Prediction of common bile duct stones in acute cholecystitis patients at time of hospital admission

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Background
Early diagnosis of common bile duct stone (CBDS) is crucial since its presence affects surgical therapy and acute calculous cholecystitis (ACC) has a comparable clinical picture whether or not a CBDS is present.
Aim
At the time of hospital admission, we sought to discover predictors of CBD stones in acute cholecystitis (AC) patients.
Methods
Between January 2020 and December 2022, we chose 90 patients who had typical ACC and had previously visited the emergency room at Minia University Hospital in Egypt. The 90 AC patients were split into two groups: the 63 AC patients without CBD stones and the 27 AC patients with CBD stones. The data were obtained and compared between the two groups include gender, age, history of chronic calcular cholecystitis (CCC), white blood cells (WBC), liver function tests (LFT), and common bile duct (CBD) diameter.
Results
By using simple logistic regression analysis for prediction of CBD stones, old age $>$ 55 years, CBD diameter more than 6 mm and elevated liver functions including total bilirubin, direct bilirubin, serum glutamic-pyruvic transaminase (SGPT), serum glutamic-oxaloacetic transaminase (SGOT), alkaline phosphatase (ALP) and gamma-glutamyl transferase (GGT) was associated with CBD stones. By using multiple logistic regression analysis, only 2 variable showing significant association with CBD stones, including old age $>$ 55 years ($P = 0.013$, odds ratio 9.26, confidence interval 1.6–53.61) and direct bilirubin ($P = 0.008$, Odds ratio 55.67, confidence interval 2.89–1072.35).
Conclusion
Age, abnormal LFTs greater than twofold, and dilated CBD $>$6 mm in AC patients increase the likelihood of concurrent CBDS. Knowing about these results might assist physicians develop clinical suspicions for an earlier diagnosis and improved management of CBDS.

Keywords:
acute cholecystitis, common bile duct stone, liver function test, predictive factors

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Introduction

Cholecystitis, a consequence of gallstones that can be acute or chronic, affects up to 90% of all gallstone cases [1]. Common bile duct stones (CBDS) have been observed in acute cholecystitis (AC) patients in 9.8% to 26.8% of cases [2]. Early diagnosis of a CBDS is crucial when a patient with AC arrives to the emergency department (ED) because its existence affects the mode of therapy [3].

Regrettably, whether a CBDS is present or not, AC presents with the same clinical presentation [4]. Moreover, individuals with AC frequently have mild elevations in serum transaminases, alkaline phosphatase (ALP), and total bilirubin upon initial laboratory assessment with or without presence of CBDS.

Concern about concurrent common bile duct stone (CBDS) is frequently expressed in circumstances when these indices are noticeably elevated [2].

Moreover, the abdominal CT scan and gallbladder ultrasound diagnostic imaging modalities used in the ED for suspected AC cases lack specificity and sensitivity for the diagnosis of CBDS [5].

The preoperative examination often entails one or more of the following investigations: endoscopic

ultrasound, magnetic resonance cholangiopancreatography, or endoscopic retrograde cholangiopancreatography (ERCP), depending on the clinical suspicion for CBDS. These tests can be costly, invasive, linked to serious side outcomes, and frequently put off receiving definitive therapy [6,7].

The American and European Societies of Gastrointestinal Endoscopy (ASGE and ESGE) recommendations' risk stratification criteria do not work well enough in patients with ACC [8]. These recommendations are mostly based on research on people without AC, which suggests that they apply to a different patient population than those who have concurrent AC [9].

It is still unknown if specific criteria apply to this particular subset of patients and whether additional testing for patients at intermediate risk should be carried out [9].

We provide straightforward clinical, laboratory, and imaging elements that are easily accessible to correctly target patients who would benefit from preoperative endoscopic intervention or imaging prior to cholecystectomy.

Patients and methods

Among all the patients who arrived to the emergency department at Minia University Hospital in Egypt with symptoms related to the gall bladder between January 2020 and December 2022, we retrospectively selected 90 patients who present with typical AC.

Biliary pancreatitis and other conditions that could result in LFT abnormalities, such as malignancy, viral or drug-related hepatitis, and Mirizzi syndrome, as well as patients who were on dialysis prior to surgery and those with ascites, congestive heart failure, or bleeding disorders, are excluded [10,11]. Individuals with biliary pancreatitis were excluded as it is typically brought on by small-sized stones that can briefly alter LFT and then spontaneously pass out [12].

The 90 AC patients were split into two groups: the 63 AC patients without CBD stones (AC-) and the 27 AC patients with CBD stones (AC+).

In accordance with the 2018 Tokyo Guidelines, AC is characterized by imaging findings that are typical of AC, local signs of inflammation (Murphy's sign or right upper abdominal pain, mass, or tenderness), and systemic signs of inflammation (fever, elevated C-reactive protein, or elevated white blood cell count).

Only patients with CBD stones, which were found by ERCP or surgery, were included in the AC + CBD group. Patients with diagnosed CBD stones by magnetic resonance cholangiopancreatography should have ERCP to confirm diagnosis and as a therapeutic. It was also recommended if the LFT levels did not improve during the follow-up period. Where necessary, ERCP was carried out as quickly as feasible.

It was not standard practice to do intraoperative cholangiography to look for potential CBD stones. Also intraoperative US and endoscopic ultrasound were unavailable.

Clinical and laboratory data

The data were obtained from the patients' medical records include clinical data, such as gender, age (more or less than 55 years), and history of chronic calcular cholecystitis (CCC) laboratory data included the white blood cell count (> 11.000/mm3) and LFT values. The LFT, including Total Bilirubin (TB), Direct Bilirubin (DB), SGPT, SGOT, ALP, and GGT. Imaging data included CBD diameter in US more than 6 mm.

Only LFT increases by two times are taken into account. When it was >2.4 mg/dl, total bilirubin was considered abnormal or high. When Direct Bilirubin exceeded 0.6 mg/dl, it was regarded as abnormal or high. At >130 U/l and >80 U/l, respectively, SGOT and SGPT were classed as abnormal. When ALP was >240 IU/l, it was considered abnormal. When GGT was >80 IU/l, it was considered abnormal.

Study design

To assess the prediction for the existence of CBD stones in AC patients, the prior parameters at ER admission were compared between the AC + group and the AC – group in this retrospective study. The results will help inform and direct future planning and therapy.

The hospital's Institutional Review Board gave its approval to this study.

Statistics

The statistical package software IBM SPSS version 25 was used to analyses the data. For qualitative data, the data were reported as a number and a percentage. Categorical variables were compared using the chi-square test. To identify the predictoes of CBD stone, univariate and multivariate logistic regression analysis were both performed. A P value of 0.05 or less was regarded as statistically significant.

Results

A total of 90 patients (36 male and 54 female) fulfilled the inclusion criteria. Choledocholithiasis was found in 27 patients (30%) and not found in 63 patients (70%) (Table 1).

According to Table 2, patients in the AC+ group were more likely to be female (70.4% vs. 55.6%), had a larger percentage of patients older than 55 (63 vs. 39.7%). In the AC+ group, the proportions of double-fold elevated LFTs were also considerably higher for total bilirubin (55.6% vs. 15.9%, *P* 0.001), direct bilirubin (63% vs. 15.9%, *P* 0.001), SGPT (59.3% vs. 15.9%, *P* 0.001), SGOT (66.7% vs. 27%, *P* 0.001), GGT (66.7% vs. 31.7). Moreover, there were substantially more dilated CBDs with diameters greater than 6 mm in the AC+ (66.7% vs. 19%, *P* 0.001).

Table 1 Patients Demographics and characteristics

	Descriptive statistics (n = 90)
CBD stone	
No	63 (70%)
Yes	27 (30%)
Gender	
Male	36 (40%)
Female	54 (60%)
age >55	
No	48 (53.3%)
Yes	42 (46.7%)
WBC>11	
No	39 (43.3%)
Yes	51 (56.7%)
Total bilirubin >2,4 mg	
No	65 (72.2%)
Yes	25 (27.8%)
direct bilirubin >0.6 mg	
No	63 (70%)
Yes	27 (30%)
SGPT>80	
No	64 (71.1%)
Yes	26 (28.9%)
SGOT>130	
No	55 (61.1%)
Yes	35 (38.9%)
ALP>240	
No	57 (63.3%)
Yes	33 (36.7%)
GGT>80 IU/l	
No	52 (57.8%)
Yes	38 (42.2%)
H/O CCC	
No	35 (38.9%)
Yes	55 (61.1%)
CBD diameter>6	
No	60 (66.7%)
Yes	30 (33.3%)

Regarding percentage of positive history of CCC, there is no difference between the AC+ group and AC- group (59.3% vs. 61.9).

By comparison of patient Demographics and characteristics between the AC + and AC – group (Table 2), no statistically significant relation was detected between the 2 groups as regard gender, elevated WBC and history of CCC. The same table demonstrates statistically significant relation was detected between the 2 groups as regard old age > 55 years (*P* value 0.042), CBD diameter (*P* value < 0.001) and elevated liver functions (TB, DB, SGPT, SGOT, ALP, and GGT) with *P* value < 0.001 for all liver functions except GGT it was 0.002.

Table 2 Comparison of patient Demographics and characteristics between the AC + and AC – group

	CBD stone		
	No N = 63	Yes N = 27	*P* value
Gender			
Male	28 (44.4%)	8 (29.6%)	*0.189*
Female	35 (55.6%)	19 (70.4%)	
Age > 55			
No	38 (60.3%)	10 (37%)	***0.042****
Yes	25 (39.7%)	17 (63%)	
WBC>11			
No	29 (46%)	10 (37%)	*0.430*
Yes	34 (54%)	17 (63%)	
Total bilirubin >2.4 mg			
No	53 (84.1%)	12 (44.4%)	<***0.001****
Yes	10 (15.9%)	15 (55.6%)	
Direct bilirubin >0.6 mg			
No	53 (84.1%)	10 (37%)	<***0.001****
Yes	10 (15.9%)	17 (63%)	
SGPT>80			
No	53 (84.1%)	11 (40.7%)	<***0.001****
Yes	10 (15.9%)	16 (59.3%)	
SGOT>130			
No	46 (73%)	9 (33.3%)	<***0.001****
Yes	17 (27%)	18 (66.7%)	
ALP>240			
No	50 (79.4%)	7 (25.9%)	<***0.001****
Yes	13 (20.6%)	20 (74.1%)	
GGT>80 IU/l			
No	43 (68.3%)	9 (33.3%)	***0.002****
Yes	20 (31.7%)	18 (66.7%)	
H/O CCC			
No	24 (38.1%)	11 (40.7%)	*0.813*
Yes	39 (61.9%)	16 (59.3%)	
CBD diameter>6			
No	51 (81%)	9 (33.3%)	<***0.001****
Yes	12 (19%)	18 (66.7%)	

Chi square test for qualitative data between the two groups.
*Significance level at *P* value < 0.05.

Table 3 Simple logistic regression analysis for prediction of CBD stones

	OR	95% CI	*P* value
Age > 55	2.58	1.02–6.55	***0.045****
Total bilirubin >2.4 mg	6.63	2.4–18.3	<***0.001****
Direct bilirubin >0.6 mg	9.01	3.21–25.31	<***0.001****
SGPT > 80	7.71	2.77–21.44	<***0.001****
SGOT > 130	5.41	2.04–14.34	***0.001****
ALP > 240	10.99	3.83–31.56	<***0.001****
GGT > 80 IU/l	4.3	1.65–11.23	***0.003****
CBD diameter > 6	8.5	3.07-23.52	<***0.001****

CI, Confidence Interval; OR, Odds Ratio. *Significant level at *P* value < 0.05.

Table 4 Multiple logistic regression analysis for prediction of CBD stones

	AOR	95% CI	*P* value
Age > 55	9.26	1.6-53.61	***0.013****
Total bilirubin >2.4 mg	2.8	0.07-115.35	*0.587*
Direct bilirubin >0.6 mg	55.67	2.89-1072.35	***0.008****
SGPT > 80	1.38	0.12–15.83	*0.796*
SGOT > 130	NA	NA	*NA*
ALP > 240	NA	NA	*NA*
GGT > 80 IU/l	NA	NA	*NA*
CBD diameter > 6	NA	NA	*NA*

AOR, Adjusted Odds Ratio; CI, Confidence Interval; NA, Not Applicable. *Significant level at *P* value < 0.05.

By using simple logistic regression analysis for prediction of CBD stones (Table 3), multiple variables showing significant association with CBD stones, including old age > 55 years, CBD diameter and elevated liver functions (total bilirubin, direct bilirubin, SGPT, SGOT, ALP, and GGT).

By using multiple logistic regression analysis for prediction of CBD stones (Table 4), only 2 variable showing significant association with CBD stones, including old age > 55 years ($P = 0.013$, Odds ratio 9.26, confidence interval 1.6–53.61) and direct bilirubin ($P = 0.008$, Odds ratio 55.67, confidence interval 2.89–1072.35).

Discussion

This study identifies basic clinical, laboratory, and imaging indicators that are readily available in patients who are admitted with an AC episode and correlates these findings with the occurrence of a CBDS. In an effort to more correctly suspect the presence of CBDS in AC patients, these measures were compared across patients with and without CBDS. This is crucial for surgeons to prevent needless costly imaging or invasive preoperative endoscopic intervention and to plan the appropriate mode of treatment.

Around one-third of patients (30%) had CBDS. This is comparable to a research by Zgheib, Hady *et al.* where more than a third of patients included (40.2%) had a concurrent CBDS [13]. Moreover, Singh *et al.* observed a significant prevalence of CBDS in their prospective analysis of 55 CCC patients, of which 21 (38.2%) had CBD blockage [14].

Compared to AC-patients, patients in the AC+ group more frequently had female patients. This supports a research by Lammert F. *et al.* that found the female gender to be a risk factor for gallstone formation [15].

contrary to de Mestral C *et al.*, who showed that everyone with a history of gallstone disease is at risk of developing CBDS with CBD blockage [16], there was no difference between the AC+ group and the AC- group in our study when it came to CCC history (59.3% vs. 61.9). Our findings indicate that it is not uncommon for gallstones to first manifest as AC aggravated by a CBD stone.

The percentage of LFTs with double-fold increases in total bilirubin, direct bilirubin, SGOT, SGPT, GGT, and ALP were likewise considerably greater among the AC+ patients included in this investigation. The results of this study are consistent with a number of other studies on AC patients who found that LFTs significantly increased in AC patients with CBDS [11,17–19]. Our results support the usefulness of LFTs as trustworthy and clinically relevant tools to assist surgeons in determining the possibility of a CBDS in AC patients.

While much greater among CBDS+ patients in our research, LFT values remained abnormal in both CBDS+ and CBDS- individuals. Nevertheless, over 50% of AC+ individuals exhibited normal or somewhat increased SGPT (40.7%), direct bilirubin (44.4%), and total bilirubin (37.%) levels. In order to forecast CBDS in AC patients, a higher cut off may be more suitable and an aberrant level of LFT should be taken with caution.

There are several potential causes of the false negative and false positive LFTs in AC patients. Theoretically, CBD stones cause elevated LFT, hepatic damage, periductal inflammation, increased intra-biliary pressure, and biliary obstruction. Nevertheless, partial stone obstruction may not increase bilirubin levels, giving falsely negative findings [20]. Furthermore, stones may spontaneously enter or depart the CBD during the time between blood collection and ERCP or surgery, leading to false positive or negative findings, respectively [20].

Bile viscosity may rise as a result of sludge or microlithiasis in the common bile duct, which would subsequently result in elevated liver function tests [21,22]. Nevertheless, because to the possibility that the contrast material administered to the CBD washed them away, they might not be seen on intraoperative cholangiography. Concurrent Sphincter of Oddi dysfunction [23–25], conjugation anomalies [26,27], Mirizzi syndrome [28], and other disorders may cause elevated liver function test results in the absence of CBDS.

This study found old age > 55 as a predictor of CBDS in AC patients using simple logistic regression analysis, which was further supported by multiple logistic regression analysis. This is consistent with the findings of Khoury, Tawfik, *et al.* A further well-known factor in the prediction of CBD stone is age, which is why it is one of the ASGE criterion [8].

Although in multivariate logistic regression analysis, abnormal direct bilirubin was the best predictor for CBDS, in simple logistic analysis Elevated liver functions, including total bilirubin, direct bilirubin, SGPT, SGOT, ALP, and GGT, were all demonstrated to be predictors for CBDS in AC patients.

This is somewhat comparable to a prospective research by Videhult *et al.* that identified ALP and bilirubin as the most dependable variables in 1171 cholecystitis patients [19]. Other liver enzymes, such as GGT, have been shown to be more accurate predictors in other investigations [29]. Moreover, a significant correlation between ALP and CBDS has been shown in earlier studies [17].

Nevertheless, a large number of other research aimed at using LFTs for the prediction of CBDS only had weak findings and came to the conclusion that no LFT results were related to CBD stones [30–32].

The exclusion of cases with potentially suspect LFT results, such as those with biliary pancreatitis, viral or drug-related hepatitis, malignancy, and Mirizzi syndrome, as well as patients with dialysis, ascites, and bleeding disorders, as well as the reliance on usual clinical practise variables, are among the study's strengths.

Also, the study included straightforward, inexpensive clinical, laboratory, and imaging (US) characteristics as initial diagnostic procedures for identifying AC patients at risk for developing a concurrent CBDS. Hence, it is crucial for doctors to accurately triage patients upon presentation in order to improve subsequent therapy and prevent needless costly, invasive, and occasionally unavailable therapies.

The use of a clinical registry database and the retrospective study methodology are two factors that contribute to some of this study's weaknesses.

To evaluate the diagnostic effectiveness of LFTs for CBDS prediction in AC patients, a sizable prospective studies in several sites is still needed. In order to more accurately categorise patients with AC as having a high or low risk of having a CBDS at time of presentation, it would also be beneficial to develop various cut-off values that clinicians could depend on when analyzing the findings of LFT tests.

Conclusion

Age, abnormal LFTs greater than twofold, and dilated CBD >6 mm in AC patients increase the likelihood of concurrent CBDS. Knowing about these results might assist physicians develop clinical suspicions for an earlier diagnosis and improved management of CBDS.

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Conflicts of interest

There are no conflicts of interest.

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