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Severity of Acute Appendicitis is Predicted by Hyperbilirubinemia: A Clinical Clue

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Abstract **Original Research Article**

***Background*:** One of the most frequent abdominal emergencies requiring emergency surgery is acute appendicitis, and appendectomy is the most common emergency procedure performed globally. There is an urgent need for a predictor of the severity of acute appendicitis since delayed identification and treatment of severe appendicitis are linked to higher risks of perforation and postoperative morbidity, mortality, and prolong hospital stay. ***Objectives*:** The aim of this study was to assess how the severity of acute appendicitis is predicted by hyperbilirubinemia. ***Methods*:** This descriptive cross-section study was carried out in the Department of Surgery at Combined Military Hospital (CMH), Cumilla, during March 2021 to Feb 2023. A total of 80 patients purposing were included in this study. Among them 30 were diagnosed as complicated appendicitis and rest 50 were simple appendicitis patients. Patients diagnosed with complicated appendicitis and simple appendicitis irrespective of age and sex were included in the study. Patients who were not given consent to participate in the study were excluded from the study. After taking consent and matching eligibility criteria, data were collected from patients on variables of interest using the predesigned structured questionnaire by interview, observation, clinical examination and hematological investigation of the patients. Statistical analyses of the results were obtained by using window based Microsoft Excel and Statistical Packages for Social Sciences (SPSS-26), where required. ***Results*:** In complicated appendicitis 40% were male and 60% were female. In simple appendicitis 40% were male and 60% were female. The mean T-Bil in complicated appendicitis was 1.187mg/dL and 1.00 mg/dL in simple appendicitis. About 46.0% patients had hyperbilirubinemia in complicated appendicitis and 32.5% in simple appendicitis. Here, 58.0% had fever >37.3^{0}C in complicated appendicitis and 33.5% in simple appendicitis. About 69.7% had positive peritoneal irritation signs in complicated appendicitis and 55.5% in simple appendicitis. Complicated appendicitis was significantly more frequent in older patients (p= 0.010), patients with hyperbilirubinemiamia (p = 0.014), high CRP level (p < 0.001), positive peritoneal irritation signs (p =0.016), and fever (p < 0.001). Multivariate analysis revealed older age (>64 years) (p < 0.001), high CRP level (p < 0.001), hyperbilirubinemia (p < 0.038), and fever (p = 0.001) (odds ratios 3.34, 1.74, 7.63, and 2.34, respectively) as risk factors for complicated appendicitis. ***Conclusion*:** In conclusion, elevated CRP levels, fever, and hyperbilirubinemia may be helpful indicators of the severity of acute appendicitis, with hyperbilirubinemia being more helpful in individuals under 65 years old than in those over 65.

Keywords: Complicated appendicitis, Simple appendicitis, Hyperbilirubinemia.

INTRODUCTION

One of the most frequent abdominal emergencies requiring emergency surgery is acute appendicitis, and appendectomy is the most common emergency procedure performed globally [1]. Based on clinical signs, a physical exam, and laboratory results, other grading systems for appendicitis have been proposed, such as the Alvarado score [2]. It might be challenging to make a diagnosis of appendicitis when the classical symptoms and indications are lacking [3]. There is an urgent need for a predictor of the severity of acute appendicitis since delayed identification and treatment of severe appendicitis are linked to higher risks of perforation and postoperative morbidity, mortality and prolong hospital stay [4]. Numerous viral disorders have

been linked to high serum bilirubin levels, according to research [5]. The majority of the time, this discovery affects newborns who have gram-negative bacterial infections. Patients with severe intraabdominal infections have also been reported to experience it. The pathophysiology is thought to result from endotoxemia or bacteremia, which limit bilirubin excretion from the bile canaliculi [6]. Escherichia coli is one of the most often isolated bacteria in cases of appendicitis, one of the most frequently diagnosed surgical disorders. It is mostly unknown if patients with appendicitis and hyperbilirubinemia are related. Only a few case reports in the literature discuss the discovery of hyperbilirubinemia in individuals who either had difficult appendicitis or severe postoperative infection following appendectomy [5, 7]. In situations of acute appendicitis, hyperbilirubinemia that is not due to biliary obstruction or liver disease may be seen. Despite the fact that several researches have discussed the importance of hyperbilirubinemia for diagnosing acute appendicitis, its clinical utility is still debatable [3, 8-12].

METHODOLOGY

This descriptive cross-sectional study was carried out in the Department of Surgery at Combined Military Hospital (CMH), Cumilla, during March 2021 to Feb 2023. A total of 80 patients were included in this study. Among them 30 were diagnosed as complicated appendicitis and rest 50 were simple appendicitis patients. Patients diagnosed with complicated appendicitis and simple appendicitis irrespective of age and sex (both male & female) were included in the study. Patients who were not given consent to participate in the study were excluded from the study. After taking consent and matching eligibility criteria, data were collected from patients on variables of interest using the predesigned structured questionnaire by interview, observation, clinical examination and hematological investigation of the patients. Statistical analyses of the results were obtained by using window based Statistical Packages for Social Sciences (SPSS-26) where required.

RESULT

Table I: Characteristics and preoperative parameters in patients with complicated (perforated or gangrenous) and simple (phlegmonous or catarrhal) appendicitis

	Complicated appendicitis (n =30)	Simple appendicitis (n =50)	p value
Age (Mean ± SD) years	50 ±2.4	38 ± 6	0.010
WBC (Mean)	12,571/µL	11,845/µL	0.067
WBC >11,000/µL	23 (75.1%)	24 (48.0%)	0.203
CRP (Mean)	9.88 mg/dL	3.14 mg/dL	<0.001
CRP >0.5 mg/dL	28 (95%)	118 (64.1%)	<0.001
T-Bil (Mean)	1.187mg/dL	1.00 mg/dL	0.07
T-Bil >1.1 mg/dL	14 (46.0%)	16.25 (32.5%)	0.014
Fever >37.3^{0}C	17 (58.0%)	17 (33.5%)	<0.001
Peritoneal irritation signs	21 (69.7%)	28 (55.5%)	0.016

CRP: C-reactive protein, WBC: white blood cell, T-Bil: total bilirubin.

Table-I shows the characteristics and preoperative parameters in patients with complicated (perforated or gangrenous) and simple (phlegmonous or catarrhal) appendicitis. The mean (± SD) age of the patients in complicated appendicitis was 50 (±2.4) and in simple appendicitis was 38 (± 6). The mean WBC in complicated appendicitis was 12,571/µL and in simple appendicitis was 11,845/µL. About 75.1% patients had high WBC counts (>11,000/µL) in complicated appendicitis and 48.0% had high WBC counts (>11,000/µL) in simple appendicitis. The mean CRP in complicated appendicitis was 9.88 mg/dL and in simple appendicitis was 3.14 mg/dL. About 95% of patients had high CRP levels in complicated appendicitis and 64.1% in simple appendicitis.

The mean T-Bil in complicated appendicitis was 1.187mg/dL and 1.00 mg/dL in simple appendicitis. About 46.0% patients had hyperbilirubinemia in complicated appendicitis and 32.5% in simple appendicitis. Here, 58.0% had fever >37.3^{0}C in complicated appendicitis and 33.5% in simple appendicitis. About 69.7% had positive peritoneal irritation signs in complicated appendicitis and 55.5% in simple appendicitis.

Complicated appendicitis was significantly more frequent in older patients (p= 0.010), patients with hyperbilirubinemiamia (p = 0.014), high CRP level (p < 0.001), positive peritoneal irritation signs (p =0.016), and fever (p < 0.001).

Figure-1 shows that, in complicated appendicitis 40% were male and 60% were female.

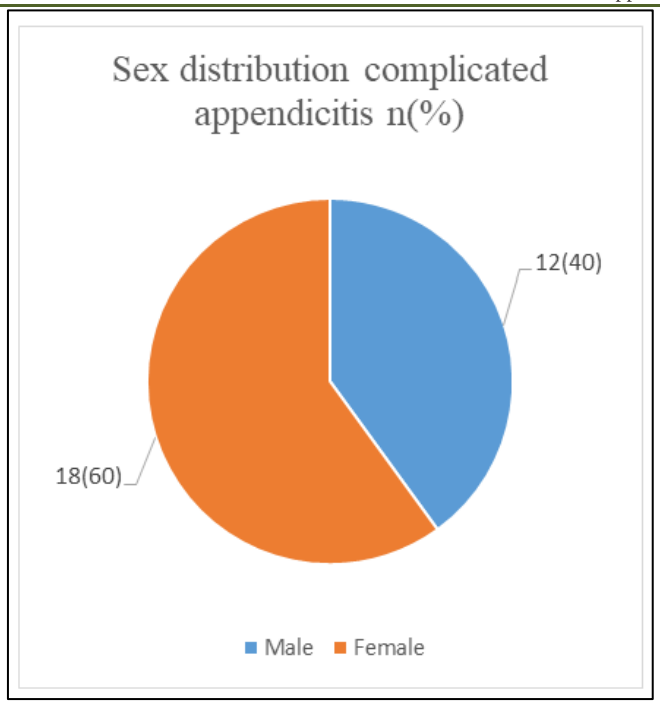

Figure-1: Distribution of the patients (complicated appendicitis) by sex (n=30)

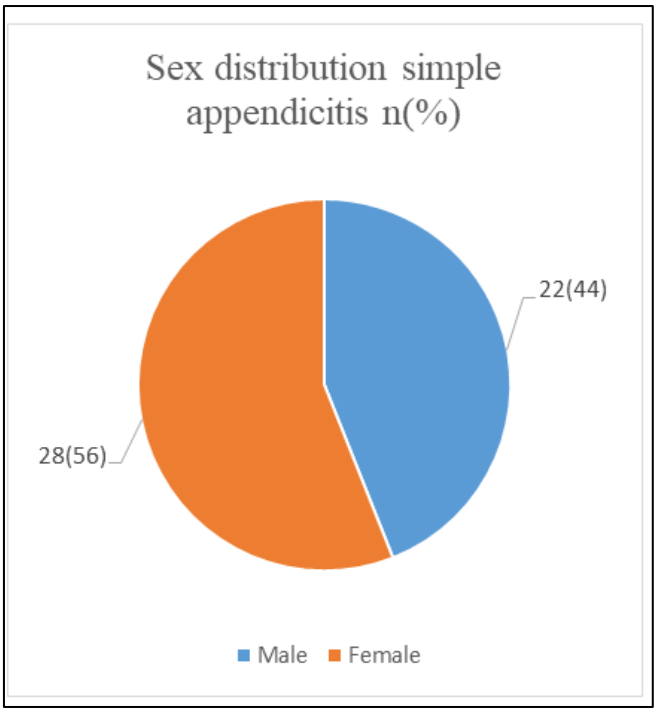

Figure-2: Distribution of the patients (simple appendicitis) by sex (n=50)

Table-II: Univariate and multivariate analyses in all patients

		Univariate analysis		**Multivariate analysis**
	OR	**95% CI**	**OR**	**95% CI**
Age (>64 years)	3.42	1.918–6.138	3.34	1.73–6.48
High CRP (>0.5 mg/dL	11.148	4.497–23.104	7.63	3.257–17.757
Hyperbilirubinemia (>1.1 mg/dL)	1.971	1.131–2.798	1.74	1.001–2.959
Fever (>37.3C)	2.962	1.791–4.281	2.34	1.499–4.057
Peritoneal irritation signs	1.781	1.104–2.808		

Multivariate analysis revealed older age (>64 years) ($p < 0.001$), high CRP level ($p < 0.001$), hyperbilirubinemia ($p < 0.038$), and fever ($p = 0.001$) (odds ratios 3.34, 7.63, 1.74, and 2.34, respectively) as risk factors for complicated appendicitis.

DISCUSSION

Acute appendicitis, which has an incidence of 7 to 22 per 10,000 people, is a frequent cause of abdominal pain in emergency department [13, 14]. Appendectomy can heal uncomplicated appendicitis (phlegmonous or catarrhal), but complex appendicitis (perforated or gangrenous) can result in consequences such as bacterial peritonitis, urinary problems, small intestinal obstruction, or the development of intra-abdominal abscesses. These complications could become fatal, emphasizing the importance of an accurate diagnosis and prompt treatment [4, 8]. However, because there are so many different symptom patterns, it can be challenging to make a conclusive diagnosis. Particularly in asymptomatic cases, most doctors are forced to conduct observation and re-evaluation, which lengthens hospital stays and delays definitive treatment, which could result in perforation [11]. The incidence of appendicitis misdiagnosis (15%) and appendiceal rupture have not changed despite the rise in diagnostic technologies like computed tomography and ultrasonography [15].

This current study shows that, in complicated appendicitis 40% were male and 60% were female. In simple appendicitis 44% were male and 56% were female. In this study the mean (± SD) age of the patients in complicated appendicitis was 50 (±2.4) and in simple appendicitis was 38 (± 6). The mean WBC in complicated appendicitis was 12,571/µL and in simple appendicitis was 11,845/µL. About 75.1% patients had high WBC counts (>11,000/µL) in in complicated appendicitis and 48.0% had high WBC counts (>11,000/µL) in simple appendicitis. The mean CRP in in complicated appendicitis was 9.88 mg/dL and in simple appendicitis was 3.14 mg/dL. About 95% of patients had high CRP levels in complicated appendicitis and 64.1% in simple appendicitis. According to Eren *et al*., high CRP levels are a crucial indication for identifying gangrenous or perforated appendicitis. High CRP levels may also be a significant predictor of complicated appendicitis since difficult appendicitis is linked to more severe inflammation than simple appendicitis [8]. Appendicitis has previously been linked to hyperbilirubinemia as a risk factor. According to Svinc *et al*., 3392 cases of perforated appendicitis were strongly linked with hyperbilirubinemia (>1.0 mg/dL) and a high neutrophil-to-lymphocyte ratio (>4.8) (odds ratios of 2.6 and 2.6, respectively [12]. In a study of 162 patients, Eren *et al*., discovered that elevated CRP (>0.5 mg/dL) and hyperbilirubinemia (>1.2 mg/dL) were linked to gangrenous or perforated appendicitis [8]. Hyperbilirubinemia was found by Nomura *et al*., as a risk factor for gangrenous appendicitis in Japan in a study of 410 patients, with an odds ratio of 1.7919 [9]. Therefore, appendiceal infection-related systemic endotoxinemia is the most likely cause of the increase in SB (serum bilirubin). It has been demonstrated by Utili *et al*., that there is a dose-dependent reduction in the excretion of bile salts from the isolated rat liver and that it is probable that Escherichia coli endotoxin causes direct injury at the cholangiolar level [16].

In this study, multivariate analysis revealed older age (>64 years) ($p < 0.001$), high CRP level ($p < 0.001$), hyperbilirubinemia ($p < 0.038$) and fever ($p = 0.001$) (odds ratios 3.34, 1.74, 7.63, and 2.34, respectively) as risk factors for complicated appendicitis. Older age was similarly found by Nomura *et al*., to be a predictor of gangrenous appendicitis. Age-related immunological impairment in patients causes inflammation to be more severe in older patients as compared to younger ones. This may help to explain why advanced age was an important predictor of complex appendicitis [9].

CONCLUSION

In conclusion, elevated CRP levels, fever, and hyperbilirubinemia may be helpful indicators of the severity of acute appendicitis, with hyperbilirubinemia being more helpful in individuals under 65 years old than in those over 65.

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