



A STUDY OF PREDICTORS OF SYNCHRONOUS COMMON BILE DUCT STONES IN PATIENTS WITH SYMPTOMATIC CHOLECYSTOLITHIASIS SCHEDULED FOR ELECTIVE CHOLECYSTECTOMY.

Gastroenterology

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ABSTRACT

Objective: The goal of this study is to identify predictors of synchronous common bile duct (CBD) stones in symptomatic cholecystolithiasis (SCL) patients scheduled for elective cholecystectomy and to stratify those at risk for CBD stones for further CBD evaluation and potentially reduce complications associated with invasive procedures for CBD evaluation. **Methods:** In this Retrospective study programme done at a tertiary hospital in South India, the Department of Surgical Gastroenterology and Minimal Access Surgery in collaboration with the Departments of Medical Gastroenterology and Radiology, data from a total of 630 patients who underwent Laparoscopic Cholecystectomy (LC) were collected and from them 87 already diagnosed cases of CBD stone were excluded, while data of 367 patients at risk for synchronous CBD stones were studied from March 2017 to November 2020 with a follow of minimum of six months. Based on pre-operative data that is clinical, Laboratory and USG abdomen a risk categorisation was done for cholangiography (ERCP or IOC)/follow-up as High, Intermediate or Low risk groups in all 367 patients at risk for possible synchronous CBD stones before they were taken for LC. The statistical analysis has been done from this data using SPSS software and maintaining a P-value <0.05 as statistically significant. **Result:** In the present study, SPSS version 20 software was used and Uni, Bi and Multivariate analysis has been done. Of 367 patients at risk for synchronous CBD stones, only 223 have synchronous CBD stones with a prevalence of 60.7%. Statistical analysis showed no particular age and gender at risk for synchronous CBD stones but with a slight male preponderance of 1.7% only. Bivariate analysis of clinical data revealed Cholecystitis (CH), Cholangitis (CG), and biliary pancreatitis (BP) are statistically significant ($p < 0.005$). multivariate analysis of biochemical findings revealed Total bilirubin (TB), serum alkaline phosphatase (S.ALP), serum gamma-glutamyl transferase (GGT), SGPT/ALT, SGOT/AST and serum amylase/lipase ($p < 0.005$). multivariate analysis of radiological findings showed CBD size, CBD image, IHBRD and pancreatitis are statistically significant for predicting synchronous CBD stones in patient with symptomatic cholecystolithiasis. Different Risk groups analysis for associated CBD stones in symptomatic patients found out that the low-risk group had 2.4%, the intermediate-risk group had 31% and the high-risk group 86.6% with statistically significant p-value ($p < 0.005$). **Conclusion:** In the present study, all the studied predicting factors in clinical, biochemical and radiological are significant to determining presence of synchronous CBD stones in patients who are at risk and diagnosed with symptomatic Cholelithiasis undergoing laparoscopic cholecystectomy pre-operatively.

KEYWORDS

Cholecystolithiasis or symptomatic Cholelithiasis (SCL); common bile duct stones (CBD's) or choledocholithiasis; laparoscopic cholecystectomy [LC]; Endoscopic Retrograde Cholangiopancreatography [ERCP]; Intra-operative cholangiopancreatography (IOC).

INTRODUCTION:

The clinical data of patients with gallstone surgery in our hospital over the past four years were retrospectively analysed to identify predictors of synchronous CBD stones in SCL patients scheduled for LC which helped to establish the synchronous unsuspected CBD stones in SCL using a selective policy of biliary studies based on clinical, biochemical, radiological and cholangiographic findings. This would help categorize at-risk patients into those requiring preoperative endoscopic retrograde cholangio pancreatography (ERCP), intraoperative cholangiography (IOC), follow or those not requiring further biliary imaging. Thus, this selective policy is intended to foresee a more judicious and rational use of invasive procedures and further reduce the complication risks associated with cholangiography (pre or intraoperative) and more so for operative CBD exploration as it is one of the most common medical diseases affecting the hepatobiliary system that necessitates surgical intervention¹. The number of patients who undergo LC for SCL has increased with the development of ultrasonography and laparoscopy². Common bile duct (CBD) stones occur 3-10% of the time in cholecystectomy patients. Although 10-20% of individuals with gallstone disorders have CBD stones, it might be difficult to precisely diagnose them before surgery³. Since preoperative diagnosis directs interventional treatment on the common bile duct, CBD stones must be found before surgery⁴. However, research indicates that even with normal liver function tests (LFT), 5 to 12% of CBD stones are completely asymptomatic. Because of this, some surgeons follow the dictum that, in the event of a positive intraoperative cholangiography (IOC), open CBD exploration should be performed⁵. Patients can be evaluated for choledocholithiasis using a variety of clinical, biochemical enzyme testing and radiographic techniques such as ultrasound, computed tomography scans (CT), and magnetic resonance cholangio pancreatography (MRCP)^{6,7}. Silent or asymptomatic, biliary colic, cholangitis, jaundice, and pancreatitis are the clinical presentations of SCL patients with CBD stones⁸. While asymptomatic CBD calculi patient selection for biliary intervention

has been flawed in part due to the lack of a sensitive non-invasive imaging modality and also because the incidence and natural history of patients selected for laparoscopic cholecystectomy have not been determined, cholangiopathy is the most predictive, with some studies showing 100% specificity⁹. Transcutaneous ultrasonography (TC-USG) abdomen (sensitivity is 50 to 80% depending primarily on CBD dilatation)¹⁰, magnetic resonance cholangiopancreatography (MRCP) (with a positive predictive value of 95%)⁵, and endoscopic ultrasonography (EUS) with sensitivity of 98% and specificity of 99%¹¹ are the modalities used for detecting CBD stones pre-operatively. However, it's still possible that most centres won't have access to MRCP and EUS¹². Experience and a learning curve are necessary to master EUS¹³. Despite being one of the frequently utilised invasive procedures for the early assessment and detection of suspected biliary blockage, endoscopic retrograde cholangiopancreatography (ERCP) is linked to complications such as pancreatitis, cholangitis, and enteric perforation¹⁴. Cholangitis, biliary blockage, and specifically severe biliary pancreatitis are the current criteria for ERCP in individuals at risk for CBD stones¹⁵. Other options include laparoscopic or open intraoperative USG, cholangiogram, choledochoscopy, and CBD exploration in increasing order of invasiveness. These invasive procedures would not be wise to apply for all patients with symptomatic gallstones undergoing cholecystectomy with possible symptoms correlated choledocholithiasis as these procedures are associated with various complications like pancreatitis, cholangitis, strictures and perforations especially related to endoscopic procedures^{16,17}.

Furthermore, up to 61% of patients who undergo ERCP will be found to be free of CBD stones, wasting their time and money¹⁸. A recent prospective analysis of 1177 consecutive ERCPs found a 1.0% procedure-related mortality rate and 15.9% morbidity rate at 30 days¹⁹. Therefore, in these situations, it is best to take a protocol-based approach to make the most of the limited healthcare resources

available locally and to minimise the risks associated with intrusive operations.

MATERIALS AND METHODS:

Data from all the diagnosed SCL patients who presented at a tertiary hospital in South India, in the Department of Surgical Gastroenterology and Minimal Access Surgery in collaboration with Departments of Medical Gastroenterology and Radiology, and scheduled for cholecystectomy were collected and studied. Among them all the pre-operative definitively diagnosed cases of CBD stones and when no risk factors for synchronous CBD stones found were excluded. All symptomatic cholecystolithiasis patients with no definitive feature to diagnose synchronous CBD stones but when they have risk factors for them are included in this present study and were evaluated from the year 2017 to the year 2020 with follow-up of a minimum of six months.

The risk factors analysed were based on clinical presentation, altered biochemistry and imaging studies of the hepato-biliary system. All the cases falling under the high-risk category were subjected to ERCP, those falling under the intermediate group were subjected to IOC and lastly, the low risk group were kept under observation by follow-up for duration of a minimum of 6 months from the time of cholecystectomy.

PROFORMA⁵¹

Table 1: Predictors Of CBD Stones In Cholecystolithiasis

Name:		Address:			
Age/sex:		Phone No.:			
IPNo.:		DOA:	DOS:	DOD:	
Risk group Data	Parameter	0) No risk	1) Low risk	2) Inter risk	3) High risk
1)CLINICAL					
	Age	<70 yrs.	70-80 yrs.	>80 yrs.	
	Biliary colic		Epigastric +/- RHC to back		
	Cholecystitis		Present H/o		
	Cholangitis				Recent H/o
	Obstructive Jaundice				Recent H/o
	Biliary Pancreatitis				Recent H/o
2) LABS					
	Total bilirubin		2-4 X normal	>4X normal	
	S.AL.P			<2.5X normal	>2.5X normal
	S.GGT			<2X normal	>2 X normal
	SGPT/ALT		<2 X normal	2-4X normal	
	SGOT/AST		<3 X normal	3-4X normal	
	S.Amylase/ Lipase		<4 X normal	>4X normal	
3)USG ABDOMEN					
	Gall bladder		Inflamed		
	CBD size	<5 mm	5-7mm	7-9mm	>9 mm
	CBD image s/o			Sludge	? stone
	IHBRD				>2 mm
	Pancreatitis (Focal)				Head / diffuse
IOC					
	Findings				
ERCP					
	Findings				
OTHER					
	Tests				
FOLLOWUP					

Defining the risk parameters included in this study –

Clinical:

Age – more than 80 yrs. fall under intermediate risk, those between 70 to 80 years. fall under low risk and less than 70 yrs. under no risk category. Biliary colic - abdominal pain originating from right hypochondrium or epigastrium or left hypochondrium, colicky in nature, radiating to back and relating to fatty meals; all pains suggesting only biliary colic or acute Cholecystitis would be categorized as a low risk group, whereas those with recent history suggestive of cholangitis, obstructive jaundice and biliary pancreatitis would fall under high-risk group.

Biochemical:

The high-risk group includes all cases with S.AL.P more than 2.5 times the normal limit or S.GGT more than 2 times the normal limit. The intermediate risk group includes all cases with total S.bilirubin more than 4 times normal or S.AL.P less than 2.5 times normal or S.GGT less than 2 times normal or SGPT/ALT 2 to 4 times normal or SGOT/AST 3 to 4 times normal or S.amylase / lipase more than 4 times normal. Low risk group includes all cases with total S.bilirubin less than 2 to 4 times normal or SGPT/ALT less than 2 times normal or SGOT/AST less than 3 times normal or S. amylase / lipase less than 4 times normal.

Imaging:

Mainly based on USG abdomen and parameters of the high-risk group were CBD size more than 9 mm or CBD image suggestive of filling defects where still a possibility of a stone cannot be ruled out or the presence of intrahepatic biliary radical dilatation [IHBRD] more than 2 mm or features of pancreatitis. Parameters for the intermediate-risk group were CBD size 7 to 9 mm or CBD image suggestive of sludge. The low-risk group parameters included were thickened gallbladder walls suggestive of acute Cholecystitis or CBD size 5 to 7 mm.

Intraoperative cholangiography [IOC] findings:

The entire intermediate risk group subjects underwent IOC and those with findings of CBD dilatation, filling defects suggestive of stones, IHBRD, and hindrance to free flow of contrast into duodenum were subjected to ERCP.

Endoscopic retrograde cholangiopancreatography [ERCP] status:

Preoperative, intraoperative or postoperatively was done if patients were under the high-risk category or IOC with abnormal findings as stated previously or CBD stones detected later during follow respectively. After successful cannulation of the bile duct cholangiogram were done, filling defects suggestive of stones was retrieved by balloon trawl, and if required sphincterotomy were performed and in the majority, bile ducts were stented to guide during LC. Bile duct stents were removed after 3 to 4 weeks after LC on OP basis.

Other imaging findings:

Routinely not done at present admission or done elsewhere include endoscopic USG, MRCP, CT scan abdomen, liver biopsy, etc.

CBD exploration:

Done either laparoscopically or open – if findings on IOC or failed ERCP.

Follow-up:

A minimum follow-up duration of 6 months from the time of cholecystectomy in all cases of the low-risk group category was done to look for residual retained or recurrent stones discovered in the common bile duct after cholecystectomy CBD stones based on clinical features, biochemistry or imaging studies. Patients were followed up personally in OPD, conversed telephonically or contacted through mailing.

Risk categorization is defined as follows:

HIGH RISK: - if at least 2 High-risk parameters from different data or 1 High risk + at least 2 Intermediate risks from different data or >3 Intermediate risks from all 3 data. All these are subjected to ERCP

INTERMEDIATE RISK:– if 1 High risk + at least 1 Intermediate risk from different data or >2 Intermediate risks from different data or 1 Intermediate risk + at least 2 Low risks from different data or > 3 Low risks from all 3 data. Subjected to IOC and proceed.

LOW RISK: - if > 2 Low risks or only 1 Intermediate risk Kept under Follow-up for a minimum of 6 months to max. 2 years / till study period

permitted

No risk: No further biliary imaging if < 2 Low risks or No risk parameters.

The efficacy of all predictors for synchronous CBD stones is analysed and discussed. An identified group of patient at high risk subjected to preoperative ERCP as they can get benefit from it, intermediate group subjected to IOC and the low risk group was kept under follow up avoiding further biliary imaging.

Inclusion criteria:

All symptomatic cholelithiasis [SCL] patients after clearance from pre-anaesthetic check-ups scheduled for cholecystectomy meeting the above study criteria were included in this study.

Exclusion criteria:

Patients with diagnosed CBD stones, hepatitis (raised prothrombin time, >6 times ALT, > 4 times AST, low albumin), prior ERCP-cleared CBD stones and SCL patients who have not met the above study criteria.

RESULTS:

Data from a total of 630 patients with SCL who underwent LC were studied at a Hyderabad tertiary hospital from 2017 to 2020 with a minimum follow-up of six months using strict inclusion and exclusion criteria. Of these, 87 diagnosed cases of CBD stones were excluded, while 367 patients at risk for synchronous CBD stones were included in the study. These 367 patients were categorized as high risk 239 (65.122%), intermediate risk 45 (12.26%), or low risk 83 (22.61%) groups based on defined risk stratification criteria taken from pre-operative data (clinical, lab, and USG abdomen). These patients were at risk for potential synchronous CBD stones before they were taken for cholecystectomy.

Table 2 – Showing the influence of demographic factors in symptomatic Cholelithiasis patients (n-367) for the presence of synchronous CBD stones (CBDS)

Demographic Predictor	Parameter	No. of Subjects	No. of CBDS	% of CBDS	Chi-square	P-value
Age	<70 yrs.	327	204	62.3	4.969	0.83
	70-80 yrs.	29	12	41.3		
	>80 yrs.	11	7	63.6		
Sex	Male	190	113	59.4	0.275	0.60
	Female	177	110	62.1		

P-value <0.05* is significant

P-value >0.05 is not significant

In this study, the number of study subjects having a synchronous CBD stone was 223 out of 367 patients at-risk symptomatic Cholelithiasis with prevalence of 60.7%. Age distribution among study subjects ranged from 12 yrs. to 99 yrs. with the mean age being 44.9 years. (SD- 17.19). The majority of the study subjects were below 70 years about 327 (89.0%) composed of almost equal gender distribution with a slight male preponderance of 190(51.7%). Statistical analysis of age has not demonstrated any particular age group at risk for synchronous CBD stones as the p-value is statistically not significant(0.83) and also no particular sex was found to have a risk for CBD stones as p-values for sex were statistically non-significant(0.60).

Table 3 – Showing the Bivariate analysis of clinical predictor factors in symptomatic Cholelithiasis patients (n-367) for the presence of synchronous CBD stones (CBDS)

Predictor factor	Parameter	Risk	No. of Subjects	No. of CBDS	% of CBDS	Chi-square	P-value
Clinical	Cholecystitis	Yes	341	197	57.7	18.069	0.00*
		No	26	26	100		
	Cholangitis	Yes	264	221	84	207.8	0.00*
		No	103	2	1.9		
	Obstructive jaundice	Yes	26	18	69.2	0.842	0.35
		No	341	205	60.1		
	Biliary pancreatitis	Yes	16	14	87.5	5.01	0.025*
		No	351	209	63.3		

P-value <0.05* - Significant*

P-value >0.05- Non Significant

Bivariate analysis of clinical data from this study revealed that practically all of the study individuals presenting symptoms were consistent with biliary colic, 367(100%).

Acute Cholecystitis was present in 341 of the 367 patients at risk for CBD stones, and of these, 197(57.7%) were later found to be carrying CBD stones. In contrast, synchronous CBD stones

Were present in 26 (100%) of the 26 subjects without acute Cholecystitis; statistical analysis revealed a significant p-value (0.000) for these two conditions.

Similar Bivariate analysis of recent cholangitis has revealed its Presence in 264 among 367 at risk patients, out of whom 221 (84%) were found to have CBD stones whereas 103 at risk without cholangitis were Harboring CBD stones in 2(2%), again correlation of recent Cholangitis and synchronous CBD stones has reached statistically Significant p-value (0.00).

Similar Bivariate analysis of recent obstructive jaundice revealed its presence in 26 of 367 at-risk, of whom 18 (69.2%) were found to have CBD stones, while 341 at-risk patients without recent obstructive jaundice were harbouring synchronous CBD stones in 205 (60.1%), again reaching statistically non-significant p-values(0.35) for the correlation between recent obstructive jaundice and synchronous CBD stones.

Similar Bivariate analysis of recent biliary pancreatitis revealed its presence in 16 of 367 at-risk individuals; of these, 14 (87.5%) were found to have CBD stones, while in 351 at-risk individuals without biliary pancreatitis, 209(59.5%) were harbouring CBD stones. However, the correlation between recent biliary pancreatitis and synchronous CBD stones has reached statistically significant p-values (0.025).

Clinical data subgroup analysis revealed that synchronous CBD stones were associated with acute Cholecystitis, cholangitis and biliary pancreatitis. In contrast, a trend towards a potential presence of CBD stones is seen in obstructive jaundice, however not enough to establish a statistically significant p-value.

Table 4: Showing multivariate analysis of pre-operative biochemical predictors for synchronous CBD stones (CBDS) in symptomatic Cholelithiasis patients (n-367)

Predictor factor	Parameter	Risk	No. of Subjects	No. of CBDS	% of CBDS	Chi-square	P-value
Bio-chemistry	T.bilirubin	Low	121	45	37.1	69.797	0.00*
		Inter	182	114	62.6		
		High	64	64	100		
	S.ALP	Low	111	30	27.0	121.18	0.00*
		Inter	151	88	58.2		
		High	105	105	100		
	S.GGT	Low	92	03	3.2	170.80	0.00*
		Inter	73	61	83.5		
		High	202	159	78.7		
	SGPT/ALT	Low	192	49	25.5	209.77	0.00*
		Inter	94	93	98.9		
		High	81	81	100		
	SGOT/AST	Low	193	50	25.9	207.45	0.00*
		Inter	104	103	99		
		High	70	70	100		
	S.amylase/lipase	Low	231	111	48	43.654	0.00*
		Inter	10	10	100		
		High	126	102	80.9		

P-value <0.05* -significant*

P-value >0.05- Non significant

In 367 patients who were at risk for developing synchronous CBD stones, a multivariate analysis of the biochemistry of the hepatic-bile-pancreatic system revealed total bilirubin levels that were within normal limits in 121 patients, raised 2 to 4 times normal in 182 patients and more than 4 times normal in only 64 patients. Rising T. bilirubin has been found to correlate well with increasing chances of having synchronous CBD stones, with highly statistically significant p-values reaching (0.000). This is because there is a linear correlation between rising bilirubin levels and the presence of CBD stones, with normal

bilirubin levels being 45(37.1%); 114 (62.6%) for rises of 2-4 times; and 64 (100%) for rises of more than 4 times.

All 367 at-risk patients had serum alkaline phosphatase (ALP) levels that were within the normal range in 111, but in the majority of cases, the levels were raised by less than 2.5 times normal in 151 and more than 2.5 times normal in 105 of the patients. Again, rising S.ALP levels were seen to be closely correlated with the development of CBD stones; normal values had 30(27.0%), 2.5 times normal values had 88(58.2%), and >4 times normal ALP had 105(100%) CBD Stones. Rising S.ALP was shown to be in good association with the existence of synchronous CBD stones in this instance, with p-values that were extremely statistically significant (0.000).

Serum Gamma glutamyl Trans peptidase (GGT) level measurements revealed similar outcomes. Most research participants 202, had GGT levels that were higher than twice normal, with 92, having GGT levels normal, and 73, having values below twice normal. CBD stones with normal GGT values were seen in 3(3.2%), 61(83.5%) if GGT were <2 times normal and 159(78.7%) if GGT values were more than 2 times normal. This is due to an increase in frequency of CBD stones that reached statistically highly significant p-values (0.000) with growing GGT levels.

Rising SGPT/ALT results were. 192 people had SGPT levels that were within normal ranges, 94 people had levels that were less than twice normal and only 81 people, had elevated levels that were more than twice normal. Normal SGPT levels resulted in 49(25.5%) cases of CBD stones, <2 times normal SGPT levels resulted in 93(98.9%) cases of CBD stones, and if SGPT raised over 2 times normal, 81(100%) cases of CBD stones were present. This correlation had a statistically significant p-value of (0.000).

367 patients who were at risk had SGOT/AST testing as per our hospital's policy. When SGOT values were evaluated, the majority of cases 193 were within normal ranges, and 50(25.9%) had CBD stones. While 103 (99%) of the 104 patients had CBD stones that were less than three times the normal level. 70(100%) of the 70 at-risk patients who had SGOT levels that were 3-4 times normal were also found to have CBD stones, with the link reaching a statistically significant p-value of (0.000).

Although serum amylase testing is done on all LC candidates according to our hospital's protocol, serum lipase testing is only done when there is a high probability of pancreatitis. In the current investigation, pancreatic enzymes were performed on 367 individuals who were at risk and were mostly within normal limits in 231 patients, less than four times normal in 10, and more than four times normal in 126 patients. CBD stones were found in 111 (48%) of the study participants with normal levels of pancreatic enzymes, 10(100%) if 4 times normal, and 102(80.9%) if >4 times normal with a highly significant p-value (0.00).

Table 5: Showing multivariate analysis of pre-operative imaging predictors for synchronous CBD stones (CBDS) in symptomatic Cholelithiasis patients (n-367)

Predictor factor	Parameter	Risk	No. of Subjects	No. of CBDS	% of CBDS	Chi-square	P-value
Imaging-TC USG	CBD size	Normal	103	14	13.59	173.06	0.00*
		Low	57	26	45.6		
		Inter	144	120	83.3		
		High	63	63	100		
	CBD image	Low	234	90	38.4	134.69	0.00*
		Inter	30	30	100		
		High	103	103	100		
	IHBRD	NO	315	179	56.8	14.457	0.00*
		YES	52	44	84.6		
	Pancreatitis	NO	206	144	69.9	11.511	0.001*
		YES	17	17	100		

P-value <0.05* - significant

P-value >0.05 - Non Significant

TC-USG is the main imaging technique used in this investigation. Since SCL patients were all referred for cholecystectomy, all of them had cholecystolithiasis and no outward signs of CBD stones. The characteristics examined in the imaging to show evidence for synchronous CBD stones included pancreatic inflammation,

gallbladder wall thickness, CBD size/diameter, CBD image and Intrahepatic biliary dilatation.

When the CBD diameter was within the normal range in 103 i.e. < 5mm and synchronous CBD stones were seen in 14(13.59%); when CBD diameter was mildly raised, such as between 5-7mm in 57 and synchronous CBD stones were seen in 26(45.6%); when the CBD diameter is moderately raised, such as between 7-9mm in 144 and synchronous CBD stones are seen in 120(83.3%); however, only in 63(10%) is the CBD diameter markedly enlarged, such as >9mm, and synchronous CBD stones are seen in all 63(100%). More study individuals were likely to have CBD stones if their overall CBD size was higher, which was found to be a good correlation with the prevalence of synchronous CBD stones. It was discovered that this imaging parameter substantially correlated with the highly significant p-value (0.00).

Luminal images of CBD were generally clear in 234 of the study participants, but they were harbouring stones in 90 (38.4%) of them, while in 30 they were not clear for any echogenic to signal any filling defects or stones, but they were in 30 (100%) of the participants. 103 individuals saw a CBD image that appeared to be soil, and practically all of them had stones. The existence of synchronous CBD stones was observed to significantly correlate with this imaging characteristic, with a statistically highly significant p-value of (0.00).

Only 52 of the study subjects had intrahepatic biliary dilatation, an indirect predictor of the severity of biliary obstruction, and the majority of these had synchronous CBD stones, with 44 (84.6%), which had a statistically significant p-value of (0.00).

Only 17 people had pancreatic inflammation, probably due to obstruction caused by stones at the common pancreatic-biliary junction, and all 17 (100%) people had synchronous CBD stones. The bulk of the study participants 206 had normal pancreas, and 144 of them 69.9% had CBD stones. The statistically significant p-value (0.001) indicates a correlation between biliary pancreatitis and synchronous CBD stones.

Table 6: Showing multivariate analysis of pre-operative risk groups for presence of synchronous CBD stones (CBDS) in symptomatic Cholelithiasis patients (n-193)

Predictor factor	Risk group	No. of Subjects	No. of CBDS	% of CBDS	Chi-square	P-value
Risk group	Low	83	2	2.4	202.113	0.01*
	Intermediate	45	14	31		
	High	239	207	86.6		

P-value<0.05*-significant*

Each study participant was assigned to one of the three risk groups based on the established criteria after all three pre-operative (clinical, lab, and imaging) data were entered into a prepared proforma. 239 study participants of the total—fell into the high-risk category, 45 fell into the intermediate category, and 83 fell into the low-risk category.

ERCP was performed on 263 patients, 239 of whom were in the high-risk group, 18 in the intermediate-risk group and 6 in the low-risk group. CBD stones were discovered and successful stone extraction was completed in 223 patients (84.7%) with a cannulation rate of 97 % (procedure couldn't be completed for technical reasons in 6 patients) comprising 207 from high risk, 14 from intermediate risk and 2 from the low-risk group. ERCP also diagnosed other conditions like Mirizzi syndrome and papillary stenosis in patients at risk. In total papillary stenosis was diagnosed in 14 subjects who comprised 12 from high risk and 2 from intermediate risk and mirizzi was diagnosed in 11 and they were from the high-risk group only. ERCP was normal in 7 patients (2 from high risk, 3 from low risk and 2 from intermediate risk.)

45 patients made up the intermediate-risk group, and they were all given IOC. The IOC results show dilated CBD in 8 patients, CBD filling defects in 8, both dilated CBD and filling defects in 6, and normal study in 23 individuals. Thus, of the 22 patients with aberrant IOC findings, 18 underwent normal (in 14 bile duct stones were extracted, 2 had papillary stenosis, and 2 had normal study), and 4 underwent 6-months of follow-up. ERCP was not necessary in 27(60%) individuals, while IOC was diagnostic in 16(35.5%) patients who needed additional ERCP.

The majority of the Low-Risk group 77(94%) did not require additional bile duct testing while being monitored, but 6 patients required subsequent biliary system evaluation requiring ERCP. Among these 6 patients, 2 patients presented after 15 months of Laparoscopic cholecystectomy with biliary pancreatitis and the other 4 with obstructive jaundice but bile duct stones were found only in 2 (In other cases possibility of spontaneous passage of bile duct stones can be contemplated).

In the current study, bivariate statistical analysis revealed that there is no correlation between increasing age and the presence of CBD stones, so no correlation has reached a statistically significant p-value for either sex to have CBD stones. Statistical analysis of clinical features with less severe symptoms showed having lower chance of CBD stones than when compared with patients having more severity though not reaching statistical significance. Similarly, subjects with increasing abnormal hepatobiliary-pancreatic biochemistry or TC-USG imaging abnormalities had significantly increased chances of having synchronous CBD stones with statistically high significant P values.

In the current study, the goal of risk stratification was to predict the overall percentage of synchronous CBD stone presence in patients with symptomatic Cholelithiasis scheduled for laparoscopic cholecystectomy to guide further CBD evaluation and the policy of selective use of cholangiography using classification table was 96.7% when compared to overall/finally observed CBD stones.

Table 7: showing predicted and observed CBD stones in patients with symptomatic Cholelithiasis (n=367)

Classification Table		Predicted		
Observed		Final diagnosis		Percentage Correct
		No Stone	Stone	
Final diagnosis	No Stone	137	07	95.1
	Stone	03	220	98.7
Overall Percentage				97.3

With a sensitivity of 0.969, specificity of 0.978, positive predictive value of 0.986 negative predictive value of 0.951 and overall accuracy of 0.97 in predicting CBD stones using pre-operative factors, statistical analysis has shown that this strategy of managing symptomatic Cholelithiasis with synchronous CBD stones by classifying patients at risk for CBD stones has been effective in managing CBD stones. Without these risk factors or pre-operative predictors, the likelihood of having bile duct stones was 1.34%; however, when all predictors were positive, the likelihood increased to 98.6%.

DISCUSSION:

The development of laparoscopy has ushered in a new age in surgery. The standard of care for symptomatic Cholelithiasis is currently laparoscopic cholecystectomy. Due to limited laparoscopic CBD exploration experience, examination for synchronous bile duct stones was a very common practice in the early laparoscopic period, either pre-operatively or during surgery.

Many studies have demonstrated that this practice of routine cholangiography is linked to unintended problems, with the dangers outweighing the benefits. There has been a sharp decline in the number of routine IOCs (intra-operative cholangiogram) performed for SCL (symptomatic Cholelithiasis) slated for LC (laparoscopic cholecystectomy) as laparoscopic experience has increased. Rapid advancements in medical technology have expanded the range of diagnostic and therapeutic options for the treatment of synchronous CBD stones. The surgeon now has a serious problem as a result of the limited health resources and the growing population. Rational use is required to select the best distribution of these resources. To prevent the complications that come with these specialized tests and to improve patient care overall, it is also crucial to avoid indiscriminate indications. All of these should increase the demand for non-invasive, low-cost diagnostic tests for CBD stones.

It is still debatable how to diagnose and treat synchronous choledocholithiasis. Different teams have proposed several management techniques, such as laparoscopic cholecystectomy with laparoscopic common bile duct exploration, an open approach to common bile duct exploration, and pre-, intra-, or post-operative

ERCP, but none of these techniques has yet provided evidence-based support for their applicability as the preferred technique. Additionally, the potential for small stones to migrate on their own and asymptotically, as well as the morbidity and mortality linked to invasive diagnostic procedures, highlight the need for newer tools and/or strategies that could guarantee high diagnostic accuracy while minimizing invasiveness.

Methodological stumbling blocks commonly impede several attempts to create precise predictive criteria^{25, 26, 27} for the existence of common bile duct stones.



FIG 1: The given figure shows: The American Society for Gastrointestinal Endoscopy algorithm for managing of patients with symptomatic cholelithiasis based on the degree of probability for choledocholithiasis⁵¹.

The treatment of symptomatic Cholelithiasis has changed from the open era to the contemporary laparoscopic age aided by rapid developments in endoscopy with the background purpose of treating potential synchronous CBD stones. It was customary to perform IOC in practically all cases during the open era and the early stages of laparoscopy up until the learning curve was overcome. This has a 2% false positivity rate and a 2-3% false negative rate.³⁸

To evaluate the bile duct before surgery, surgeons have a variety of methods at their disposal, including TC-USG, ERCP, MRCP, and EUS, to name a few of the most common alternatives now used in clinical practice. These pre-operative modalities have a failure rate of between 5 and 10%.²² with a missed diagnosis rate of 44.95%; preoperative ultrasonography does a poor job at diagnosing linked CBD stones in gallstone patients. Alanine aminotransferase, concomitant acute cholecystitis, and CBD diameter were identified as important characteristics that may affect the accuracy of the diagnosis, according to the results of statistical analysis.⁴² Routine preoperative ERCP is not widely accepted because it is linked to serious complications such as pancreatitis and perforation. It has a morbidity and mortality rate of 3 to 6.4% and 0.2% to 0.8%, respectively.^{23, 42, 24} In contrast to ERCP, which provides the potential for a therapeutic intervention if necessary, USG, CT, and MRI are only diagnostic procedures. IOC is a common procedure that is safe and effective for determining the anatomy of the bile duct and the presence of stones.

Therefore, it is advised that IOC be used routinely during cholecystectomy.⁴³ Preoperative MRCP has been suggested by numerous authors as an alternate method for identifying CBD stones. The negative predictive value of MRCP was quite high, and the sensitivity and specificity of MRI were reported to be 88.9% and 100%, respectively.²¹ Patients who are MRCP negative for choledocholithiasis can be given ERCP, although continuous monitoring is necessary in case of recurrent cholangitis or pancreaticobiliary cancer.⁴¹ However, due to the limited interpretation of the grey scale, most of MR imaging's potential is lost. Theoretically, MR imaging produces more than 2,000 distinct shades of grey, each corresponding to a distinct digital value ranging from pure white to pure black.^{21, 36} The biology of human vision, however, restricts the number of shades of grey that the human eye can detect on a monitor or a radiographic film to no more than 16, which limits the basis of interpretation by a radiologist. As a result, a substantial amount of information that would be helpful is ignored. Even with 3D reconstruction, the limitations of MRCP in detecting stones smaller than 5 millimetres or stones present in the final segment of the CBD over the papillary sphincter still apply. The hardest stone to find is one that is in the final 5 millimetres of the common bile duct.³⁶ In addition; the requirement for routine MRI procedures could be criticized for being both costly and an excessive use of the existing resources.

Table 8: Showing the statistical data from various techniques to detect synchronous CBD Stones in symptomatic Cholelithiasis.

AUTHOR	SENS	SPEC	PPV	NPV	ACCUR
MRCP- Mari M et al21	0.91	0.84	0.89	0.88	0.90
ERCP48	0.98	1.00	1.00	0.98	
ENDO-USG46	0.97	0.79	0.95	0.88	0.94
IOC Korman et al38			0.75		0.88
Intra-op imaging44	0.93	0.99			
Intra-op. palpation- CBD					0.96
HELICAL-CT 47	95.5				
3D Cholangioscopy Michele et al37	0.71	0.91	0.75	0.87	
PRESENT STUDY-Strategy based	0.96	0.97	0.63	0.93	0.96

There have been various attempts in the past^{25,26,27,30} to analyse factors or indicators that might aid a surgeon in selecting the proper investigation for CBD stones, particularly in cases when the indication for invasive cholangiography is ambiguous. These initiatives received attention since they were all made to lessen needless invasive cholangiography and its associated consequences, such as the need for anaesthesia. Following CBD explorations, early consequences may include cholangitis, pancreatitis, enteric perforations, particularly duodenal, and remote problems such as bile duct strictures.

It is never easy to choose the gold standard method (GSM) for diagnosing synchronous CBD stones in SCL. Due to the great propensity of calculi to shift spontaneously from the CBD, there is currently no absolute GSM, including surgical approaches.³⁴ To diagnose synchronous CBD stones in SCL, EUS is the most accurate tool among those currently on the market for evaluating the CBD, with positive predictive values ranging from 94.9% to 100% and specificity from 97% to 100%.²² Therefore, it is believed that the diagnostic outcomes of EUS are comparable to or even better than those of ERCP or intra-operative CBD exploration.²²

The following factors make EUS less frequently used for CBD evaluation than TC-USG: need for anaesthesia, availability in specialized centres, invasiveness, subjectivity due to the need for expert interpretation, which can result in inter-observer variations, scope maintenance, cost due to the need for a dedicated setup and trained staff, and portability as compared to TC-USG. The use of less invasive pre-operative indicators or risk factors to stratify at-risk patients for CBD stones to select for further CBD evaluation from both a diagnostic and a therapeutic point of view before these patients are taken for LC is therefore definitely feasible until EUS becomes widely used as TC-USG.

In the current clinical study program, we collected data from 367 patients at risk for Synchronous CBD stones, out of 630 patients with SCL who underwent LC from March 2017 to November 2020 using strict inclusion and exclusion criteria. However, 87 diagnosed cases of

CBD stones were excluded. This disease's prevalence (60.7%) was discovered to be nearly comparable to previous studies' findings.³⁹

Table 9: Showing the prevalence of gall bladder stones and CBD stones.

Prevalence	Girard 39	PRESENT STUDY
Gall bladder stones	10471	367
CBD stones diagnosed	654	223
CBD stones suspect %	11	58.2
CBD stones yield %	75	62.67

Among the clinical data analysed, age and gender were poorly correlated for the presence of synchronous CBD stones. In other similar studies from France²⁷, there was a significant correlation between increasing age to the presence of CBD stones especially in females, which could be because of a good number of elderly subjects.

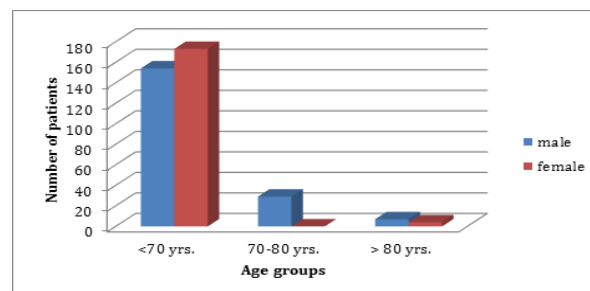


FIG 2: Age distribution in the present study.

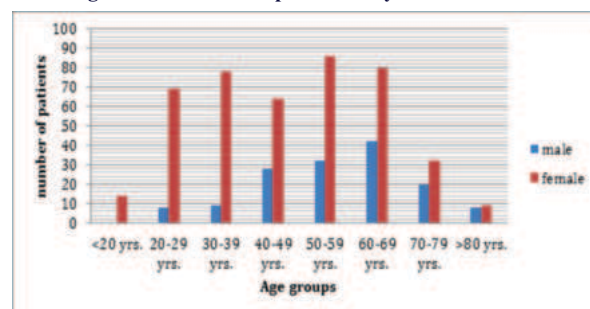


FIG 3: Age distribution in a similar study³⁷.

Clinical presentation in this present study has revealed biliary pancreatitis, cholangitis and acute Cholecystitis in decreasing order to be found to correlate with an increasing chance of harbour synchronous CBD stones. This clinical presentation is almost similar to other studies³⁴.

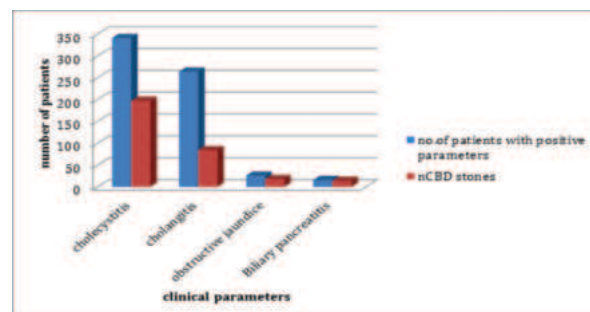


FIG 4: Clinical presentation and synchronous CBD stones in the present study.

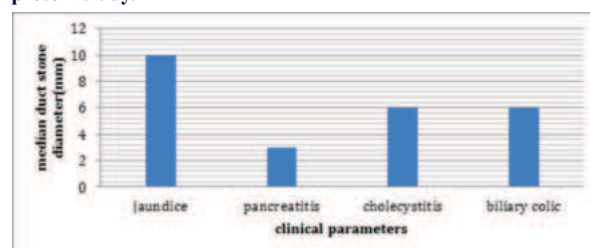


FIG 5: Clinical presentation in a similar study³³.

According to the current investigation, SGPT/ALT, SGOT/AST, serum gamma-glutamyl transferase (GGT), serum alkaline phosphatase (ALP), total serum bilirubin (TSB), and S. Amylase/lipase is the biochemical predictor strongly associated with the occurrence of synchronous CBD stones. While comparable research from the UK²⁰, Singapore²⁵, and France²⁷ has revealed that S.GGT, ALP, TSB, and SGPT are strongly linked to the likelihood of synchronous CBD stones.

S.GGT was found to have a strong connection with synchronous CBD stones in the study from the United Kingdom²⁰, especially if combined with acute Cholecystitis. According to research from France and Singapore, TSB and ALP are reliable indicators for synchronous CBD stones.

Preoperative assessment of the common bile duct by measuring liver function and the common bile duct diameter (5mm + 1mm per decade after 50 yrs.) the day before cholecystectomy has been shown to eliminate the need for routine operative cholangiography in SCL at-risk for synchronous CBD stones, according to research by David S. Watkins et al⁴⁰ using a combination of USG abdomen and biochemistry.

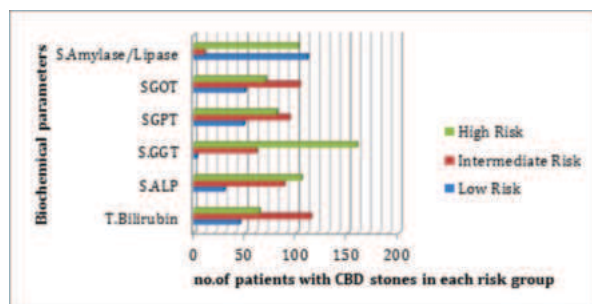


FIG 6: Biochemical findings and synchronous CBD stones in the present study.

There hasn't been an increase in postoperative morbidity from missing bile duct injuries or common duct stones when combined with the selective use of operational cholangiography. This technique eliminates the requirement for routine IOC when evaluating the bile duct before cholecystectomy. In the current investigation, imaging markers such as CBD diameter, CBD filling deficiencies, IHBRD and biliary pancreatitis, were also linked to synchronous CBD stones. A prospective RCT group²², followed by EUS and another group, has thoroughly explored imaging employing USG for CBD evaluation. Of these characteristics, the largest connection was with CBD filling defects and CBD diameter, a finding that was also observed in related studies^{30,22}.

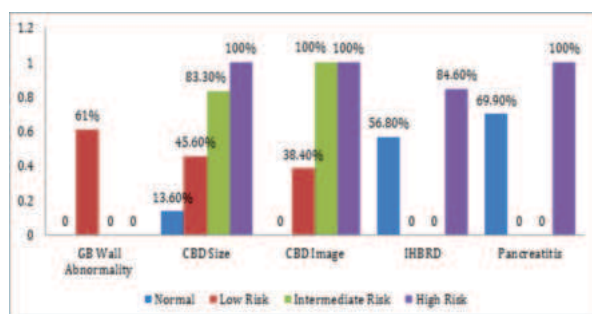


FIG 7: Radiological findings and synchronous CBD stones in the present study.

There are frequencies of 2 cases of persistent or residual CBD stones in this study, which are more likely to result in long-term issues both of which are reported as obstructive jaundice during follow-up.

Operative removal of stones from the common bile duct in addition to laparoscopic cholecystectomy was not thought to be technically feasible in the early days of laparoscopic biliary surgery. To remove common bile duct stones, open surgical removal or, more frequently, ERCP/sphincterotomy became the accepted method. However, ERCP has risks that include mortality of up to 1%, pancreatitis, haemorrhage, cholangitis, and duodenal perforation (5% to 11%)⁴⁵.

The selective approach, where at-risk patients were grouped for further biliary investigations, such as ERCP or IOC or, if not significant, kept under follow-up, greatly facilitated the ability to choose patients for ERCP preoperatively. The risk grouping strategy will likely decrease the incidence of non-therapeutic ERCPs. In the current study, 223 patients (84.7%) had therapeutic ERCP, while 25 patients (11.2%) did not, demonstrating that this study's approach considerably lowered the proportion of non-therapeutic ERCPs from 20 to 50 per cent³² to 11.2% in the current study.

Although there is little information on the long-term expectant care of asymptomatic bile duct stones, surgeons who don't undertake routine surgical imaging typically choose this approach. In low-risk patients who did not fall or need any additional biliary imaging as in intermediate or high-risk groups, clearance of calculi may have occurred without major problems after cholecystectomy, which is supported by this study. This finding (the current study had a follow-up time of 6 months) is consistent with earlier studies that looked at subjects for at least 6 months to 2 years³¹. According to prior studies^{26, 33-35}, it's probable that more calculi would have vanished after 6 weeks, favouring continued expectant care. Expectant management was proven to be both safe and economical in a recent study comparing the immediate and expectant management of 8 and 14 patients, respectively, with small CBD calculi (less than 5 mm) detected intraoperatively.

CONCLUSION:

Application of pre-operative predictors including Clinical (acute Cholecystitis, cholangitis, biliary pancreatitis) Biochemical (Total serum bilirubin, Alkaline phosphatase, S. Gamma-glutamyl transferase, S.SGPT/ALT, S.SGOT/AST, Amylase /lipase) Radiological (CBD diameter, CBD filling defects and intrahepatic biliary radical dilatation [IHBRD]) parameters for synchronous CBD stones in symptomatic cholelithiasis patients scheduled for elective laparoscopic cholecystectomy, seems to be effective in diagnosis and plays a fundamental role in patient selection for further cholangiography studies (like Intra-operative cholangiography or ERCP), more therapeutic than diagnostic ERCP and contributing to reduce inherent complications of invasive cholangiography.

Pre-operative diagnosis of patients likely to have CBD stones and targeted intervention reduces inadvertent complications from 20 to 50% to 11.2%.

A combined analysis of clinical features, biochemistry and USG abdomen taken just before surgery in patients with symptomatic Cholelithiasis would help in decision-making for bile duct evaluation in all at-risk patients in whom possible diagnosis of synchronous CBD stones cannot be excluded.

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Ethical clearance:

No Approval for this study was obtained from the hospitals scientific and ethics committee as this is a retrospective and observational study.

Statistical analysis:

Standard statistical tools software **SPSS version 20** were applied to analyse the predictors for synchronous CBD stones in patients at risk with SCL.

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