Medicine®

OPEN

Liver function tests as predictors of common bile duct stones in acute cholecystitis patients with a chronic history
A retrospective cohort study on the ACS-NSQIP database

Hady Zgheib, MD[a], Cynthia Wakil, MD[a] iD, Nader Al Souky, MD[a], Aurelie Mailhac, MPH[b], Faek Jamali, MD, FACS, FSSO[c], Mazen El Sayed, MD, MPH[a,d], Hani Tamim, PhD[b,e,*]

Abstract

Liver function tests (LFTs) use for common bile duct stone (CBDS) prediction in acute cholecystitis (AC) patients is challenging, especially in patients with chronic cholecystitis (CC) history.

This study aims to describe characteristics of AC patients with CC history and assess LFTs' utility for CBDS prediction in these patients.

A retrospective cohort study was conducted on adults with a diagnosis of AC and CC history included in the National Surgical Quality Improvement Program database from 2008 to 2016. Patients were categorized into CBDS- (without CBDS) and CBDS+ (with CBDS). Multivariate logistic regression was used to determine CBDS predictors.

This study included 7458 patients, of which 40.2% were CBDS+. CBDS+ patients were more commonly females (64.4% vs 54.7%, $P < .001$). Mean levels of bilirubin (1.70 vs 0.90, $P < .001$), SGOT (105.9 vs 49.0, $P < .001$) and ALP (164.6 vs 103.8, $P < .001$) were significantly higher among CBDS+ patients.

Significant positive predictors of CBDS were female gender, increased BMI, and abnormal bilirubin, ALP and SGOT. AC patients with CC history are more likely to have CBDS. Abnormal LFTs are significantly associated with CBDS in this patient population. Familiarity with these findings can help raise clinical suspicion of providers for earlier evaluation and management of CBDS.

Abbreviations: AC = Acute Cholecystitis, ACS = American College of Surgeons, ALP = Alkaline Phosphatase, ASA = American Society of Anesthesiologists, BMI = Body Mass Index, CBD = Common Bile Duct, CBDS = Common Bile Duct Stones, CC = Chronic Cholecystitis, ED = Emergency Department, ERCP = Endoscopic Retrograde Cholangiopancreatography, ICD = International Classification of Disease, LFT = Liver Function Tests, NSQIP = National Surgical Quality Improvement Program, SGOP = Serum Glutamic-Oxaloacetic Transaminase.

Keywords: acute cholecystitis, common bile duct stone, diagnostic screening, liver function test, predictive value

a Department of Emergency Medicine, b Faculty of Medicine, Clinical Research Institute, c Department of Surgery, Division of General Surgery, d Emergency Medical Services and Pre-hospital Care Program, e Department of Internal Medicine; American University of Beirut, Beirut, Lebanon.

* Correspondence: Hani Tamim, Department of Internal Medicine, Clinical Research Institute, Fellowship and Residency Research Program, American University of Beirut Medical Center, Beirut, Lebanon (e-mail: hani_t@hotmail.com).

1. Introduction

Chronic cholecystitis (CC) is characterized by a prolonged subacute dysfunction in the emptying of the gallbladder that can be mechanical or functional in nature, with or without concomitant gallstones.[1] Apart from chronic symptoms, it can progress to a more severe form requiring urgent intervention known as acute cholecystitis (AC).[1] Cholecystitis, whether acute or chronic, occurs as a complication of gallstones in up to 90% of cases.[2] The development of gallstones is associated with several risk factors including female gender, pregnancy, age, obesity and decreased physical activity.[3] Gallstones can block any section along the biliary tree. They most commonly reside in the cystic duct but can also block the common bile duct (CBD).[4] AC patients have been reported to have a concomitant common bile duct stone (CBDS) in 9 to 26.8% of cases.[5,6]

When a patient presents with AC to the Emergency Department (ED), early detection of a CBDS is important as its presence impacts surgical management.[7] Unfortunately, AC has the same clinical picture, regardless of the presence (CBDS+) or absence (CBDS-) of a CBDS.[4] Moreover, the diagnostic imaging techniques for a suspected AC case in the ED, namely abdominal CT scans or gallbladder ultrasounds, lack specificity and sensitivity for the detection of CBDS.[8] As such, despite being invasive, expensive, and not readily available in an ED setting, an

endoscopic retrograde cholangiopancreatography procedure (ERCP) is generally recommended before surgery when a CBDS is suspected.[8]

Liver function tests (LFTs) have been investigated as clinical predictors of CBDS and are commonly included in the ED diagnostic work up of AC patients.[6] Due to the direct effect of the obstructing CBDS, LFTs are more commonly abnormal in CBDS+ patients.[9,10] Nevertheless, in the absence of CBDS, AC patients may still have abnormal LFT results.[6,11] Actually, most studies that did identify a correlation between LFTs and the presence of CBDS illustrate their limitations for the prediction of CBDS in AC patients.[6,11,12]

Moreover, on one hand, among patients without CBDS, CC cases have been reported to have significantly lower LFTs when compared to AC cases.[13] On the other hand, a study by Peng WK, Sheikh Z, Paterson-Brown S et al, on patients without CBDS showed no significant differences in LFTs between AC and CC patients.[14] As such, the chronicity of hepatocellular damage may contribute to a normalization of LFT results. In that case, an AC exacerbation as well as a CBDS may have a different impact on LFT results of AC patients who have a history of CC. As a result, physicians may need to rely on different LFT cut offs for the prediction of CBDS in these patients. In the literature, data on LFT patterns among AC patients with a CC history is scarce.

The aim of this study was to describe the characteristics of patients with a diagnosis of AC and a history of CC and to assess the utility of LFTs in predicting the presence of a CBDS in this patient population.

2. Materials and methods

2.1. Setting & study population

This is a retrospective cohort study of all adult patients with a diagnosis of AC and a history of CC included in the American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP) database between the years of 2008 and 2016.[15] This database was previously described in a study conducted by Zgheib H, Wakil C, Shayya S et al, on the utility of LFTs in AC patients.[6]

An Institutional Review Board exemption was obtained from the American University of Beirut before conducting this study because it's a secondary data analysis using the HIPAA de-identified database. Adults, with a past medical history of CC, diagnosed with AC in the period ranging from 2008 till 2016, were identified in the ACS NSQIP database. These cases were selected using their corresponding International Classification of Disease (ICD) 9 and 10 diagnosis codes (see Table S1 Supplemental Digital content, http://links.lww.com/MD/G356, which lists the ICD 9 and 10 codes for AC diagnosis). To avoid any selection bias, all adult patients with any of the ICD 9 and 10 codes corresponding to AC diagnosis were then screened for ICD 9 and 10 codes for CC history to be included in the study sample (see Table S1 Supplemental Digital content, http://links.lww.com/MD/G356, which lists the ICD 9 and 10 codes for CC history). Excluded patients were those known to have a malignancy, namely those with disseminated disease or presenting within 90 days from their radiotherapy session or 30 days from their chemotherapy. In addition, patients found to have missing data on LFTs, ascites, congestive heart failure or coagulopathies, or on dialysis pre-operatively were excluded from the study.[16] Following patients' selection, participants were categorized into

CBDS- and CBDS+ patients respectively based on the absence or presence of CBDS according to ICD 9 and 10 codes (see Table S1 Supplemental Digital content, http://links.lww.com/MD/G356, which indicates the ICD 9 and 10 codes for CBDS- and CBDS+ patients).

2.2. Data collection

The following variables were collected from the NSQIP database: demographics (age, race, and gender), American Society of Anesthesiologists (ASA) score that assesses the physical status of patients before surgery,[17] comorbidities, sepsis rates, Body Mass Index (BMI) and LFTs taken preoperatively namely serum glutamic-oxaloacetic transaminase (SGOT), alkaline phosphatase (ALP) and total bilirubin. LFT measurements were done according to standardized hospital laboratory techniques. For bilirubin, any value ≤ 1.2 mg/dL was considered normal and any value >1.2 mg/dL was abnormal. For SGOT, a value ≤ 40 U/L was considered normal while a value > 40 U/L was abnormal. For ALP, a value ≤ 120 IU/L was considered normal while a value > 120 IU/L was abnormal.

2.3. Data analysis

A descriptive analysis of all AC cases with CC in general, and of CBDS+ and CBDS- cases in particular was conducted. Continuous variables were presented as means ± standard deviations and categorical variables were presented as frequencies with percentages. A bivariate analysis was then carried out using Student's t-test and Pearson's Chi-square test, to compare patients' characteristics between CBDS+ and CBDS- groups. No procedure was performed to handle missing data as all variables had less than 5% of data missing. The correlation between LFTs and the presence of CBDS was investigated. The LFTs' results were initially described and then compared between CBDS+ and CBDS- groups. Furthermore, forward stepwise multivariate logistic regression was used to determine the predictors of CBDS in AC patients with a CC history. All statistical analyses were performed using SAS 9.4. Statistical significance was set at a bilateral P-value of .05.

3. Results

3.1. Patient characteristics

This study's population consisted of 7,458 patients with AC and CC, of which 59.8% had no CBDS (CBDS- group) and 40.2% had a CBDS (CBDS+ group). Table 1 presents the characteristics of patients included in this study. The mean age of our study population was of 53.5 (± 18.6) years and more than half (58.6%) were females. CBDS+ patients were more commonly females (64.4% vs 54.7%, P < .001), had a slightly higher BMI (31.1 vs 30.7, P-value of .02) yet were less likely to be diabetic (12.9% vs 16.1%, P < .001) when compared to the CBDS- patients (Table 1).

3.2. Laboratory results

Table 2 displays the results of LFTs among CBDS- and CBDS+ patients. Mean levels of total bilirubin (1.7 vs 0.9, P < .001), SGOT (105.9 vs 49.0, P < .001) and ALP (164.6 vs 103.8, P < .001) were significantly higher among CBDS+ patients. Mean SGOT results remained abnormal in both CBDS+ and CBDS-

Table 1

Demographics and characteristics of patients with acute cholecystitis and a chronic history with (CBDS⁺) or without (CBDS⁻) common bile duct stone.

Variables	All AC[†] (n = 7458)	CBDS⁻[‡] (n = 4457)	CBDS⁺[§] (n = 3001)	*P*-value
Age (years), mean ± SD	53.5 ± 18.6	53.7 ± 17.8	53.2 ± 19.7	.23
Race, n (%)				
Black	680 (10.5)	397 (10.7)	283 (10.3)	.05
White	5377 (83.2)	3109 (83.7)	2268 (82.6)	
Others	404 (6.3)	209 (5.6)	195 (7.1)	
Gender, n (%)				
Male	3084 (41.4)	2016 (45.3)	1068 (35.6)	<.001
Female	4366 (58.6)	2437 (54.7)	1929 (64.4)	
Diabetic, n (%)	1105 (14.8)	719 (16.1)	386 (12.9)	<.001
Hypertensive, n (%)	3078 (41.3)	1893 (42.5)	1185 (39.5)	.01
BMI, mean ± SD	30.9 ± 7.7	30.7 ± 7.8	31.1 ± 7.7	.02
ASA, n (%)				
1	669 (9.0)	396 (8.9)	273 (9.1)	.49
2	3915 (52.5)	2312 (52.0)	1603 (53.5)	
3	2604 (35.0)	1580 (35.5)	1024 (34.2)	
4-5	259 (3.5)	161 (3.6)	98 (3.3)	
WBC, mean ± SD	8.951 ± 3.960	9.238 ± 4.046	8.527 ± 3.790	<.001
Hematocrit, mean ± SD	38.3 ± 5.0	38.8 ± 5.1	37.6 ± 4.9	<.001
Septic, n (%)	1032 (13.9)	610 (13.7)	422 (14.1)	.64

AC= Acute cholecystitis; CBDS⁻= Acute cholecystitis without common bile duct stone (CBDS); CBDS⁺= Acute cholecystitis with CBDS; SD= Standard Deviation; BMI= Body Mass Index; ASA= American Society of Anesthesiologists (ASA) score, a global score that assesses the physical status of patients before surgery; WBC= White Blood Cell count.

patients although significantly higher among CBDS+ patients. Whereas CBDS+ patients had all mean LFTs within abnormal ranges, CBDS- patients had normal mean results for total bilirubin and ALP.

Furthermore, the CBDS+ group had a significantly higher proportion of patients with abnormal LFTs, including total bilirubin (44.4% vs 16.6%, *P* <.001), SGOT (58.3% vs 25.6%, *P* <.001) and ALP (54.3% vs 21.6%, *P* <.001). However, a significant amount of CBDS+ patients were found to have normal total bilirubin (55.6%), SGOT (41.7%) and ALP (45.7%) such as a significant amount of CBDS- patients were found to have abnormal total bilirubin (27.8%), SGOT (38.8%) and ALP (34.7%) (Table 2).

3.3. Predictors of CBDS

Table 3 shows the results of the stepwise multivariate regression analysis in which all clinically and/or statistically significant variables on bivariate analysis were included. Among AC patients with a CC history, females were 1.56 times more likely to have a CBDS and diabetics were significantly less likely to have a CBDS (OR = 0.79, 95% CI 0.68–0.92). Elevated BMI was a significant positive predictor for the presence of CBDS with an odds ratio of 1.01 whereas high WBC counts and low hematocrit levels were significant negative predictors of CBDS with odds ratios of 0.97 and 0.98, respectively. Abnormal bilirubin, ALP and SGOT were found to increase the odds of having a CBDS by 2.52, 2.22 and 1.60 respectively (Table 3).

Table 2

Individual liver function test results in acute cholecystitis patients with a chronic history with (CBDS⁺) or without (CBDS⁻) common bile duct stone.

LFTs	All AC	CBDS⁻	CBDS⁺	*P*-value
Total bilirubin (mg/dL), mean ± SD	1.22 ± 1.37	0.90 ± 0.96	1.70 ± 1.72	<.001
Total bilirubin*, n (%)				
Normal	5386 (72.2)	3718 (83.4)	1668 (55.6)	<.001
Abnormal	2072 (27.8)	739 (16.6)	1333 (44.4)	
SGOT (U/L), mean ± SD	71.9 ± 110.2	49.0 ± 83.0	105.9 ± 134.3	<.001
SGOT*, n (%)				
Normal	4567 (61.2)	3315 (74.4)	1252 (41.7)	<.001
Abnormal	2891 (38.8)	1142 (25.6)	1749 (58.3)	
ALP (IU/L), mean ± SD	128.3 ± 101.3	103.8 ± 74.9	164.6 ± 112.3	<.001
ALP*, n (%)				
Normal	4866 (65.3)	3493 (78.4)	1373 (45.7)	<.001
Abnormal	2592 (34.7)	964 (21.6)	1628 (54.3)	

LFTs= Liver function tests; AC= Acute cholecystitis; CBDS⁻= Acute cholecystitis without common bile duct stone (CBDS); CBDS⁺= Acute cholecystitis with CBDS; SD= Standard Deviation; SGOT= Serum Glutamic-Oxaloacetic Transaminase; ALP= Alkaline phosphatase.

* Cut-off values were set at 1.2 milligrams per deciliter (mg/dL) for bilirubin, 40 units per liter (U/L) for SGOT and 120 international units per liter (IU/L) for ALP.

Variable	*Adjusted OR (95% CI)	*P*-value
Female gender	1.56 (1.38–1.74)	<.001
Diabetes	0.79 (0.68–0.92)	.002
BMI	1.01 (1.00–1.02)	.01
WBC	0.97 (0.96–0.99)	<.001
Hematocrit	0.98 (0.97–0.99)	.003
Total Bilirubin	2.52 (2.22–2.86)	<.001
SGOT	1.60 (1.33–1.93)	<.001
ALP	2.00 (1.70–2.36)	<.001

OR = Odds ratio; CI = Confidence interval; BMI = Body Mass Index; WBC = White Blood Cell count; SGOT= Serum Glutamic-Oxaloacetic Transaminase; ALP = Alkaline phosphatase.

* Adjusted for all clinically and/or statistically significant variables on bivariate analysis namely age, female gender, diabetes, hypertension, BMI, WBC, Hematocrit, sepsis, total bilirubin, SGOT and ALP.

4. Discussion

This study is the largest to date to examine LFT results in patients with a CC history and presenting with an AC episode and to correlate these results with the presence of a CBDS. Its findings including a difference in LFT patterns between patients with and without CBDS are important for ED physicians to better interpret LFTs and more accurately suspect the presence of CBDS in AC patients with a history of CC.

More than a third (40.2%) of patients included in this study had a concomitant CBDS. Similarly, a high incidence rate of CBDS was reported by Singh et al in their prospective study on 55 CC patients of whom 21 (38.2%) had CBD obstruction.[18] However, these rates are higher than in cases of AC without any chronic history for which the prevalence of CBDS ranges from 7 to 26.8%.[5,6] In fact, any individual with a history of gallstone disease is also at risk of developing CBDS with CBD obstruction being more common in patients with recurrence of symptoms.[19] As such, because CC is most commonly attributed to gallstones, when presenting to the ED with AC, patients with a history of CC are more likely to have a concomitant CBDS.

Moreover, in this study, CBDS+ patients had a significantly higher proportion of females and a slightly higher BMI compared to CBDS- patients. Indeed, female gender and obesity are known to be risk factors for the development of gallstones.[3] However, CBDS+ patients were significantly less likely to be diabetic with an OR of 0.79. These findings are in line with those of a previous study conducted on AC patients in which the CBDS+ group had a slightly lower proportion of diabetic patients.[6] Diabetes, however, is known to be associated with an increased triglyceride level, gallbladder stasis and hepatic insulin resistance, which increase the risk of developing gallstones.[20] Nevertheless, it may have a protective effect on the progression of a gallstone into a CBDS. This finding needs to be investigated further in future studies.

Additionally, mean LFT results of total bilirubin, SGOT and ALP among patients included in this study were significantly higher in CBDS+ patients. These study findings are in agreement with several previous studies on AC patients revealing a significant increase in LFTs in AC patients with CBDS.[9–12] These findings thus validate the utility of LFTs as clinically applicable and reliable tools to help ED physicians decide on the likelihood of a CBDS in AC patients with a history of CC.

In this study, mean SGOT results remained abnormal in both CBDS+ and CBDS- patients although significantly higher among CBDS+ patients. In fact, even AC patients without CBDS have some degree of hepatocellular injury.[21] In CC patients, however, SGOT levels did not differ between patients with gallstones and those with CBD obstruction.[18] These findings imply that the acute inflammation and hepatocellular injury contribute to the elevation in SGOT in AC patients. As such, an abnormal level of SGOT should be interpreted with caution and relying on a higher cut off may be more appropriate for the prediction of CBDS in AC patients.

Moreover, whereas all mean LFTs included in this study were within abnormal ranges in CBDS+ patients, mean total bilirubin and mean ALP were normal in CBDS- patients. These findings are in line with those of Videhult P, Sandblom G, Rudberg C et al who described ALP and bilirubin as the most reliable CBDS predictors in AC patients.[12] Likewise, significantly higher levels of bilirubin and ALP were found among CC patients with CBD obstruction when compared to those with gallstones.[18] Generally, an increase in ALP generally signals the presence of biliary tract pathology and bilirubin increases in both biliary and hepatocellular conditions. As such, normal bilirubin and ALP results may be helpful in ruling out CBDS in AC patients with a chronic history.

Despite having a chronic history, the CBDS+ patients in this study had a significantly higher proportion of patients with abnormal LFTs compared to CBDS- patients. CBDS+ patients regardless of presence of CC history are still significantly more likely to display abnormal LFT results compared to CBDS- patients. Generally, in case of AC, if a CBDS acutely obstructs the bile ducts, liver necrosis may result. Subsequently, aminotransferase levels usually rise and fall first followed by bilirubin and ALP, which rise more slowly.[3] LFTs remain therefore useful in the diagnostic workup for CBDS prediction among AC patients with a chronic history however results should be interpreted with caution. In fact, a significant amount of CBDS+ patients included in this study had normal results such as a significant amount of CBDS- patients had abnormal results. Previously, in AC patients, elevated LFTs were reported to have limited value in predicting the presence of CBDS.[9,12] Nevertheless, the association between elevated LFTs and CBDS seems to be weaker among AC patients with a CC history.[6] Similarly to our study, Videhult P, Sandblom G, Rudberg C et al, report high rates of normal results for ALP and bilirubin among CBDS+ patients and high rates of abnormal results for ALP and bilirubin among CBDS- patients, especially in patients with a history of cholecystitis.[12] These findings illustrate the limitations of LFTs for the prediction of CBDS in AC patients in general and in those with a chronic history in particular.

This study also identified CBDS predictors in AC patients with a chronic history: Women are significantly more likely to have CBDS while diabetics are significantly less likely to have CBDS. Total bilirubin, ALP and SGOT were all shown to be of some discriminatory value for CBDS in AC patients with a chronic history. However, an abnormal bilirubin was the strongest predictor for CBDS, followed by ALP and SGOT. This finding is consistent with a previous study on hyperbilirubinemia without CBD abnormalities that concluded that is it uncommon for patients with chronic calculous cholecystitis to have an elevated bilirubin but no CBDS.[22] Moreover, in previous studies, a strong association has been established between ALP and CBDS,[9,12] and a study focusing on liver changes associated

with AC even showed that none of the patients with acalculous AC had an elevated ALP.[23] Abnormal results of bilirubin and ALP are thus more reliable than SGOT for CBDS prediction among AC patients with a chronic history. As previously reported LFTs are always better interpreted in combination, as an abnormal SGOT alone may be attributed to the acute inflammation.[6]

The strengths of this study include the incorporation of a significant sample of confirmed cases of AC with a CC history, the exclusion of cases with potentially questionable LFT results, namely patients with dialysis, ascites and bleeding disorders, and the reliance on common variables used in daily clinical practice. The study confirmed the role of LFTs as reliable first-line diagnostic tests for the identification of AC patients with a chronic history at risk of having a simultaneous CBDS. It also shed light on the increased risk of having a CBDS, which prompts physicians to keep a higher index of suspicion for CBDS in AC patients with a chronic history. It is thus important to properly triage patients on presentation as either having or not having any chronic history for physicians to better interpret LFTs and optimize patient care.

Some limitations of this study are related to use of a clinical registry database and to the retrospective study design. The database has missing data, miscoding, and unreported variables of potential value such as ALT and GGT. It is also limited by the lack of established criteria used for diagnosis of CC. Important confounders such as cirrhosis are also not available in the database and were not used in this study. Furthermore, the sample chosen is restricted to the ACS NSQIP database of affiliated hospitals, and does not constitute a nationally representative sample. A large-scale prospective study in multiple centers is necessary to assess the diagnostic performance of LFTs for CBDS prediction in AC patients with a chronic history. It would also be worthwhile to generate different cut-off values for physicians to rely on when interpreting LFT results of AC patients with or without any chronic history in order to better classify these patients as high or low risk of having a CBDS.

5. Conclusions

AC patients with a chronic history of cholecystitis are more likely to have a concomitant CBDS. Abnormal LFTs are also significantly associated with the presence of CBDS in this patient population. Familiarity with these findings can help raise clinical suspicion of providers for earlier evaluation and better management of CBDS.

Author contributions

Conceptualization: Hady Zgheib, Faek Jamali, Mazen El Sayed.
Formal analysis: Aurelie Mailhac, Hani Tamim.
Investigation: Cynthia Wakil, Nader Al Souky.
Methodology: Hady Zgheib, Faek Jamali, Mazen El Sayed, Hani Tamim.
Supervision: Hady Zgheib, Faek Jamali, Mazen El Sayed, Hani Tamim.
Writing – original draft: Cynthia Wakil, Nader Al Souky, Aurelie Mailhac.

Writing – review & editing: Hady Zgheib, Cynthia Wakil, Nader Al Souky, Aurelie Mailhac, Faek Jamali, Mazen El Sayed, Hani Tamim.

References

[1] Jones MW, Ferguson T. Chronic Cholecystitis. In: *StatPearls*. Treasure Island (FL)2019.
[2] Indar AA, Beckingham IJ. Acute cholecystitis. BMJ 2002;325:639–43.
[3] Lammert F, Gurusamy K, Ko CW, et al. Gallstones. Nat Rev Dis Primers 2016;2:16024.
[4] Njeze GE. Gallstones. Niger J Surg 2013;19:49–55.
[5] Gouveia C, Loureiro R, Ferreira R, et al. Performance of the choledocholithiasis diagnostic score in patients with acute cholecystitis. GE Port J Gastroenterol 2018;25:24–9.
[6] Zgheib H, Wakil C, Shayya S, et al. Utility of liver function tests in acute cholecystitis. Ann Hepatobiliary Pancreat Surg 2019;23:219–27.
[7] Dasari BV, Tan CJ, Gurusamy KS, et al. Surgical versus endoscopic treatment of bile duct stones. Cochrane Database Syst Rev 2013; CD003327.
[8] Ansaloni L, Pisano M, Coccolini F, et al. WSES guidelines on acute calculous cholecystitis. World J Emerg Surg 2016;11:25.
[9] Thapa PB, Maharjan DK, Suwal B, Byanjankar B, Singh DR. Serum gamma glutamyl transferase and alkaline phosphatase in acute cholecystitis. J Nepal Health Res Counc 2010;8:78–81.
[10] Ahn KS, Yoon YS, Han HS, Cho JY. Use of liver function tests as first-line diagnostic tools for predicting common bile duct stones in acute cholecystitis patients. World J Surg 2016;40:1925–31.
[11] Padda MS, Singh S, Tang SJ, Rockey DC. Liver test patterns in patients with acute calculous cholecystitis and/or choledocholithiasis. Aliment Pharmacol Ther 2009;29:1011–8.
[12] Videhult P, Sandblom G, Rudberg C, Rasmussen IC. Are liver function tests, pancreatitis and cholecystitis predictors of common bile duct stones? Results of a prospective, population-based, cohort study of 1171 patients undergoing cholecystectomy. HPB (Oxford) 2011;13:519–27.
[13] Fikry AA, Kassem AA, Shahin D. Elevated liver enzymes in patients with cholecystitis. J Surgery 2014;2:38.
[14] Peng WK, Sheikh Z, Paterson-Brown S, Nixon SJ. Role of liver function tests in predicting common bile duct stones in acute calculous cholecystitis. Br J Surg 2005;92:1241–7.
[15] American College of Surgeons (ACS): National Surgical Quality Improvement Program (NSQIP). 2011. https://www.facs.org/quality-programs/acs-nsqip.
[16] Johnston DE. Special considerations in interpreting liver function tests. Am Fam Physician 1999;59:2223–30.
[17] Doyle DJ, Garmon EH. American Society of Anesthesiologists Classification (ASA Class). In: *StatPearls*. Treasure Island (FL) 2019.
[18] Singh M, Tiwary S, Patil D, Sharma D, Shukla V. Gamma-Glutamyl Transpeptidase (GGT) as a marker in obstructive jaundice. Internet J Surgery 2007;9:
[19] de Mestral C, Rotstein OD, Laupacis A, Hoch JS, Zagorski B, Nathens AB. A population-based analysis of the clinical course of 10,304 patients with acute cholecystitis, discharged without cholecystectomy. J Trauma Acute Care Surg 2013;74:26–30. discussion 30-21.
[20] Biddinger SB, Haas JT, Yu BB, et al. Hepatic insulin resistance directly promotes formation of cholesterol gallstones. Nat Med 2008;14:778–82.
[21] Chang C-W, Chang W-H, Lin C-C, Chu C-H, Wang T-E, Shih S-C. Acute transient hepatocellular injury in cholelithiasis and cholecystitis without evidence of choledocholithiasis. World J Gastroenterol 2009;15:3788.
[22] Kurzweil SM, Shapiro MJ, Andrus CH, Wittgen CM, Herrmann VM, Kaminski DL. Hyperbilirubinemia without common bile duct abnormalities and hyperamylasemia without pancreatitis in patients with gallbladder disease. Arch Surg 1994;129:829–33.
[23] Geraghty JM, Goldin RD. Liver changes associated with cholecystitis. J Clin Pathol 1994;47:457–60.