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Case Report

Acute calcular cholangitis in a diverse multi-ethnic population

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ABSTRACT

Introduction: Of the common complications of gallstones, acute cholangitis (AC) is the most rapidly lethal entity, making accurate diagnosis and early treatment imperative. Studies that report on the risk factors for the development of AC secondary to bile duct stones are rare. The aim of the present study is to identify clinical, laboratory and radiological factors that can predict which patients may develop cholangitis.
Patients and methods: The study is a retrospective case–control study based on patients admitted to Hamad General Hospital from June 2008 to November 2012 with a diagnosis of AC secondary to CBD stones. The control subjects were patients admitted during the same period with obstructive lithiasic jaundice, but not complicated by cholangitis. Countries of origin, age, sex, history of diabetes mellitus, hypertension, chronic liver disease, previous similar attack, previous cholecystectomy, previous bariatric surgery procedure, small bowel resection, significant weight loss and Crohn's disease were studied. Also, complete blood count (CBC), prothrombin time (PT), liver enzymes (ALT and AST), bilirubin, alkaline phosphatase, albumin, amylase creatinine and blood urea nitrogen (BUN) were studied. Finally the diagnostic investigations and the surgical and endoscopic procedures have been reported. Statistical analysis was performed.
Results: A total of 112 patients of 24 different nationalities (70 men and 42 women) were included in this study. Fifty-three patients (43.4%) presented with AC (cases group), and 59 (56.6%) were admitted for management of obstructive jaundice. Although Asians had a greater prevalence of cholangitis (57.4%) compared to Middle Easterners (35.7%) and Africans (33.3%), this was not statistically significant ($P = 0.066$). Laboratory tests significantly correlated to AC were leukocytosis ($P < 0.001$), elevated Bilirubin ($P = 0.005$), prolonged prothrombin time ($P = 0.001$), elevated INR ($P = 0.001$), elevated serum Creatinine ($P = 0.001$) and BUN ($P = 0.001$). In univariate analysis, the logistic regression model showed that dark urine, fever, elevated WBC and BUN were strongly associated with cholangitis.
Conclusions: Typical clinical signs of acute cholangitis, history of chronic liver disease, together with certain biochemical criteria are strongly associated with occurrence of acute lithiasic cholangitis. Further study on a larger sample of patients is required to confirm these findings and as an attempt to create a reproducible and simple scoring system able to predict and consequently facilitate early intervention in such cases.

1. Introduction

Cholangitis refers to inflammation of the biliary ductal system from a bacterial infection. The bile of healthy subjects is generally aseptic. However, bile culture is positive for microorganisms in 16% of patients undergoing a non-biliary operation, in 72% of patients with acute cholangitis, in 44% of patients with chronic cholangitis, and in 50% of those with biliary obstruction [1]. Bacteria in bile are identified in 90% of patients with choledocholithiasis accompanied by jaundice [2]. Patients with incomplete obstruction of the bile duct present a higher positive bile culture rate than those with complete obstruction of the bile duct [3].

Biliary infection alone does not cause clinical cholangitis unless biliary obstruction raises the intraductal pressure in the bile duct to levels high enough to cause cholangiovenous or cholangiolymphatic reflux [4]. Thus, acute cholangitis progresses from local biliary infection to the systemic inflammatory response syndrome (SIRS), and advanced disease leads to sepsis with or without organ dysfunction [5].

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While analysis of the conditions related to the development of acute cholangitis is warranted, most studies have focused primarily on the treatment and outcomes of acute cholangitis; thus, the predisposing factors for the development of acute cholangitis are not fully understood, and studies that report on the risk factors for acute cholangitis in patients with bile duct stones are rare [6]. Therefore, it is important to identify the factors that predispose patients to acute cholangitis and to determine the proper timing for the performance of biliary drainage [7].

Cholangitis is reported in all races. No study is published in the literature, according to our search, comparing patients from different racial origins. As residents in Qatar are very diverse in their racial origin, we hypothesize that acute cholangitis is more common among certain races, so the incidence and course of acute cholangitis is studied among the thirteen different nationalities included in our study.

The aims of this study were to first identify at an early stage clinical, biochemical, and etiologic variables that may be useful in predicting AC in patients with obstructive jaundice. A second goal was to determine whether AC is more common among certain ethnic groups.

2. Methods

This is a case–control study design. Study subjects were selected from patients admitted to Hamad General Hospital, which is the only referral hospital in the state of Qatar during the period from June 2008 to November 2012. The study protocol was fully approved by legal ethical committee in Hamad Medical Corporation (approval number: HMC 41020019).

All cases diagnosed as AC secondary to CBD stones on admission to the emergency department of Hamad General Hospital were eligible. The control subjects were patients admitted during the same period because of calcular obstructive jaundice, but not complicated by cholangitis. The major source of information was medical records.

History of diabetes mellitus, hypertension, chronic liver disease, previous similar attack, previous cholecystectomy, previous bariatric surgery procedure, small bowel resection, significant weight loss and Crohn's disease were documented for all cases. Laboratory investigations such as complete blood count (CBC), prothrombin time (PT), serum liver enzymes (ALT and AST), serum bilirubin, serum alkaline phosphatase, serum albumin, serum amylase and serum creatinine and blood urea nitrogen (BUN) were all documented for all cases. All patients underwent trans-abdominal ultrasound examination, with some undergoing abdominal CT scans or Magnetic Resonance Cholangiopancreatography (MRCP). ERCP reports, operative notes, and discharge summaries were also reviewed.

In the control group, the admission diagnosis was calcular obstructive jaundice. All data collected in the cases group were also documented in the control group in exactly the same manner.

2.1. Statistical methods

Categorical and continuous variables were expressed as frequency (percentages) and mean ± SD respectively. A student t-test was used to compare differences between cases and control. Associations of categorical variables with cases and controls were assessed using chi-square test. When expected cell frequency was inadequate, a Fisher Exact test was used instead. Variables that appeared significant in univariate analysis were further analyzed in a logistic regression model applying backward stepwise model selection procedure. A two-sided P value of ≤0.05 was considered to be statistically significant. All statistical analyses were done using SPSS 19.0 statistical package (SPSS Inc. Chicago, IL).

3. Results

A total of 112 patients (70 men and 42 women) were included in this study with a mean age of 45.7 ± 14.1 years (range, 20–92 years). These patients were of 24 different nationalities and the most common were Qatari (15.6%) and Indian (12.3%). Of the 112 patients, 53 (43.4%) presented with AC (cases group) and 59 (56.6%) were admitted for management of CBD stones or obstructive jaundice (control group).

Six cases required emergency endoscopic retrograde cholangiopancreatography (ERCP) with drainage of the biliary tree (11.4%), and AC improved rapidly after biliary decompression in those patients. The rest of the patients in the cases group (n = 47) improved on antibiotic and supportive measures. One patient died from uncontrolled septicemia despite successful decompression of the biliary obstruction; this patient had underlying chronic liver disease, while two patients expired after discharge due to unrelated chronic diseases. Laparoscopic cholecystectomy and intraoperative cholangiogram were performed in all cases except in the patient who died from septic shock. No mortality was recorded among patients included in the control group.

There were no differences in age between cases and controls. However, men were more likely to have AC than women (P > 0.002). Despite the fact that we included patients of 24 different nationalities in the study, no statistical correlation was found between nationality and incidence of AC. Moreover, there was no statistically significant association between patient's ethnicity and outcome in both groups. Although Asians had greater prevalence of AC (57.4%) compared to Middle Easterners (35.7%) and Africans (33.3%), this was not statistically significant (P = 0.066) (Table 1).

Among presenting symptoms, fever and dark urine were more common among cases. Patient history was not associated with AC except for history of chronic liver disease (P = 0.003) (Table 1).

Some laboratory findings were significantly correlated to AC such as leukocytosis (P < 0.001), elevated Bilirubin (P = 0.005), prolonged prothrombin time (P = 0.001), elevated INR (P = 0.001), elevated serum Creatinine (P = 0.001) and BUN (P = 0.001) (Table 2).

Table 1
History and clinical examination data on admission in control and cases groups.

	Controls (n = 59)	Cases (n = 53)	P-value
Age (years)	45.6 ± 15.5	45.3 ± 13.2	0.922
Gender			
Male	31 (44.3)	39 (55.7)	0.022
Female	28 (66.7)	14 (33.3)	
Ethnicity			
Middle Eastern	27 (64.3)	15 (35.7)	
Asian	26 (42.6)	35 (57.4)	0.066
African	6 (66.7)	3 (33.3)	
Symptoms			
Pain	55 (52.4)	50 (47.6)	0.999
Fever	18 (33.3)	36 (66.7)	<0.001
Vomiting	36 (60.0)	24 (40.0)	0.096
Yellowish discoloration	15 (50.0)	15 (50.0)	0.731
Dark urine	6 (31.6)	13 (68.4)	0.043
Patient history			
Similar disease	37 (54.4)	31 (45.6)	0.648
Weight loss	3 (75.0)	1 (25.0)	0.620
Bariatric procedure	0 (0.0)	1 (100.0)	0.473
Small bowel resection	0 (0.0)	1 (100.0)	0.473
Crohn's disease	0 (0.0)	3 (100.0)	0.103
Previous cholecystectomy	38 (56.7)	29 (43.3)	0.296
Chronic liver disease	1 (9.1)	10 (90.9)	0.003
Hypertriglyceridemia	5 (83.3)	1 (16.7)	0.210
Signs			
Tenderness	43 (46.2)	50 (53.8)	0.003
Jaundice	27 (44.3)	34 (55.7)	0.051
Fever	10 (20.8)	38 (79.2)	<0.001