Hyperbilirubinemia, a Predictor of the Severity of Acute Appendicitis

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Abstract

Introduction: Appendicitis is a challenging diagnosis to make especially in children/elderly and the diagnosis is mostly made on clinical grounds. To operate upon a case of suspected acute appendicitis is a double challenge for a budding surgeon and can be a nightmare if it turns out to be a complicated appendicitis (e.g., Gangrenous or Perforated) especially when the surgeon is on their own as the findings are relatively unexpected. The surgeon can perform better with planning if they are knowledgeable or have a high index of suspicion about the complexity of the situation. Raised serum bilirubin in acute complicated appendicitis can help in better understanding the severity of the situation, especially the complicated cases like perforated and/or gangrenous appendix.

Aim: This retrospective study's aim was to assess high bilirubin levels in acutely inflamed appendicitis and to look for its value in severity of acute inflammation of appendix. b: In this study, serum bilirubin was raised in 60% of cases of perforated/gangrenous appendicitis.

Conclusion: Therefore, a simple, cheap, and readily available blood test like Serum Bilirubin can be of great value and importance in the management of complicated appendicitis.

Keywords: Appendicitis; Appendicitis, Perforated; Appendicitis, Gangrenous; Appendectomy; Hyperbilirubinemia

Introduction

Acute appendicitis is one of the commonest cases on any given acute surgical on call intake. In acute appendicitis mucosal ulceration occurs early and this facilitates invasion of bacteria into the muscularis propria of the appendix thereby causing classical acute suppurative appendicitis. Subsequent events lead to oedema, elevated intraluminal pressure, and ischemic necrosis of mucosa, causing tissue gangrene and perforation. This process is associated with progressive bacterial invasion most likely facilitated by bacterial toxin. This severity of appendicitis and bacterial toxins puts a huge burden of septic load on liver which liver cannot metabolise causing S. Bilirubin to rise. As it is almost always a trainee who is going to be operating these cases in the event of need for a surgical intervention, a trainee may be caught off guard when faced with an unexpected presentation of a perforated / gangrenous appendix[1-3]. A raised Serum Bilirubin can be a red flag sign/ a word of caution for the operating surgeon about the complexity of the situation he/she is going to encounter. Serum Bilirubin is one of the basic, easily available, and inexpensive tests giving us a lot of information about the severity of the disease and thus better preparation for safe surgery.

Methods:

A retrospective study was performed in a 100 bedded secondary care adult teaching hospital in Saudi Arabia with approximately 35,000 annual emergency department visits. The authors used the medical records of the patients suspected of having appendicitis who presented to the emergency department between 2011 and 2016. We identified 117 patients with acute appendicitis after excluding those with other causes of hyperbilirubinemia among the 831 patients that underwent appendectomy. This

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retrospective chart review of the medical records, including laboratory, operative surgery notes and histologic results, was conducted to identify the diagnostic investigation in cases of perforated / gangrenous appendicitis.

Results

Among the 831 patients who underwent appendectomy, 781 (94%) cases were proven histo-pathologically as acute appendicitis. WBC were high in 58% of cases. Bilirubin was high in 72% of cases while fever was seen in 12.3% and tenderness in right iliac fossa in 97% of cases respectively. Out of 781 positive patients, 161 (20%) patients had perforated appendix/gangrenous appendicitis i.e., 90 patients had perforated and 71 had gangrenous appendicitis respectively. 117 (15%) patients had hyperbilirubinemia, whereas ALT was raised in only 64 (8%) patients in total with specifically in gangrenous/ perforated appendicitis it was present in only 45 patients (28%). Hyperbilirubinemia was seen in 97 patients (60%) with gangrenous/perforated appendicitis, with a cut-off point of >1.3 mg and has a sensitivity of 85%, specificity of 89%, a positive predictive value of 93%, and a negative predictive value of 96%.

Discussion

Acute appendicitis is one of the most common general surgical emergencies and appendicectomy being one of the first few independent/observed procedures for any surgical trainee[1]. Facing a gangrenous appendix or a perforated appendix is difficult scenario for a relatively new trainee in either open or laparoscopic surgery[2,3]. Having some beforehand knowledge of the condition of appendix is very valuable and vital in the surgical field and help can be sought at the opportune time.

Investigations to know the extent/severity of the acute appendicitis without radiological imaging is of interest. The ideal kind of investigation should be easy to get, not costly, quick and can be repeated easily if required. Observing serum bilirubin level merits consideration as it seems to elevate in perforated/ gangrenous appendicitis, its determination is fast and can be performed in Biochemistry panel with other commonly performed blood tests also can be repeated as and when required. White blood cell count (WBC) and C-reactive protein (CRP) have already been found somewhat to predict the severity of acute appendicitis, but without definitive and convincing results[4,5]. WBC and CRP elevation are markers of infection/elevation but will never suggest the complexity of situation like perforated/gangrenous appendix moreover WBC/CRP will be normal in a good number of cases of acute appendicitis.

Table 1: results and percentage of various blood test.

		No.	%
Total number of Appendicectomies done		831	
Leucocytosis	Positive	482	58%
	Negative	349	42%
Neutrophilia	Positive	467	56%
Bilirubin	Raised >1.1	117	14.9%
	Gangrenous / Perforated	97	60%
ALT (10-50)	Raised >50	64	08%
	Gangrenous / Perforated	45	28%
Histopathological examination (HPE)	Positives	781	94%
	Negative	50	6%
Perforated Appendix		91	11%
Gangrenous		70	9%

There are several diagnostic scoring systems such as the Alvarado score[6-8], the modified Alvarado score for use in paediatric patients[9,10], Paediatric Appendicitis Score[11], RIPASA (RajaIsteri Pengiran Anak Saleha Appendicitis) score for use in Asian patients[12] and a newer Appendicitis Inflammatory Response (AIR) score[13]. Most often these scoring systems combine symptoms (duration of pain, migration of pain, nausea, vomiting), signs (tenderness, fever) and/ or laboratory measurements (leucocytosis, CRP). All these scores point towards the diagnosis of acute appendicitis and not perforation or gangrene viz severity of acute appendicitis. Most surgical centres (especially in the West) attempt to reduce surgical procedures performed during the night and delaying appendectomy for 12-24 hrs does not seem to increase complications[14]. Conservative treatment with antibiotics has also been suggested for uncomplicated acute appendicitis in selected patients[15-17]. Appendiceal perforation/gangrene/ abscess combined with peritonitis always mandates an urgent operation or percutaneous drainage. Thus, there is definite need for a quick and safe investigation to specifically differentiate uncomplicated appendicitis with complicated acute appendicitis (perforated/gangrenous appendicitis). Elevated serum bilirubin level is commonly observed in patients suffering from a severe septic condition[18,19]. Rise of serum bilirubin, was reported, but the importance of the raised total bilirubin has not been stressed.

It was shown that in appendicitis mucosal ulceration

occurs early and this facilitates invasion of bacteria into the muscularis propria of the appendix thereby causing classical acute suppurative appendicitis[20]. Subsequent events lead to oedema, elevated intraluminal pressure, and ischemic necrosis of mucosa, causing tissue gangrene and perforation[21,22]. This process is associated with progressive bacterial invasion most likely facilitated by bacterial toxins. The number of organisms isolated from patients with gangrenous appendicitis is five times greater than those with acute suppurative appendicitis. The same findings were found significantly higher in peritoneal culture in patients with gangrenous/perforated appendicitis[23]. This elevated load of bacteria/toxins in appendicitis causes either direct invasion or translocation into the portal venous system. Direct invasion of bacteria into the hepatic parenchyma interferes with the excretion of bilirubin into the bile canaliculi by a mechanism that is thought to be caused by the bacterial endotoxin and is biochemical in nature rather than obstructive. There is evidence of bacterial translocation from inflamed gastrointestinal tract or peritonitis to the liver via the portal vein and the development of hepatitis and pyogenic liver abscess[24,25]. Two classical findings were described: firstly, simultaneous inflammation of the intestine (e.g., appendix), peritoneum and development of pyogenic liver abscesses, and secondly, bacteriological similarities of the gastrointestinal tract and pyogenic liver abscesses. These bacteria commonly reach liver from intra-abdominal organs, commonly from the appendix. Thus, it is beyond doubt hepatocellular dysfunction due to septic overload causing both at the level of hepatocytes (Hepatocellular) and intra-hepatic cholestasis despite the increased cardiac output and hepatic blood flow and decreased peripheral resistance.

Present study revealed that isolated hyperbilirubinemia without much elevation in the liver enzymes is an independent predictor for a complicated appendicitis. This was also shown by a study by Estrada et al[23] and other studies[26,27] showing nearly a threefold risk of perforated appendicitis in patients with total bilirubin levels greater than 1 mg/dL. Since the rise in Serum Bilirubin level was significantly higher in patients with appendiceal perforation, it has a definite predictive potential in these cases. Therefore, obtaining Serum Bilirubin values upon admission can be used in with or without more modern diagnostic tests such as CT scan, MRI, ultrasonography to help determine the presence of perforation and thus aid in prompt clinical management or where these tests are not available/ costly or where the risks of ionising radiations are too high.

Conclusion:

Serum Bilirubin estimation, a simple cheap and easily available test in every laboratory, can be added to the routine investigation list of clinically suspected case of acute appendicitis for the confirmation and the severity of the diagnosis. Rise of bilirubin level in cases of acute appendicitis should alarm the clinician of the severity of acute appendicitis, thus is a significant marker for complexity of appendicitis with possibility of perforation or gangrene and should prompt for early, timely intervention with safer surgery. It demands further research and generalised consensus for its use in all the cases of acute abdomen especially right iliac fossa pain.

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