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Original Research Article

Hyperbilirubinemia and appendicular perforation peritonitis

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ABSTRACT

Background: This study aims to assess the relationship between appendiceal perforation peritonitis and serum bilirubin levels, as has been reported previously in the literature.
Methods: A retrospective observational study was conducted at tertiary care hospital of India, namely Government Medical College-Srinagar, Maulana Azad Medical College-Delhi and Government Medical College-Jammu over a period of five years (January 2014 to December 2018). Authors collected and analysed the data of 306 patients, who had reported to the surgery emergency of the afore mentioned hospitals with complaints of acute abdominal pain and were later confirmed and managed as appendiceal perforation peritonitis (localized or generalized). Also, liver function tests of these 306 patients had been sent at the time of admission.
Results: Authors had 202 males and 104 females with an average age of 35 years in this study group. Hyperbilirubinemia was noted in 226 patients, with an average serum bilirubin level 1.8 mg/dl. In patients having total leucocyte counts higher than 11000 cells/cumm, the average serum bilirubin level was 2 mg/dl.
Conclusions: It may be safely concluded that a pre-operative evaluation of serum bilirubin levels may help us in better diagnosing appendiceal perforation when used in conjunction with other routine and advanced diagnostic modalities.

Keywords: Appendiceal, Peritonitis, Perforation, Hyperbilirubinemia

INTRODUCTION

Acute appendicitis is one of the commonest causes of abdominal pain leading to emergency surgery with an overall time risk of getting appendicitis being approximately 7-12%.[1] Despite being a common surgical condition and the availability of a wide array of modern diagnostic tools, it is not uncommon to have a delayed or mis-diagnosis of acute appendicitis due to its myriad clinical presentations.[2]

A search of the available literature points to an association between a variety of infectious diseases and severe intra- abdominal infections, as in appendiceal perforation peritonitis (Figure 1), with an elevated serum bilirubin levels; the pathogenesis being thought of as impaired bilirubin excretion from bile canaliculi due to bacteremia or endotoxemia.[3-5]

Many authors have reported that elevated bilirubin levels do help in diagnosing appendiceal perforation, if used in conjunction with other available diagnostic modalities.[2,6] Moreover, many authors have found hyperbilirubinemia in patients having severe post-operative infection after an appendectomy or with complicated appendicitis.[7-9] (Figure 2).

This study aims to assess the relationship between appendiceal perforation peritonitis and serum bilirubin levels, as has been reported previously in the literature.

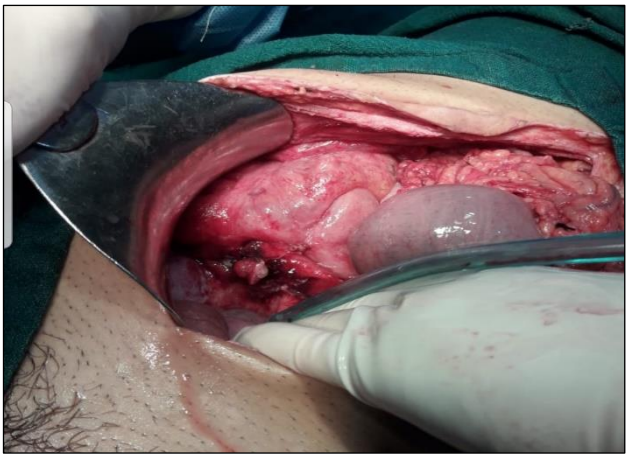

Figure 1: Appendiceal perforation peritonitis.

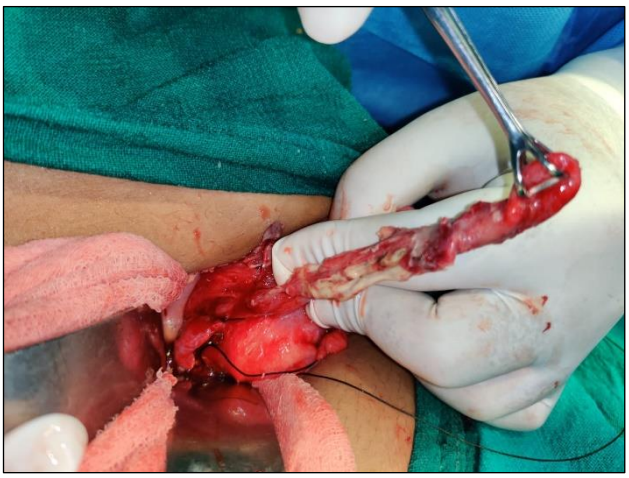

Figure 2: Perforated appendix with lump.

METHODS

This was a retrospective observational study conducted at tertiary care hospital of India, namely Government Medical College-Srinagar, Maulana Azad Medical College-Delhi and Government Medical College-Jammu over a period of five years (January 2014 to December 2018), as the author served at these institutes as a senior resident and consultant during the afore mentioned period. Authors collected and analysed the data of 306 patients, who had reported to the surgery emergency of the afore mentioned hospitals with complaints of acute abdominal pain and were later confirmed and managed as appendiceal perforation peritonitis (localized or generalized). Histopathology examination also confirmed the presence of gangrenous and perforated appendices. These 306 patients had got a pre-operative liver function tests done. Authors included only these 306 patients in this study as these had no other known medical comorbidity, were more than 12 years of age and had got a pre-operative liver function test done. All the patients of this study group had been operated upon after giving a detailed informed consent. Serum bilirubin levels were determined with photometric testing using 2,4-dichloroaniline based on the principle that direct bilirubin forms a red coloured azo compound with diazotised 2,4-dichloroaniline in an acidic solution. The reference range total and direct bilirubin was less than 1.2 and 0.2 mg/dl.

RESULTS

Of the 306 study subjects, 202 (66%) were males and 104 (34%) were females (Table 1). The youngest and the eldest patients in this study were 13 and 68 years old, respectively, with an average age of 35 years.

Hyperbilirubinemia was detected in 226 (74%) patients. Total serum bilirubin levels ranged from 0.8 to 3.1 mg/dl, the average being 1.8 mg/dl. Males and females had an average serum bilirubin levels corresponding to 1.6 and 2.1 mg/dl, respectively. Also, it was found that patients having a total leucocyte count (TLC) higher than 11000 cells/mm^3 had raised serum bilirubin levels averaging 2 mg/dl. 214 (70%) of this patient were from a rural region while 92 (30%) were from urban areas. Of the 306 study subjects, a positive intra-peritoneal pus culture report was found in 205 (67%) patients, with E. coli being the commonest pathogen isolated.

Table 1: Gender and serum bilirubin levels of this study group.

Gender	Males (n=202, 66%)	Females (n=104, 34%)
Hyperbilirubinemia	Present 226 (74%)	Absent 80 (26%)
Residence	Rural 214 (70%)	Urban 92 (30%)
Average serum bilirubin (mg/dl)	Males 1.6	Females 2.1

DISCUSSION

Acute appendicitis is a leading cause of emergency surgeries in pediatric as well as the adult age groups and there is a significant increase in morbidity and mortality in appendiceal perforation.[2]

Hyperbilirubinemia has been suggested as a new diagnostic tool for appendiceal perforation and severe intra-abdominal infection leading to sepsis.[10] The exact pathogenesis is not known but it has been postulated that it may be due to the dysfunction of the hepatocytes because of bacteria or endotoxemia leading to impaired or depressed excretion of bile in canaliculi.[11,12]

This study group comprised of 306 patients who fulfilled this studies inclusion criteria. Of these 306 test subjects, 202 were males and 104 were females corresponding to 66% and 44%, respectively. Khan in his study of 45 study subjects had 25 (55%) males and 20 (45%)females, whereas Chaudhary et al had 40 (80%) males and 10 (20%) females in their study group.[10,113] These

differences in the distribution of males and females with regards to this study and those conducted by Khan and Chaudhary et al, are probably due to the larger sample size of this study (>300 compared to <50) and that all the patients in this study had appendiceal perforation peritonitis whilst there's included acute appendicitis and it's complications.

The age of this study subjects ranged from 13 (youngest) to 68 (eldest) years with an average age of 35 years. Estrada et al had a median age of 33 years for patients with acute suppurative appendicitis and 31 years for patients having gangrenous perforated appendicitis and their age range was 5-66 years and 7-61 years, respectively, for the two groups.[6] This difference in this study and the one conducted by Estrada et al with regards to age of the study subjects could be due to the fact that they had included pediatric age group patients in their study whilst authors did not include them.

Among 214 patients amongst this study group were residing in a rural area and 92 were from urban areas. This predominance of people living in rural areas in this study can be due to the fact that as authors are a developing nation, the rural populace in this state does not have the same level of access to tertiary care hospitals or centres as compared to the urban populace, thus leading to a delay in the presentation of rural patients to a tertiary care centre and hence more complicated cases often are from the rural populace.

Hyperbilirubinemia (total serum bilirubin) was present in 226 (74%) of this study group patients. The minimum and maximum levels of serum bilirubin corresponded to 0.8 and 3.1 mg/dl, respectively, with an average of 1.8 mg/dl. Many authors have reported similar findings of hyperbilirubinemia in patients suffering from appendiceal perforation peritonitis.[6,10,13]

The average levels of serum bilirubin in male and female patients of this study group were 2.1 and 1.6mg/dl, respectively. Also, it was noted that patients having total leucocyte counts of more than 11000 cells/mm^3 had hyperbilirubinemia with an average serum bilirubin level of 2.2 mg/dl, thereby under lining the fact that patients having sepsis had greater levels of hepatic dysfunction. Liver injury due to administration of anaesthetic drugs, blood transfusions or medication was ruled out in this study group as the investigations (CBC, LFT, KFT, etc.) were sought at the time of admission before any of the above was instituted. Many authors concur that in appendicitis, bacterial overgrowth occurs leading to gangrene and perforation peritonitis subsequently. These bacteria are then transported to the portal venous system by direct invasion or translocation reaching the hepatic parenchyma and interfering with the excretion of bilirubin into the bile canaliculi, probably by the production of bacterial endotoxins. Hence the subsequent hyperbilirubinemia is biochemical rather than obstructive.[14-16] Estrada et al had observed in their study that the likelihood of appendiceal perforation was three times higher for patients having hyper-bilirubinemia.[6] Ramaswami et al have concluded in their study that total serum bilirubin levels have a predictive potential for diagnosing appendicular perforation.[17] Mallikarjuna et al have deduced from their study that patients having appendicular perforation have significant hyperbilirubinemia as compared to patients having uncomplicated appendicitis and that there is sufficient evidence to support its addition to the routine panel of investigations required to diagnose acute appendicitis and its complicatiopns.[18]

The commonest pathogen isolated in this study groups intraperitoneal [swab] cultures was *E. coli*. Similar results have been reported in the literature.[6]

CONCLUSION

It may be safely concluded that a pre-operative evaluation of serum bilirubin levels may help us in better diagnosing appendiceal perforation when used in conjunction with other routine and advanced diagnostic modalities.

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