Risk Factors Associated with Acute Cholecystitis Among Patients with Gallstones

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Abstract

Acute cholecystitis is one of the most common complications of gallstone disease and represents an important cause of hospital admission. This case-control study was conducted to evaluate the socio-demographic and medical profile of patients with acute cholecystitis and to identify the risk factors associated with the disease. The study included 155 patients diagnosed with acute cholecystitis who were admitted to hospitals in Basrah and 155 age- and sex-matched controls during the period from 1st March to 31st July 2014. Data were collected through direct interviews using a specially designed questionnaire developed for the purpose of the study. Information obtained included socio-demographic characteristics, past medical history, parity, drug history, and family history of acute cholecystitis. In addition, body weight and height were measured for all participants. The results showed that acute cholecystitis occurred predominantly among females. The most affected age group was 31–40 years among females and ≥61 years among males. The most common presenting symptoms among patients with acute cholecystitis were right upper abdominal pain, nausea, vomiting, and fever. Univariate analysis demonstrated that a history of diabetes mellitus, a history of cardiovascular disease, and the presence of three or more gallstones were significantly associated with an increased risk of acute cholecystitis. However, logistic regression analysis revealed that none of these variables represented an independent significant risk factor for acute cholecystitis. The study highlights the importance of evaluating clinical and medical characteristics associated with acute cholecystitis among patients with gallstone disease.

Keywords: Acute cholecystitis, Gallstones, Risk factors, Diabetes mellitus, Cardiovascular disease

INTRODUCTION

Acute calculous cholecystitis (AC) is one of the most common complications of cholelithiasis and represents a major cause of hospital admission and surgical intervention worldwide. Gallstone disease affects more than 20 million Americans annually and results in healthcare costs exceeding 6.3 billion dollars. (1,2) The need for cholecystectomy in patients with gallstones depends largely on the presence and severity of symptoms. While some patients may experience mild dyspeptic symptoms or intermittent abdominal discomfort, others develop severe gallbladder inflammation in the form of acute cholecystitis, which requires urgent medical and surgical management. (3,4) Laparoscopic cholecystectomy has become the treatment of choice for symptomatic gallstones; however, the procedure remains technically challenging in acute cholecystitis because of the increased risk of bile duct injury and postoperative morbidity. (5,6) Identifying patients at increased risk for developing AC may therefore help physicians perform earlier intervention and prevent serious complications.

The gallbladder is a hollow organ located beneath the right lobe of the liver and functions mainly in the storage and concentration of bile. (8,9) Anatomically, it consists of the fundus, body, and neck, which continues as the cystic duct and joins the common hepatic duct to form the common bile duct. (10) The gallbladder stores approximately 30–60 mL of bile and releases it into the duodenum in response to cholecystokinin stimulation after food intake, particularly fatty meals. (11) Bile assists in fat digestion and absorption, while the gallbladder concentrates bile by reabsorbing water and electrolytes. (11)

Gallstones are crystalline concretions formed within the gallbladder through precipitation of bile components. (12) They may remain asymptomatic or migrate into the biliary tract, leading to complications such as acute cholecystitis, cholangitis, pancreatitis, and gallstone ileus. (12) Gallstones are commonly classified into cholesterol stones, pigment stones, and mixed stones according to their composition. (13,14) Gallstone disease is particularly common among females, obese individuals, multiparous women, and people over forty years old, summarized traditionally as the "fair, fat, fertile, female, and forty" risk profile. Epidemiological studies indicate that 10–20% of adults in Western countries develop gallstones, and approximately one-third may progress to acute cholecystitis. (15,16,17) Gallstone disease is also common in southern Iraq, as demonstrated in studies conducted in Basrah. (18,19)

Several risk factors contribute to the development of acute cholecystitis. Female gender, advanced age, obesity, pregnancy, parity, diabetes mellitus, cardiovascular disease, oral contraceptive use, sickle cell anemia, ethnicity, and genetic predisposition all increase the likelihood of gallstone formation and gallbladder inflammation. (20,21,22,23,24,25,26,27, 28,29,30,31,32,33,34,35,36) Diabetes and cardiovascular disease are particularly associated with severe forms of AC because vascular compromise and gallbladder ischemia may worsen inflammation. (23,30)

Patients with acute cholecystitis are commonly present with right upper quadrant or epigastric pain, fever, nausea, vomiting, and tenderness on abdominal examination. (38,41) Diagnosis depends on clinical findings, laboratory investigations, and imaging studies including ultrasonography, which remains the most sensitive and commonly used diagnostic modality. (42,43,44,45) Management involves stabilization, fluid replacement, antibiotics, antibiotics, analgesia, and surgical intervention when indicated. (47,48,49,50,51,52,53,54,55,56)

The present study aimed to evaluate the socio-demographic and medical profile of patients with acute cholecystitis and to identify the risk factors associated with acute cholecystitis among patients with gallstones.

METHODS

This case-control study was conducted in Basrah, Iraq, during the period from 1st March to 31st July 2014 to investigate the socio-demographic and medical risk factors associated with acute calculous cholecystitis. The study included 155 patients with a confirmed diagnosis of acute calculous cholecystitis admitted to Basrah General Hospital (135 cases) and Al-Sader Teaching Hospital (20 cases). The diagnosis of acute cholecystitis was established clinically by expert surgeons and confirmed by abdominal ultrasonography.

Clinical diagnosis was based on the presence of typical manifestations of acute cholecystitis, including right upper quadrant abdominal pain and positive Murphy's sign in all patients. Ultrasonographic confirmation was based on the presence of gallstones together with one or more characteristic findings, including gallbladder wall thickness greater than 4 mm, presence of pericholecystic fluid, and positive ultrasonographic Murphy's sign. (57,58)

Patients with gallstones and a normal gallbladder, chronic cholecystitis, or acalculous cholecystitis were excluded from the study.

The control group consisted of 155 age- and sex-matched individuals who attended the ultrasonography unit at Basrah General Hospital. Controls were selected from both inpatient and outpatient departments. All controls had asymptomatic gallstones that were detected incidentally during routine abdominal ultrasonography performed for unrelated medical indications. (59) All ultrasonographic examinations for both cases and controls were performed by the same specialist radiologist to ensure consistency of assessment.

Data were collected using a specially designed questionnaire developed for the purpose of the study. Information obtained included socio-demographic characteristics, type of abdominal pain, past medical history, parity, history of oral contraceptive pill use, family history of acute cholecystitis, and other relevant clinical data. Data collection was conducted through direct face-to-face interviews by the

investigator. The purpose of the study was explained to all participants, and verbal informed consent was obtained prior to participation. No participant refused inclusion in the study.

Body weight and height were measured directly by the investigator for both cases and controls using the same weighing scale and a standard measuring tape. Body mass index (BMI) was calculated using the formula: weight in kilograms divided by height in meters squared (kg/m²). BMI was categorized into underweight (<18.5 kg/m²), normal weight (18.5–24.9 kg/m²), overweight (25–29.9 kg/m²), and obese (≥30 kg/m²). (61)

The studied variables included age, parity, medical history of diabetes mellitus, cardiovascular disease, sickle cell disease, history and duration of oral contraceptive pill use, family history of acute cholecystitis, ultrasonographic findings, number and size of gallstones, gallbladder wall thickness, and presence of pericholecystic fluid. Age was categorized into five groups: 20–30, 31–40, 41–50, 51–60, and ≥61 years. Parity was classified as nulliparous or multiparous (1–4 births). (60)

Ethical and administrative approval to conduct the study was obtained from the Basrah Health Directorate before commencement of data collection.

Data were entered and analyzed using the Statistical Package for Social Sciences (SPSS) version 16. Chi-square test, degrees of freedom, and logistic regression analysis were used to evaluate the association between selected risk factors and acute calculous cholecystitis. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated. A p-value of less than 0.05 was considered statistically significant.

RESULTS

A total of 155 patients with acute cholecystitis and 155 age- and sex-matched controls were included in the study. Females constituted the majority of cases (58.7%), with a female-to-male ratio of approximately 1.4:1. The most affected age group among females was 31–40 years, whereas among males it was ≥61 years. The mean age was higher among males compared with females.

Table 1. Demographic characteristics of patients with acute cholecystitis

Variable	Male	Female	Total
Number of cases	64 (41.3%)	91 (58.7%)	155 (100%)
Mean age ± SD (years)	53.59 ± 15.82	41.37 ± 10.8	—

Age group (years)	Male n (%)	Female n (%)	Total n (%)
20–30	8 (12.5)	11 (12.1)	19 (12.2)
31–40	11 (17.2)	34 (37.5)	45 (29.0)
41–50	3 (4.7)	31 (34.1)	34 (22.0)
51–60	2 (3.1)	7 (7.6)	9 (5.8)
≥61	40 (62.5)	8 (8.8)	48 (31.0)

Right upper abdominal pain associated with nausea, vomiting, and fever was the most common presenting symptom among patients with acute cholecystitis (81.3%). Regarding parity among females, no statistically significant association was found between parity and risk of acute cholecystitis (P = 0.73).

Table 2. Clinical presentation and parity among patients with acute cholecystitis

Initial symptom	No.	%
Epigastric pain and right upper abdominal pain	11	7.1
Epigastric pain, right upper abdominal pain, nausea and fever	18	11.6
Right upper abdominal pain, nausea, vomiting and fever	126	81.3
Total	155	100

Parity	Cases n (%)	Controls n (%)	Total n (%)
Nulliparous	14 (15.4)	18 (19.8)	32 (17.6)
1–4	28 (30.8)	27 (29.7)	55 (30.2)
≥5	49 (58.8)	46 (50.5)	95 (52.2)

Chi-square = 0.613, P = 0.73

History of diabetes mellitus and cardiovascular disease showed significant associations with acute cholecystitis, whereas sickle cell disease was not significantly associated with disease occurrence.

Table 3. Association between medical history and risk of acute cholecystitis

Risk factor	Cases n (%)	Controls n (%)	Odds Ratio (95% CI)	P-value
Diabetes mellitus	17 (11.0)	0 (0.0)	2.123 (1.881–2.397)	0.0001
Cardiovascular disease	31 (20.0)	15 (9.7)	2.333 (1.203–4.524)	0.011
Sickle cell disease	64 (41.3)	54 (34.8)	1.315 (0.831–2.083)	0.242

No statistically significant association was identified between oral contraceptive pill use, duration of use, or family history of acute cholecystitis and the risk of disease occurrence.

Table 4. Association between reproductive and family history factors and acute cholecystitis

Variable	Cases n (%)	Controls n (%)	Odds Ratio (95% CI)	P-value
Oral contraceptive pill use	41 (45.1)	42 (46.2)	0.957	0.882
Family history of acute cholecystitis	61 (39.4)	53 (34.2)	1.249 (0.786–1.983)	0.346

Duration of oral contraceptive use	Cases n (%)	Controls n (%)
<1 year	13 (14.2)	11 (12.1)
1–3 years	15 (16.5)	17 (18.5)
>3 years	13 (14.2)	14 (15.4)

The number of gallstones showed a statistically significant association with acute cholecystitis, with patients having three or more stones being at greater risk. In contrast, stone size was not significantly associated with disease occurrence.

Table 5. Association between gallstone characteristics and acute cholecystitis

Variable	Cases n (%)	Controls n (%)	P-value
Number of stones			0.034
1 stone	17 (11.0)	34 (21.9)	
2 stones	36 (23.0)	31 (20.0)	
≥3 stones	102 (66.0)	90 (58.1)	
Stone size			0.56
<2 cm	128 (82.6)	124 (80.0)	
≥2 cm	27 (17.4)	31 (20.0)	

Although overweight and obesity were common among study participants, no statistically significant association was found between body mass index and the risk of acute cholecystitis (P = 0.843).

Table 6. Body mass index and risk of acute cholecystitis

BMI category	Cases n (%)	Controls n (%)	Total n (%)
Underweight	15 (9.7)	13 (8.3)	28 (9.1)
Normal weight	50 (32.3)	51 (33.0)	101 (32.6)
Overweight	51 (33.0)	57 (36.7)	108 (34.8)
Obese	39 (25.0)	34 (22.0)	73 (23.5)

Chi-square = 0.829, P = 0.843

Logistic regression analysis was performed to determine independent predictors of acute cholecystitis. Although diabetes mellitus, cardiovascular disease, and number of gallstones were associated with acute cholecystitis in univariate analysis, none remained statistically significant independent predictors after adjustment.

Table 7. Logistic regression analysis of selected risk factors for acute cholecystitis

Independent variable	B	Chi-square	P-value	OR
History of diabetes mellitus	-41.315	0.000	0.997	0.000
History of cardiovascular disease	-20.406	0.000	0.997	0.000
Number of gallstones	0.468	2.222	0.136	1.597

DISCUSSION

Acute cholecystitis (A.C) represents a spectrum of clinicopathological conditions ranging from chronic cholecystitis with intermittent biliary colic to severe acute inflammation associated with prolonged abdominal pain, fever, leukocytosis, and cholestasis.(15) Because acute cholecystitis is associated with increased operative difficulty and postoperative morbidity, identification of patients at high risk for developing the disease is important to allow early surgical intervention before complications occur.

The present study demonstrated that females constituted the majority of patients with acute cholecystitis, accounting for 58.7% of cases, with a female-to-male ratio of approximately 1.4:1. This finding is consistent with most previous studies, which reported female predominance in gallbladder disease.(62,63) Hormonal factors, particularly the effects of estrogen on cholesterol metabolism and bile composition, may explain the higher frequency of gallstone-related disease among women. The most affected age group among females was 31–40 years, whereas male patients tended to be older, with a mean age of 53.59 ± 15.82 years compared with 41.37 ± 10.8 years among females. These findings differ from other studies reporting that acute cholecystitis occurs predominantly among elderly patients.(64,65)

Regarding clinical presentation, most patients with acute cholecystitis presented with right upper abdominal pain associated with nausea, vomiting, and fever (81.3%). Similar clinical findings were reported by other investigators.(66,67) These manifestations are considered typical features of acute gallbladder inflammation and usually prompt patients to seek urgent medical care.

The present study found no statistically significant association between parity and the risk of acute cholecystitis. However, previous studies have shown that pregnancy may predispose women to biliary tract disease because hormonal changes during pregnancy increase bile stasis and cholesterol saturation.(68) Other studies also demonstrated that obesity and overweight among women may further increase the risk of gallbladder disease during and after pregnancy.(69,70) Furthermore, pregnancy has been identified as a risk factor for hospitalization related to gallstone disease during the postpartum period. (71)

No significant association was observed between sickle cell disease and the risk of acute cholecystitis in the current study. Nevertheless, gallstones are known to occur commonly in patients with sickle cell disease because of chronic hemolysis and increased bilirubin production. Elective laparoscopic cholecystectomy is therefore recommended in these patients to reduce complications and avoid diagnostic confusion between acute cholecystitis and sickle cell crisis. (72,73)

The current study showed that family history of acute cholecystitis was associated with an increased risk of disease occurrence. This finding is comparable to other studies that reported a significant relationship between positive family history and gallbladder disease, suggesting a possible genetic or familial predisposition. (65)

A significant association was found between diabetes mellitus and acute cholecystitis in the present study. Traditionally, diabetic patients with asymptomatic gallstones were believed to have a higher risk of developing symptoms and complications because autonomic neuropathy may mask the classical symptoms of acute cholecystitis.(74) However, another study reported that asymptomatic gallstones in diabetic patients do not necessarily carry a higher risk of complications.(75) In contrast, other investigators found that diabetes mellitus and metabolic syndrome are associated with complicated gallstone disease. (76)

The study also demonstrated a significant association between cardiovascular disease and the risk of acute cholecystitis. Similar findings were reported in previous studies. (77,78) The relationship between cardiovascular disease and gallbladder inflammation may be related to shared risk factors such as obesity, metabolic syndrome, and vascular compromise affecting gallbladder perfusion.

No statistically significant association was identified between oral contraceptive pill use and acute cholecystitis. Similar findings were reported in previous studies suggesting that modern oral contraceptive formulations may not significantly increase the risk of gallbladder disease. (79,80) Nevertheless, some researchers recommended

evaluating the effects of oral contraceptive pills on bile composition and gallbladder function rather than waiting for clinical disease to develop.(79)

The number of gallstones showed a significant association with acute cholecystitis in the current study. Patients with multiple gallstones were more likely to develop symptoms and complications. Similar findings were reported in studies demonstrating that multiple small gallstones increase the likelihood of biliary obstruction and gallbladder inflammation. (81)

In contrast, stone size was not significantly associated with the risk of acute cholecystitis in the present study. However, another study suggested that large gallstones measuring more than 2.5 cm may increase the risk of symptomatic and complicated gallbladder disease. (76)

Body mass index (BMI) was not significantly associated with acute cholecystitis in this study. This finding differs from other studies reporting obesity and overweight as important risk factors for gallbladder disease and acute cholecystitis. (76) The absence of statistical significance in the current study may be related to sample size or the distribution of BMI categories among participants.

CONCLUSION AND RECOMMENDATIONS

The present study concluded that acute cholecystitis was more common among females, with the highest frequency occurring in females aged 31–40 years and males aged 61 years or older. The most common clinical presentation included right hypochondrial pain associated with nausea, vomiting, and fever. Univariate analysis demonstrated significant associations between acute cholecystitis and a history of diabetes mellitus, cardiovascular disease, and the presence of three or more gallstones. However, logistic regression analysis showed that none of these variables represented independent significant risk factors for acute cholecystitis. Based on these findings, prophylactic cholecystectomy is not recommended routinely for patients with asymptomatic gallstones, including those with diabetes mellitus, cardiovascular disease, or multiple gallstones. Further large-scale studies involving larger sample sizes from both sexes are recommended to confirm or refute these findings and to better identify independent risk factors associated with acute cholecystitis.

Conflicts of Interests: None

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Ethical Approvals: Ethical approval for the study was obtained from the relevant institutional review board, and informed consent was acquired from all participants prior to their inclusion in the study.

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