observed that hyperbilirubinemia in acute appendicitis and its complications was probably due to hepatocyte dysfunction because of deranged hepatocyte permeability to bilirubin or the depressed ductule enzyme (Na-K ATPase) causing cholestasis.[10]

Authors also noted that hyperbilirubinemia was present in a higher number of patients having appendiceal perforation (74%) as compared to those having acute appendicitis (30%), pointing to the fact that bacteria and their endotoxins play an important role in this cholestasis, as Whiting et al, had demonstrated depressed excretion of bile in canaliculi in their study assessing the role of TNF-alpha in endotoxin mediated cholestasis.[15] Similar results about hyperbilirubinemia in severe abdominal infections have been reported by various authors in the literature.[11,16-19] An association between pro-inflammatory cytokine and nitric oxide triggered cholestasis and general gastrointestinal perforation, associated with poor prognosis, has been reported as well.[20,21]

The pathogenesis of hyperbilirubinemia in severe intra-abdominal infections, as associated with appendiceal perforation, is hypothesized to be due to bacteremia or endotoxemia causing impaired bilirubin excretion from bile canaliculi.[18,22]

CONCLUSION

Hyperbilirubinemia is seen in acute appendicitis but predominantly in appendiceal perforation. As serum bilirubin estimation is an inexpensive investigation it should be routinely incorporated in the pre-operative workup of patients having acute appendicitis or its complications, so that when used in conjunction with the other available investigative modalities it may better help us to diagnose appendiceal perforation pre-operatively leading to its better management.

ACKNOWLEDGEMENTS

All the authors collected and analysed the data and wrote the final manuscript.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

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Cite this article as: Bali RS, Rajni, Watali Y, Gupta SK, Gupta G. Evaluating serum bilirubin levels in acute appendicitis and appendiceal perforation. Int J Res Med Sci 2020;8:859-62.