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Role of Gamma Glutamyl Transferase in the Diagnosis of Common Bile Duct Stones

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Abstract

Background: Laparoscopic cholecystectomy has been the gold standard in the treatment of gallstone disease, and most of cholecystectomies are performed this way today. However, it is recognized that 3-33% of patients with symptomatic gallstones might harbor common bile duct (CBD) stones.

Aim of Study: To evaluate the sensitivity and accuracy of GGT in the diagnosis of silent common bile duct stones in patients diagnosed with gall stones and scheduled for cholecystectomy.

Patients and Methods: We established this prospective observational study on 30 patients who are diagnosed with gall bladder stones with normal or elevated gamma glutamyltransferase referred to General Surgery Department, Ain Shams University and General Surgery Department, El Sahel Teaching Hospital.

Results: It was found that there common bile duct stones was significantly higher in cases with high GGT compared to cases with normal GGT (p=0.033). It was found that multiple common bile duct stones was significantly higher in cases with high GGT compared to cases with normal GGT (p=<0.001). In addition, the decision of doing ERCP before laparoscopy was significantly higher in cases with high GGT compared to cases with normal GGT (p=<0.001).

Conclusion: Abnormally elevated serum GGT level may be a potentially useful marker for the early prediction of asymptomatic choledocholithiasis secondary to cholecystolithiasis.

Key Words: *Endoscopic retrograde cholangiopancreatography – Common bile duct.*

Introduction

LAPAROSCOPIC cholecystectomy has been the gold standard in the treatment of gallstone disease, and most of cholecystectomies are performed this way today **[1]**. However, it is recognized that 3-33% of patients with symptomatic gallstones might harbor common bile duct (CBD) stones **[2]**.

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The surgical approaches used for cholecystolithiasis with secondary choledocholithiasis include laparotomy, laparoscopic common bile duct exploration and endoscopic retrograde cholangiopancreatography (ERCP) **[3]**. With the advent of minimally invasive surgery and accelerated rehabilitation surgery, minimally invasive surgery procedures such as endoscopic procedures have become the main methods for treating extrahepatic biliary calculi **[4]**.

Stones can cause obstruction in the common bile duct. The patient can have abdominal pain, fever, jaundice and other manifestations, and choledochal dilatation can be seen by abdominal ultrasound in symptomatic choledocholithiasis, which is easily diagnosed **[5]**. In contrast, most cases of secondary choledocholithiasis do not have symptoms and are often missed in diagnosis **[6]**.

On one hand, this may lead to the persistent presence of common bile duct stones and related complications. On the other hand, it may lead to an increased incidence of postoperative residual stones and related life-threatening complications, exacerbating the pain and economic burden for patients after laparoscopic cholecystectomy. Therefore, an important issue has become how to easily and efficiently identify secondary asymptomatic choledocholithiasis in patients with common cholecystolithiasis **[7,8]**.

Patients are often suspected of having choledocholithiasis when they present with right upper quadrant pain with elevated liver enzymes in a primarily cholestatic pattern **[9]**. However, some patients may have floating biliary stones without causing symptoms or clinical manifestations **[10]**.

Gamma-glutamyltransferase (GGT) is one of the most commonly requested laboratory tests and

is a key test used for the laboratory evaluation of liver damage. Serum GGT is mainly derived from the liver and is produced by hepatocyte mitochondria, excreted by the biliary tract, and primarily distributed in the liver cytoplasm and intrahepatic bile duct epithelium **[11]**.

It also indicated that an abnormal increase in serum GGT plays an important role in predicting cholecystolithiasis combined with secondary asymptomatic choledocholithiasis, and it may be an effective serological index for routine screening. With the exception of obvious jaundice, a raised GGT level has been suggested to be the most sensitive and specific indicator of CBD stones **[10]**.

There are two reasons for increased GGT. First, the presence of stones may cause local inflammatory damage to the bile duct epithelium, resulting in excessive GGT production. Therefore, even the latest literature suggests that serum GGT is also an inflammatory marker **[12]**. Second, the presence of stones has a mechanical stimulatory effect on the bile duct epithelium, inducing the epithelial layer to increase GGT synthesis, combined with poor bile excretion, eventually leading to an abnormal increase in serum GGT **[10]**.

The current literature is poor with clinical trials evaluating GGT as a predictor for asymptomatic biliary stones in patients undergoing cholecystectomy. That is why we conducted the current study.

Aim of the work:

This study aims to evaluate the sensitivity and accuracy of GGT in the diagnosis of silent common bile duct stones in patients diagnosed with gall stones and scheduled for cholecystectomy.

Patients and Methods

Study design: Prospective observational study.

Study setting: This study carried out at General Surgery Department, Ain Shams University and General Surgery Department, El Sahel Teaching Hospital from 8/2022 to 2/2023.

Study population: The current study included patients with gall bladder stones.

Inclusion criteria: Adult patients diagnosed with gall bladder stones with normal or elevated gamma glutamyltransferase. Both genders (age 18-60 years old).

Exclusion criteria: Concomitant hepatic disorders (hepatitis or malignancies), concomitant biliary disorders (mirizzi syndrome, acute cholangitis), pregnancy, patients with obstructive jaundice manifestations e.g (yellowish discoloration of skin, scelera and mucosa - dark urine - pale stool - right hypochondrial pain - itching sensation etc..), patients diagnosed with biliary pancreatitis, age (below 18 or above 60 years old), uncontrolled Diabetes Mellitus (Hb A1c more than 7%), patients on medications that may cause idiopathic increase in gamma glutamine transferase (carbamazepine, oral contraceptive pills, phenobarbital, phenytoin and valproic acid).

Sample size calculation:

A sample size of 30 patients diagnosed with gall bladder stones with normal or elevated gamma glutamyltransferase and no jaundice were involved in this study.

Methods:

Preoperative assessment:

All patients had been subjected to:

I- Detailed History taking and demographic data is collected.

Patient preparation:

I- *History taking:* Personal history including name, age, gender, occupation, habitat and occupation, current complaint including abdominal pain, fatty dyspepsia, jaundice, fever, and vomiting, analysis of each complaint regarding onset, course, duration, what increases, what decreases, and associations, review of other GI symptoms, and review of other systems, current medical comorbidities and its medications and previous surgical history.

II- Complete general and local Examination:

General examination: Vital signs (Blood pressure, pulse, temperature, respiratory rate; and blood pressure), body mass index (BMI), complexion (for pallor or jaundice), chest & heart examination and limbs examinations.

Abdominal examination: Inspection, superficial palpation: For liver, spleen & loin and deep palpation for abdominal masses or deep tenderness.

III- Laboratory investigations:

Serum gamma glutamyltransferase had been obtained for all patients scheduled for cholecystectomy: The quantitative determination of GGT will be performed with an enzymatic colorimetric test using L-c-glutamyl-3-carboxy-4-nitroanilide at a temperature of 37 C, which is the reference method recommended by the International Federation of Clinical Chemistry and Laboratory Medicine

(IFCC), complete blood count (CBC), liver function tests including albumin, bilirubin (total and direct), liver transaminases and international normalized ratio (INR), coagulation profile, serum creatinine and serum Hb A1c.

IV- Ultrasound examination:

A pelviabdominal ultrasound will be ordered for all patients to confirm the diagnosis of gall stones. It will be done on GE RT 3200/Toshiba core-vision pro-diagnostic ultrasound system SSA -350 machine with a transducer of 3.5 MHz or 5 MHz frequency. Study will be done after the patients had undergone an overnight fasting for 8 to 12 hours. Scans will be done in longitudinal, transverse and oblique planes. It will be performed by an experienced radiologist. The collected parameters will include: Liver status (normal, fatty, fibrotic or cirrhotic), gall bladder wall thickness, number and size of stones, common bile duct diameter and the presence of common bile duct stones.

V- Magnetic resonance cholangiopancreatography (MRCP):

It will be considered the gold standard tool for confirming common bile duct stones. MRCP will be performed for all patients scheduled for lap cholecystectomy on a 1.5-Tesla MagnetomAvanto system (Siemens, Erlangen, Germany). The patients will be ordered to fast for 6 hours before MRCP. All patients will be imaged with a body phased-array receive coil. 5mm thick sections will be taken from right dome of diaphragm to lower edge of liver. It had been used to test the accuracy of gamma glutamyltransferase in the diagnosis of common bile duct stones.

The following data had been collected:

- Common bile duct diameter.
- The presence of stones.
- Number and size of these stones.

Laparoscopic cholecystectomy had been scheduled in patients with normal MRCP findingsirrespective to gammaglutamyltransferase level. In confirmed diagnosis of common bile duct stones by MRCP, therapeutic ERCP had been scheduled irrespective to gamma glutamyltransferase level.

Intraoperative assessment (Laparoscopic cholecystectomy): Intraoperative identification of gall bladder, cystic duct and common bile duct had been done confirming no apparent abnormalities.

Postoperative follow-up: Post operative follow-up had been done after 1 month of laparoscopic cholecystectomy by ordering the following laboratory investigations. Serum gamma glutamyltransferase. Complete blood count (CBC). Liver function tests including albumin, bilirubin, liver transaminases.

Ethical considerations:

Written informed consent for the procedure and data analysis had been obtained from all he patients.

Statistical analysis:

The collected data will be, tabulated, and statistically analyzed using SPSS program (Statistical Package for Social Sciences) software version 26.0, Microsoft Excel 2016 and MedCalC program software version 19.1. escriptive statistics were done for numerical parametric data as mean ± SD (standard deviation) and minimum & maximum of the range and for numerical non parametric data as median and 1 st & 3rd inter-quartile range, while they were done for categorical data as number and percentage. Inferential analyses were done for quantitative variables using independent *t*-test in cases of two independent patients with parametric data and Mann Whitney U in cases of two independent patients with non-parametric data. Wilcoxon signed-rank test was used to compare two related samples or repeated measurements on a single sample to assess whether their population mean ranks differ. Repeated measures ANOVA (F test): was used for continuous data to test for significant difference between more than two dependent parametric data along different time points. Inferential analyses were done for qualitative data using Chi square test for independent patients. The level of significance was taken at p-value <0.05 is significant, otherwise is non-significant. The p-value is a statistical measure for the probability that the results observed in a study could have occurred by chance.

Results

Table (1): Demographic characteristics among the studied patients.

	Total patients (n=30)	
	N	%
Gender:		
Male	14	46.7
Female	16	53.3
Age (years):		
Mean ± SD	40.37±11.47	
Median	42.5	
Range	19.0-60.0	
BMI (Kg/m ^{2}):		
Mean ± SD	27.93±1.55	
Median	28.0	
Range	25.0-31.0	

Table (1) shows demographic characteristics among the studied patients. The age of patients included in our study was ranged from 19 years to 60 years with mean (± SD) was 40.37±11.47 years.

Fourteen (46.7%) cases were males and 16 (53.3%) were female with male to female ratio was 0.88: 1.

The mean BMI was 27.93±1.55Kg/m^2 and ranged from 25Kg/m^2 to 31Kg/m^2.

Table (2): Distribution of the studied patients as regards preoperative CBC.

	Studied patients (No.=30)				
	Mean	± SD	Median	Min.	Max.
Hemoglobin (g/dL)	11.27	±1.08	11.20	9.80	15.20
WBCs (10^3/L)	8007.30	±1488.98	7858.00	4700.00	10900.00
Platelets count (10^9/L)	218.33	±15.60	217.00	195.00	253.00

SD = Standard deviation.

This table show that:

The mean hemoglobin was 11.27±1.08g/dl. The mean WBCs was 8007.30±1488.98 x10^3/L.

In addition, the mean platelets count was 218.33 ±15.60 x 10^9/L.

Table (3): Distribution of the studied patients as per another preoperative liver function tests.

	Studied patients (No.=30)				
	Mean	± SD	Median	Min.	Max.
ALT	64.80	±12.99	66.00	34.00	96.00
AST	49.00	±9.49	49.50	28.00	63.00
Total Bilirubin (mg/dL)	0.77	±0.17	0.79	0.40	1.10
GGT (IU/L)	295.67	±249.20	202.00	27.00	825.00
ALP (IU/L)	204.67	±171.85	149.50	39.00	658.00
INR	0.98	±0.12	0.97	0.70	1.20
PT/sec	12.58	± 0.78	12.70	10.90	13.90

SD = Standard deviation.

This table show that the mean ALT and AST were 64.80±12.99IU/L and 49.00±9.49IU/L respectively.

The mean total bilirubin, GGT and ALP were 0.77±0.17, 295.67±249.20 and 204.67±171.85 respectively.

Table (4): Distribution of the studied patients as per ultrasound findings.

Description	Studied patients (No.=30)	
	N	%
Liver status:		
Fatty liver	14	46.7
Normal	16	53.3
Gall bladder wall thickness:		
Normal	14	46.7
Thick	16	53.3
Number of stones:		
Multiple	23	76.7
Single	7	23.3
Size of stones:		
<4mm	12	40.0
>4mm	18	60.0
CBD dilation:		
Dilated	16	53.3
Not dilated	14	46.7
CBD diameter (mm):		
Mean± SD	11.87±1.48	
Median	12.25	
Range	9.0-14.0	
The presence of common bile duct stones:		
No	23	76.7
Yes	7	23.3

SD = Standard deviation.

Regarding ultrasound findings, more than half (53.3%) had normal liver and thick gall bladder wall was seen in 53.3% cases.

Most cases had multiple gall stones, as they constituted 76.7% of patients.

The size of stones were more than 4 mm in 60% cases. Common bile duct was dilated in 53.3% cases with mean diameter of 11.87±1.48mm. common bile duct stones was found in seven cases (23.3%) as shown in Table (5).

Table (5): Distribution of the studied patients as per MRCP result.

Description	Studied patients (No.=30)	
	N	%
Number of stones:		
None	14	46.7
Multiple	13	43.3
Single		
CBD diameter (mm):	3	10.0
Average caliber	14	46.7
Dilated	16	53.3
Mean± SD	11.87±1.87	
Median	12.10	
Range	10.0-14.0	
Decision:		
ERCP, sphincterectomy, CBD swept wihballon then laparoscopic cholecystectomy laparoscopic cholecystectomy	12	40.0
ERCP, stone extraction and stenting then laparoscopic cholecystectomy	14	46.7
Intraoperative:		
No apparent abnormalities in	4	13.3
gall bladder, cystic duct and CBD	30	100.0

SD = Standard deviation.

By MRCP, single stone was detected in three cases while 43.3% cases had multiple stones.

Common bile duct had average caliber in 46.7% cases and dilated in 53.3% cases with mean CBD diameter measured by MRCP was 11.87±1.87 mm. laparoscopic cholesestectomy was done in 46.7% cases while ERCP was done first then laparoscopic cholesestectomy in 53.3% cases. Intraoperative data showed that there was no apparent abnormalities in gall bladder, cystic duct and CBD as shown in Table (5).

Table (6): Distribution of the studied patients as per preoperative GGT.

Description	Studied patients (No.=30)	
	N	%
GGT:		
Normal	10	33.3
High	20	66.7

SD = Standard deviation.

Regarding GGT, ten cases (33.3%) had normal GGT level while 20 cases (66.7%) had high GGT level.

Table (7): Distribution of the studied patients as per another postoperative liver function tests.

	Studied patients (No.=30)				
	Mean	± SD	Median	Min.	Max.
ALT	59.47	±10.96	60.00	30.00	80.00
AST	45.10	±9.23	45.00	25.00	60.00
Total Bilirubin (mg/dL)	0.65	±0.15	0.66	0.34	0.98
GGT (IU/L)	38.73	±6.48	39.00	26.00	50.00
ALP (IU/L)	83.97	±5.82	84.00	73.00	96.00

SD = Standard deviation.

This table show that the mean ALT and AST were 59.47±10.96IU/L and 45.10±9.23IU/L respectively.

The mean total bilirubin, GGT and ALP were 0.65±0.15, 38.73±6.48 and 83.97±5.82 respectively.

Table (8): Relation between GGT and ultrasound findings.

Variable	Normal GGT (N=10)		High GGT (N=20)		Chi-square test	
	No.	%	No.	%	Test value	*p*-value
Liver status:						
Fatty liver	6	60.0	8	40.0	X^2=1.07	0.301
Normal	4	40.0	12	60.0		
Gall bladder wall thickness:						
Normal	6	60.0	8	40.0	X^2=1.07	0.301
Thick	4	40.0	12	60.0		
Number of stones:						
Multiple	6	60.0	17	85.0	X^2=2.329	0.127
Single	4	40.0	3	15.0		
Size of stones:						
<4mm	4	40.0	8	40.0	X^2=0.0	1.00
>4mm	6	60.0	12	60.0		
The presence of common bile duct stones:						
No	10	100.0	13	65.0	X^2=4.57	0.033
Yes	0	0.0	7	35.0		

p-value <0.05 is significant.
SD: Standard deviation.
X^2 = Chi-Square test.

This table shows:

It was found that there common bile duct stones was significantly higher in cases with high GGT compared to cases with normal GGT (*p*=0.033).

This table shows:

It was found that multiple common bile duct stones was significantly higher in cases with high GGT compared to cases with normal GGT (p= <0.001). In addition, the decision of doing ERCP before laparoscopy was significantly higher in cases with high GGT compared to cases with normal GGT (p=<0.001).

For detecting CBD stones, GGT had sensitivity and specificity of 100% and 71.4%, respectively, when a cut-off value of 71.4u/l was applied (Table 10).

Table (9): Relation between GGT and MRCP findings.

Variable	Normal GGT (N=10)		High GGT (N=20)		Chi-square test	
	No.	%	No.	%	Test value	p-value
Number and size of these stones:						
Multiple	0	0.0	13	65.0	X^2=17.1	<0.001
None	10	100.0	4	20.0		
Single	0	0.0	3	15.0		
Decision:						
ERCP	0	0.0	16	80.0	X^2=17.1	<0.001
Laparoscopic	10	100.0	4	20.0		

p-value <0.05 is significant.
SD: Standard deviation.
X^2 = Chi-Square test.

Table (10): ROC curve analysis for GGT in the prediction of CBD stones.

	AUC	95% CI	Sensitivity	Specificity	PPV	NPV	Accuracy	p-value
GGT	0.839	0.681-0.957	100%	71.4%	77.8%	100%	85.7%	<0.001

PPV: Positive predictive value. NPV: Negative predictive value.

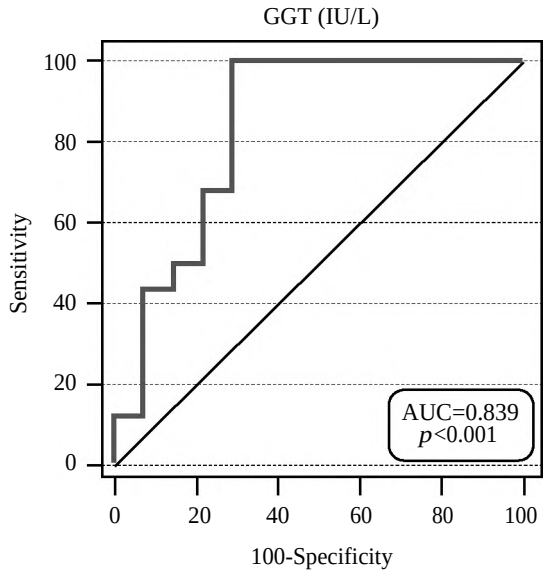

Fig. (1): ROC curve analysis for GGT in the prediction of CBD stones.

Discussion

Cholelithiasis is a common and frequently occurring disease worldwide. Simple gallbladder stones are the main component of cholelithiasis, and approximately 10-30% of gallstone patients also suffer from choledocholithiasis **[13]**.

For gallbladder stones combined with symptomatic common bile duct stones, the clinician can easily confirm the diagnosis preoperatively. However, some patients with cholecystolithiasis combined with choledocholithiasis are easily missed by clinicians due to asymptomatic choledocholithiasis. If these patients only undergo laparoscopic cholecystectomy, residual postsurgical common bile duct stones will be at risk of complications such as acute cholangitis **[14]**.

The GGT is a cell surface enzyme plays an important role in cellular metabolism against oxidative stress; accordingly, GGT can regulate redox-sensitive functions such as antioxidant defense, cell proliferation, and apoptosis homeostasis. GGT plays an important role in oxidative stress by converting glutathione to cysteine, glutamate, and glycine in cellular metabolism **[15]**.

The GGT is distributed in all organs of the body, with a higher concentration in the biliary epithelium. It is closely related to the occurrence and development of various diseases **[16,17]**.

In the diagnosis and treatment of biliary-related diseases, especially cholelithiasis, GGT has always been a popular biochemical indicator. Cholelithiasis is a common benign biliary tract disease, with its pathological process leading to biliary tract injury and changes in various metabolic enzymes in bile duct epithelial cells, among which GGT, ALP, and other liver enzymatic indicators have auxiliary diagnostic values for choledochal stones with obstructive jaundice **[18]**.

Some cholecystolithiasis patients are unwilling to undergo early surgical treatment for outpatient follow-up. If they are not screened for asympto-

matic choledocholithiasis, stones may exist in the common bile duct for a long time without symptoms, which can lead to long-term chronic bile duct inflammation and even cholangiocarcinoma. On the other hand, if asymptomatic choledocholithiasis is not found before surgery in patients with gallstones, laparoscopic cholecystectomy alone may result in complications such as jaundice, acute cholangitis and acute pancreatitis. Therefore, it is important to perform routine secondary asymptomatic choledocholithiasis screening on cholecystolithiasis patients to improve the vigilance of clinicians and to avoid these harmful complications **[10]**.

We aimed to evaluate the sensitivity and accuracy of GGT in the diagnosis of silent common bile duct stones in patients diagnosed with gall stones and scheduled for cholecystectomy.

We established this prospective observational study on 30 patients who are diagnosed with gall bladder stones with normal or elevated gamma glutamyltransferase referred to General Surgery Department, Ain Shams University and General Surgery Department, El Sahel Teaching Hospital.

Our study showed that the age of patients included in our study was ranged from 19 years to 60 years with mean (± SD) was 40.37±11.47 years. Fourteen (46.7%) cases were males and 16 (53.3%) were female with male to female ratio was 0.88: 1. The mean BMI was 27.93±1,55Kg/m^2 and ranged from 25Kg/m^2 to 31 Kg/m^2.

In the same context with Mei et al. **[10]** who retrospectively enrolled 829 patients with cholecystolithiasis to investigate the serum GGT in predicting the diagnosis of asymptomatic choledocholithiasis secondary to cholecystolithiasis and found that the mean age of the observational group was 50.29±10.07 years, included 382 males and 447 females and BMI was 20.76±4.51kg/m^2.

Also, Lin et al. **[19]** retrospectively enrolled 466 patients who underwent surgical treatment of cholelithiasis and found that the mean age was 58±14.50 of 198 and 268 male and female patients, respectively.

Our findings revealed that, the mean total bilirubin, GGT and ALP were 0.77±0.17, 295.67± 249.20 and 204.67±171.85 respectively.

Also, Mei et al., **[10]** observed that the mean ALT was 35.04 ±9.18U/L, and the mean AST was 38.96 ±10.65U/L, the mean GGT was 154.56±39.53 and ALP was 171.51±41.74.

Our study showed that more than half (53.3%) had normal liver and thick gall bladder wall was seen in 53.3% cases. Most cases had multiple gall stones, as they constituted 76.7% of patients. The size of stones were more than 4 mm in 60% cases. Common bile duct was dilated in 53.3% cases with mean diameter of 11.87±1.48mm. common bile duct stones was found in seven cases (23.3%).

Also, Jovanovic´ et al., **[12]** meanCBD diameter on abdominal ultrasound on test group 11. 1mm and validation group 11.2 mm, presence of hypertechoic structure in CBD on abdominal ultrasound on test group 52.4% and validation group 49% while the presence of CBD stones on ERCP on test group 78.6% and validation group 77%.

Our results supported by Mei et al., **[10]** study who observed that patient group were diagnosed with cholecystolithiasis by B-mode ultrasonography before operation, which was subsequently confirmed by surgery. Some patients in the observation group underwent preoperative magnetic resonance cholangiopancreatography (MRCP) examination, which indicated choledo-cholithiasis, and all patients were diagnosed with choledocholithiasis during surgery.

The examination methods of choledocholithiasis include abdominal B-ultrasound, computed tomography (commonly known as CT), MRCP, ERCP and endoscopic ultrasound (EUS). Abdominal B-ultrasound can accurately diagnose cholecystolithiasis and is the first choice for the examination of cholecystolithiasis **[20]**.

However, the location of the common bile duct is deep, and due to disturbance by abdominal wall fat and gastrointestinal gas, there is no expansion or no apparent expansion of the upper common bile duct, or there is stenosis and curvature of the common bile duct. Therefore, it is often difficult to detect common bile duct stones with external B-ultrasound, and its diagnostic accuracy for sediment-like stones is only 55%. CT examination has a high diagnostic rate for high-density calculi with a large diameter, but the diagnostic accuracy for low-density or small stones is low **[21]**.

The MRCP is more sensitive for the diagnosis of common bile duct stones, but the feasibility in patients with pathological obesity or with foreign metal materials in the body (such as a cardiac pacemaker) is low. It is also expensive and increases the economic burden on patients and may lead to waste of medical resources, so it is not appropriate as a routine preoperative screening method. ERCP can identify the location and size of common bile

duct stones, and thus is still the gold standard for the diagnosis and treatment of choledocholithiasis. However, this method is invasive, difficult to operate and causes many complications, so it cannot be used as an optimal routine screening method [33].

The EUS can avoid the interference of abdominal wall fat and gastrointestinal gas and obtain clear bile duct ultrasound imaging, making it a useful tool for diagnosing common bile duct stones. However, EUS is not yet performed in most primary hospitals [23].

The procedure also has difficulties during operation. For example, due to stenosis of the stomach outlet and duodenum, the endoscope cannot successfully reach the duodenal bulb, and patients experience a lot of pain, so EUS is not yet considered to be a better routine screening method. Therefore, it is of great clinical significance to find a small-trauma, convenient, fast, reliable and inexpensive examination method for asymptomatic choledocholithiasis screening. According to the literature, factors such as serum bilirubin, ALP and GGT have some predictive effects on the diagnosis of choledocholithiasis [24]. However, these studies were limited to symptomatic choledocholithiasis, and there have been few studies on secondary asymptomatic choledocholithiasis [25].

Our study observed that it was found that the common bile duct stones was significantly higher in cases with high GGT compared to cases with normal GGT (p=0.033). It was found that multiple common bile duct stones was significantly higher in cases with high GGT compared to cases with normal GGT (p=<0.001). In addition, the decision of doing ERCP before laparoscopy was significantly higher in cases with high GGT compared to cases with normal GGT (p=<0.001).

This indicates that changes in this indicators is related to asymptomatic choledocholithiasis, and an abnormal increase of this indicators may be a risk factor for cholecystolithiasis with common bile duct stones [12].

Additionally, in Mei et al., [10] study when compared observational group and control group and observed that Serum GGT and ALP levels were significantly higher in the observation group than in the control group (p<0.05). There were no significant differences in serum aspartate aminotransferase, alanine aminotransferase, direct bilirubin and total bilirubin levels between the two groups (p>0.05).

Additionally, ALT, AST, ALP, and GGT were significantly higher in patients diagnosed with CBD stones compared to control group [26].

Our results showed that for detecting CBD stones, GGT had sensitivity and specificity of 100% and 71.4%, respectively, when a cut-off value of 71.4u/l was applied. This came in agreement with Mei et al., [10] who found that the area under the ROC curve (AUC) were 0.881 (95%CI: 0.830-0.932), for GGT. The correspondent cut-off values of GGT were 95.5 U/L sensitivity was 90.8% and specificity was 83.6%.

Moreover, Lin et al., [26] found that GGT (AUC of 0.761, sensitivity of 78.1%, and specificity of 63.58%), in Common Bile Duct Stones however, largest AUC for the diagnostic efficacy of common bile duct stones were GGT (AUC of 0.704, sensitivity of 69.88%, and specificity of 68.24%), for CBD pathology with MRCP-Negative Patients.

In contrast with our results, Jovanovic et al. [12] found that There is no doubt that the isolated elevation of serum gamma glutamyl transaminase (GGT) is not a firm predictive factor for choledocholithiasis (CDL) in itself, but what we learned was that the combination of an elevated GGT, common bile duct (CBD) diameter and the presence of a hyperechoic structure in CBD on ultrasound (US) could be used to construct a predictive model for the presence of CBD stones on ERCP [12]. That predictive model is a clinical decision tool which provides sufficient diagnostic accuracy to help us classify patients with high and low probabilities for the presence of CBD stones on ERCP.

In our findings, Reciever- operating characteristic (ROC) curve analysis showed that the AUC, sensitivity and specificity of serum GGT were high. It also indicated that an abnormal increase in serum GGT plays an important role in predicting cholecystolithiasis combined with secondary asymptomatic choledocholithiasis, and it may be an effective serological index for routine screening. With the exception of obvious jaundice, a raised GGT level has been suggested to be the most sensitive and specific indicator of CBD stones.

There are two reasons for increased GGT. First, the presence of stones may cause local inflammatory damage to the bile duct epithelium, resulting in excessive GGT production. Therefore, even the latest literature suggests that serum GGT is also an inflammatory marker [12]. Second, the presence of stones has a mechanical stimulatory effect on the bile duct epithelium, inducing the epithelial layer to increase GGT synthesis, combined with

poor bile excretion, eventually leading to an abnormal increase in serum GGT. Therefore, if the GGT exceeds the cut-off level in serum liver function in gallstone patients, we should be vigilant that the patient is most likely afflicted with secondary asymptomatic choledocholithiasis, and MRCP or ERCP examination should be performed to confirm the diagnosis. This can avoid biliary tract inflammatory disease or tissue malignant transformation caused by the long-term presence of asymptomatic choledocholithiasis. A suitable surgical plan can also be developed to prevent intraoperative accidents, serious postoperative complications and other risks due to missed diagnosis **[10]**.

Conclusion:

Abnormally elevated serum GGT level may be a potentially useful marker for the early prediction of asymptomatic choledocholithiasis secondary to cholecystolithiasis.

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دور جاما غلوتاميل ترانسفيراز في تشخيص حصوات القناة المرارية

يعتبر استئصال المرارة بالمنظار هو المعيار الذهبي في علاج مرض حصوة المرارة، ويتم إجراء معظم عمليات استئصال المرارة بهذه الطريقة اليوم. ومع ذلك، فمن المعروف أن ٣-٣٣٪ من المرضى الذين يعانون من حصوات مرارية مصحوبة بأعراض قد تحتوي على حصوات القناة الصفراوية الشائعة.

تشمل الأساليب الجراحية المستخدمة في تحص المرارة مع تحص صفراوي ثانوي شق البطن، واستكشاف القناة الصفراوية بالمنظار وتنظير القناة الصفراوية بالمنظار. مع ظهور الجراحة طفيفة التوغل وجراحة عادة التأهيل السريعة، أصبحت إجراءات الجراحة طفيفة التوغل مثل إجراءات التنظير الداخلي هي الطرق الرئيسية لعلاج الحصوات الصفراوية خارج الكبد.

يعد جاما جلوتاميل ترانسفيراز أحد الاختبارات المعملية الأكثر شيوعاً وهو اختبار رئيسي يستخدم للتقييم المختبري لتلف الكبد. يشتق المصل جاما جلوتاميل ترانسفيراز بشكل أساسي من الكبد ويتم إنتاجه عن طريق خلايا الكبد الميتوكوندريا، وتفرز عن طريق القناة الصفراوية، ويتم توزيعها بشكل أساسي في سيتوبلازم الكبد وظهارة القناة الصفراوية داخل الكبد.

كما أشارت إلى أن الزيادة غير الطبيعية في جاما جلوتاميل ترانسفيراز في الدم تلعب دوراً مهماً في توقع تحص المرارة جنباً إلى جنب مع تحص كوليدو الصفراوي الثانوي بدون أعراض، وقد يكون مؤشراً مصلياً فعالاً للفحص الروتيني. باستثناء اليرقان الواضح، تم اقتراح مستوى جاما جلوتاميل ترانسفيراز المرتفع ليكون المؤشر الأكثر حساسية وتحديداً لأحجار القناة الصفراوية الشائعة.

لقد هدفنا إلى تقييم حساسية ودقة جاما جلوتاميل ترانسفيراز في تشخيص حصوات القناة الصفراوية الصامتة الشائعة في المرضى الذين تم تشخيص إصابتهم بحصوات المرارة والمقرر لها استئصال المرارة.

هذه دراسة قائمة على الملاحظة تم إجراؤها في قسم الجراحة العامة، جامعة عين شمس وقسم الجراحة العامة، مستشفى الساحل التعليمي من ٨/٢٠٢٢ إلى ٢/٢٠٢٣.

شملت الدراسة الحالية المرضى بحصوات المرارة مع عاماً غلوتاميل ترانسفيراز العادي أو المرتفع تم جمع بيانات التاريخ التفصيلي والبيانات الديموغرافية.

إتمام الفحص العام والمحلي.

الفحوصات المخبرية : تم الحصول على مثل جاما جلوتاميل ترانسفيراز لجميع المرضى المقرر لهم استئصال المرارة صورة دم كاملة، اختبارات وظائف الكبد بما في ذلك الألبومين، البيليروبين (الكلي والمباشر)، ناقلة أمين الكبد. وظائف التخثر. الكرياتينين في الدم. سكر تراكمي بالدم. الفحص بالموجات فوق الصوتية. تصوير البنكرياس والقنوات الصفراوية بالرنين المغناطيسي. استئصال المرارة بالمنظار. متابعة ما بعد الجراحة. تمت المتابعة بعد العملية الجراحية بعد شهر واحد من استئصال المرارة بالمنظار عن طريق طلب الفحوصات المختبرية التالية. مصل جاما غلوتاميل ترانسفيراز. صورة دم كاملة. اختبارات وظائف الكبد بما في ذلك الزلال والبيليروبين وترانس أميناس الكبد.

\النتائج :وجد أن وجود حصوات في القناة الصفراوية كانت أعلى بشكل ملحوظ في الحالات ذات جاما غلوتاميل ترانسفيراز المرتفع مقارنة بالحالات ذات جاما غلوتاميل ترانسفيراز الطبيعي. وجد أن حصوات القناة الصفراوية المتعددة كانت أعلى بشكل ملحوظ في الحالات ذات جاما غلوتاميل ترانسفيراز المرتفع مقارنة بالحالات ذات غلوتاميل ترانسفيراز الطبيعي. بالإضافة إلى ذلك، كان قرار إجراء تصوير البنكرياس والقنوات الصفراوية بالرنين المغناطيسي قبل تنظير البطن أ على بشكل ملحوظ في الحالات ذات جا ما غلوتا ميل ترانسفيراز المرتفع مقارنة بالحالات ذات غلوتاميل ترانسفيراز الطبيعي. للكشف عن حصوات الكانابيديول، كان لدى جاما غلوتاميل ترانسفيراز حساسية وخصوصية بنسبة ١٠٠٪ و ٧١.٤٪، على التوالي، عند تطبيق قيمة حدية قدرها ٧١.٤ وحدة لكل ليتر.

\الإستنتاج : قد يكون مستوى غلوتاميل ترانسفيراز المرتفع بشكل غير طبيعي في الدم علامة مفيدة محتملة للتنبؤ المبكر بتحصي القناة الصفراوية بدون أعراض ثانوية.