European Journal of Molecular & Clinical Medicine

ISSN2515-8260 Volume 09, Issue 01, 2022

A study to analyze pre-operative parameters with intra-operative and histopathological findings in cholelithiasis

[1]Dr.BalaMurali Krishna Mudiyam MS, [2]Dr.M Lakshman Kumar Yadav, [3]Dr. J Mayur Kumar,[4]Dr. M Gururaj

[1]Associate professor,Department of General Surgery, Viswabharathi Medical College, Andhra Pradesh, India

[2,3,4]Assistant Professor, Department of General Surgery, Viswabharathi Medical College, Andhra Pradesh, India

Corresponding Author: Dr. M Gururaj

Abstract

The common etiology of conversion from LC to open cholecystectomy is uncontrollable bleeding, adhesions, inflammation, anatomical variations, trauma of bile duct, presence of malignant pathologies and technical failure. The conversion rate to OC remains approximately 2-5% in most series. Patients were selected according to inclusion and exclusion criteria after taking informed consent and reassuring them keeping confidentiality of their data. In all the 200 patients, patients diagnosed as cholelithiasis and who underwent laparoscopic cholecystectomy or converted to open-cholecystectomy were included in the study. After explaining complete details of the procedure and complications to the patients, the surgery was performed under general anesthesia. In our study out of 200 patients, age from 21-60(n=102) years have difficulty in operation with >40mins of duration of operation with P value <0.001 and the difference is statistically highly significant by Fisher's exact probability test.Incidental Carcinoma of gallbladder in 1 (0.5%), Gallbladder polyp in 1 (0.5%), CC in 136 (68%), AC in 46 (23%), AGC in 5 (2.5%) & MGB in 11 (5.5%).

Keywords: Histopathological findings, gallbladder, cholecystectomy

Introduction

The gallbladder is second only to the appendix as the intra-abdominal organ most commonly requiring surgical intervention. The definitive management of symptomatic gallstones is surgical. First successful removal of gallbladder was done by Carl Langenbuch in 1882 for gall stone disease.

Attempts at laparoscopic cholecystectomy (LC) was started in the early 1980s and although the first documented laparoscopic cholecystectomy was performed by Erich Muhe in Germany in 1985, number of workers credit Philip Mouret from France as pioneer of first human laparoscopic cholecystectomy. Laparoscopic cholecystectomy has rapidly become the procedure of choice for routine gallbladder removal and is currently the most commonly performed major abdominal procedure in Western countries[1].

A National Institutes of Health consensus statement in 1992 stated that laparoscopic cholecystectomy provides a safe and effective treatment for most patients with symptomatic gallstones and has become the treatment of choice for many patients. Laparoscopic cholecystectomy has become a therapeutic gold standard in symptomatic cholelithiasis.

The common etiology of conversion from LC to open cholecystectomy is uncontrollable bleeding, adhesions, inflammation, anatomical variations, trauma of bile duct, presence of malignant pathologies and technical failure. The conversion rate to OC remains approximately 2-5% in most series. This is more common in the elderly and in the setting of acute cholecystitis. In these situations cholecystectomy will be more difficult and therefore experience and proper care are necessary to avoid technical errors that could lead to devastating complications. Secondly, there are specific instances when open surgery should

be considered a wiser approach. Conversion to open cholecystectomy has been associated with increased overall morbidity, surgical site and pulmonary infections, and longer hospital stay[2].

Cholelithiasis produces diverse histopathological changes in gallbladder mucosa namely acute inflammation, chronic inflammation, glandular hyperplasia, granulomatous inflammation, cholesterolosis, dysplasia and carcinoma. Traditionally, all cholecystectomy specimens performed for symptomatic cholelithiasis were evaluated histologically. The primary objective of such evaluation is to confirm the clinicoradiological diagnosis. Identification of unsuspected findings including incidental gallbladder malignancy audit and research purposes, and quality control issues are further reasons for such evaluation. Although symptomatic cholelithiasis is considered a benign disease entity, gallstones are a known risk factor for gallbladder malignancy and stones may coexist with gallbladder malignancy[3, 4].

In India, the incidence of gallbladder carcinoma is very high in the north (e.g., incidence in Delhi is 4.5 per 100 000 for men and 10·1 per 100 000 for women) compared with the south (e.g.,in Chennai, Mumbai, Trivandrum, and Bangalore incidence is 1.2 per 100000 for men and 0.9 per 100 000 for women). Gall stones, present in 60%-90% of patients with gallbladder carcinoma as compared to 20%-25% of an age-matched population, are the most important risk factor for gallbladder carcinoma. A history of symptoms of gall stone disease was a major risk factor (odds ratio 4.4, 95% confidence interval: 2.6-7.5) in a large case-control study.

Most of the places of North India and North-eastern states of India are surrounded by the rivers and lifestyle is quite different. The region mostly occupied with different ethnic groups with different cultures and it is obvious that their day to day lifestyle is unique from rest of the country[5].

Discarding gallbladder specimens without histopathological examination is best avoided. Selective approach for sending these specimens to the laboratory results in missing discrete pathologies like premalignant benign lesions such as porcelain gallbladder, carcinoma-in-situ and early carcinomas. Early carcinoma of gallbladder notoriously remains undiagnosed without histopathology as it neither produces clinical symptoms or signs nor provides any clues on ultrasound assessment. Cholecystectomy performed with provisional diagnosis of benign diseases based on clinical, Ultrasonographical and computerized tomographic scanning misses a significant number of early malignant lesions of gallbladder. To avoid such blunders with bad consequences, therefore, every cholecystectomy specimen should be routinely examined histologically. Incidental carcinoma has been reported as 0.3-1.5% of cholecystectomies done for cholelithiasis[6].

Difficult laparoscopic cholecystectomy is a distressing condition. The definition of difficult laparoscopic cholecystectomy (DLC) is not well established and may vary according to experience of surgeon. Several entities during LC may be accepted as DLC like increased operation time, difficulty in dissection of Calot’s triangle or gallbladder and complications occurring during cholecystectomy.

Through this study, we have studied predicting difficulties in Laparoscopic cholecystectomy by clinical, biochemical (LFT) and ultrasound findings, analyzing pre-operative parameters with intra-operative & HPE findings.

Methodology

This is prospective and descriptive study of patients who were admitted in General Surgery ward and diagnosed to have cholelithiasis by ultrasound findings.

Patients were selected according to inclusion and exclusion criteria after taking informed consent and reassuring them keeping confidentiality of their data. In all the 200 patients, patients diagnosed as cholelithiasis and who underwent laparoscopiccholecystectomy or converted to open-cholecystectomy were included in the study. After explaining complete details of the procedure and complications to the patients, the surgery was performed under general anesthesia.

Pre-operative history taking which included age of the patient in years, sex of the patient, duration of pain in right upper abdomen, whether the patient had experienced pain abdomen in last two months, history of jaundice, vomiting, nausea and dyspepsia, diabetes mellitus, pancreatitis and history suggestive of acute cholecystitis.

Pre-operative clinical examination which included thorough per abdominal examination, with special emphasis on presence of tenderness in right hypochondrium and palpation of gallbladder.

Pre-operative baseline investigations necessary for fitness which include ECG, Chest X-ray PA view, Urine R/E,KFT, complete haemogram, blood sugar level (fasting) and estimation of serum enzyme levels of Serum Total Bilirubin, Serum Indirect bilirubin, Serum direct bilirubin, Serum Aspartate Transferase (AST), Alanine Transferase (ALT) Gamma glutamyl transpeptidase (GGPT) and Alkaline phosphatase (ALP), Viral markers (HBsAg, HCV-antibody, HIV-antibody). The value were said to be deranged if it was outside the range for normal recommended.

Pre-operative transabdominal sonography was done by Philips ultrasound on B mode, gray scale and real time scan with 3.5MHz probe as a routine in the pre-operative workup. It included number and size of gall stones in gall bladder, if the gall bladder was contracted or distended with its wall thickness(<3mm or >3mm), with Acute or Chronic cholecystitis features.

The procedure of laparoscopic cholecystectomy and the risk of conversion to open were explained to patients, with a special emphasis for those patients with a higher risk of conversion. All patients received 1 gm Ceftriaxone i.v. at time of induction of anesthesia and another 2 doses at 8 and 16 hours postoperatively. All operations performed under general anesthesia by standard four port laparoscopic technique: The surgeon stand on left side of patient. Pneumoperitoneum was created by carbon dioxide gas.

The laparoscopic surgery was performed by General surgeons with more than 5years experience in laparoscopic surgery; therefore, the learning curve effect do not apply to this study. The operating surgeon was blinded to these findings. The operative findings were objectively graded as difficult or easy laparoscopic cholecystectomy according to the following criteria: if duration of operation, more than 40 minutes, taken from insertion of the Veress needle or trocar until the closure of the port site[66],was considered a difficult laparoscopic cholecystectomy.

The decision for the conversion to open cholecystectomy was based on the clinical judgment of the surgeon.

Every gallbladder after the operation was sectioned serially from neck to fundus and carefully washed with 0.15Normal Saline. Detailed gross examination was done and all specimens were subjected to histopathological examination using hematoxylin and eosin stain. The histopathological report given by pathologist was considered as final diagnosis.

Difficulties were predicted during laparoscopic cholecystectomy by clinical findings, biochemical tests and preoperative ultrasound findings and preoperative parameters (ultrasound report) were be analyzed with intra-operative findings and histopathological findings.

The study Performa has been prepared to suit the proposed study. All relevant data were entered in it. A copy of the study performa is attached with the thesis.

A copy of the patient information sheet and the informed consent form were given to all the participants.

Results

Table 1: Predicting difficulties by Clinical palpable Gallbladder(n=200)

Gall bladder	Duration of operation				Total		P-value
	< 40 min		>40 min				
	Count	%	Count	%	N	%	
Palpable	0	0.00%	15	7.50%	15	7.50%	0.001*
Non-Palpable	87	43.50%	98	49.00%	185	92.50%	
Total	87	43.5%	113	56.50%	200	100%	

*P value =0.001(i.e. p<0.05) significant.

In our study, among 200 patients, who were having clinically palpable (7.50%) gallbladder (n=15) had difficulty in operation with duration >40mins and the difference is statistically significant with p-value 0.001 i.e., p<0.05 by Fisher's exact probability test.

Table 2: Predicting difficulties by Liver enzymes (bio-chemical n=200)

Liver enzymes		Duration of enzymes				P-value
		<40 min		>40 min		
		Count	%	Count	%	
Total Bilirubin	Normal	86	43.00%	100	50.00%	0.004*
	Increase	1	0.50%	13	6.50%	
ALP (Alkalinephosphate)	Normal	70	35.00%	34	17.00%	0.001*
	Increase	17	8.50%	79	39.50%	
AST(Aspartateaminotransferase)	Normal	75	37.50%	57	28.50%	0.001*
	Increase	12	6.00%	56	28.00%	
ALT(Alanineaminotransferase)	Normal	81	40.50%	88	44.00%	0.003*
	Increase	6	3.00%	25	12.50%	
GGPT(Gamma-Glutamyl transpeptidase)	Normal	63	31.50%	27	13.50%	0.001*
	Increase	24	12.00%	86	43.00%	
IB(IndirectBilirubin)	Normal	86	43.00%	98	49.00%	0.004*
	Increase	1	0.50%	15	7.50%	
DB(DirectBilirubin)	Normal	86	43.00%	100	50.00%	0.004*
	Increase	1	0.50%	13	6.50%	

In our study out of 200 population, the patients with increase in ALP (n=79, 39.5%), increase in AST (n=56,28%) and increase in GGPT (43%) in their liver function tests had difficulty in operation with >40min of duration of operation with p value 0.001 which is significant and patients with increase in Total bilirubin (n=13, 65%), increase in Indirect bilirubin (n=15, 7.50%) and increase in Direct bilirubin (n=13, 6.50%) had difficulty in operation with >40min of duration of operation with P value 0.004 and difference is statistically significant with Fisher's exact probability test.

Table 3: Predicting difficulties by ultrasound findings (n=200)

Ultra sound finding		Duration of operation				p-value
		<40 min		>40 min		
		Count	%	Count	%	
USGB(Ultra sound of gallbladder)	Contracted	59	29.50	53	26.50	0.004*
	Distended	28	14.00	60	30.00	
USGW(Ultra sound of gall bladder wall thickness in millemeter)(mm)	< 3 mm	70	35.00	36	18.00	0.001*
	>3 mm	17	8.50	77	38.50	
USGS (Ultra sound finding of stone)	SS(Singlestone)	1	0.05	32	16.00	0.001*
	MS (Multiple stone)	86	43.00	81	40.50	
CBD(Common bile duct)	DL(Dilated)	0	0.00	2	1.00	0.506
	ND(Non-dilated)	87	43.50	111	55.50	

In our study, out of 200 patients with gallbladder wall >3mm thickness (n=77, 38.50%), multiple stones (n=81, 40.50%) in their ultrasonography had difficulty in operation with >40min as duration of operation with P value 0.001and difference is statistically significant with Fisher's exact probability test. Patient with contracted (n=53, 26.50%), distended (n=60, 35%) gallbladder in ultrasonograph had difficulty in operation with >40min of duration of operation with P value 0.004 and their difference is statistically significant by Fisher's exact probability test.

Table 4: Analyzing ultrasound finding of stone detection with operative findings

USGS (Ultra sound finding of stone)	Operative finding stone						p-value
	SS(Single Stone)		NS(No stone)		MS(Multiple stone)		
	Count	%	Count	%	Count	%	
SS(Singe stone)	29	14.50%	1	0.50%	3	1.50%	<0.001*
MS(Multiplestone)	0	0.00%	0	0.00%	167	83.50%	<0.001*

*P-value=<0.001(i.e., P< 0.05) significant.

In our study out of 200 patients, detection of stone and number in gallbladder by ultra sound as single (p value <0.001) and multiple stone (p value <0.001) when analyzed with operative findings the difference is statistically significant by Fisher's exact probability test.

Table 5: Sensitivity, Specificity, PPV, NPV and DA of USG for detection of stone in gallbladder

Ultra sound gallbladderstone	Operative finding of stone	
	SS (single stone)	MS (multiple stone)
Sensitivity	100%	100%
Specificity	98.83%	100%
PPV	93.94%	100%
NPV	100%	100%
DA	99%	100%

Table 6: Histopathological findings

HPE (Histopathological findings)												
Total population (n=200)	AC (Acute calculus cholecystitis)		AGC(Acute gangrenous cholecystitis)		CAGB (Carcinoma gall bladder)		CC(Chronic calculus cholecystitis)		GBP(Gall bladder polyp)		MGB(Mucocele of gall bladder)	
	Count	%	Count	%	Count	%	Count	%	Count	%	Count	%
Female(n=141)	34	17.00	5	2.50	1	0.50	90	45.00	0	0.00	11	5.50
Male (n=59)	12	6.00	0	0.00	0	0.00	46	23.00	1	0.50	0	0.00

In our study, out of 200 specimens sent for histopathological examination, among males (n=46, 23%) and females (n=90, 45%) chronic calculus cholecystitis is maximum (n=136, 68%) followed by AC (n=46, 23%), MGB (n=11, 5.5%), GBP (male: 1, 0.5%) & CAGB (female: 1,0.5%).

Table 7: Type of operation

USGF(Ultra sound gallbladder final)	Type of operation			
	COC(Converted to opencholecystectomy)		LC(Laparoscopic cholecystectomy)	
	Count	%	Count	%
AC(Acute cholecystitis)	2	1.00%	54	27.00%
CC(Chronic cholecystitis)	2	1.00%	136	68.00%
MGB(mucocele of gallbladder)	0	0	6	3%

In our study out of 200 patients operated for cholelithiasis, laparoscopic cholecystectomy was done in 196(AC n=54, 27% + CC n=138, 68% + MGB n=6, 3%) and open cholecystectomy was converted in 4 (2%) cases.

Table 8: Duration of operation among different age groups (n=200)

Age(n=200)	Duration of Operation				P-value
	<40 min		>40 min		
	Count	%	Count	%	
≤20(n=15)	8	4.00%	7	3.50%	0.433
21-40(n=135)	70	35.00%	65	32.50%	<0.001*
41-60(n=46)	9	4.50%	37	18.50%	<0.001*
61-80(n=4)	0	0.00%	4	2.00%	0.134

In our study out of 200 patients, age from 21-60(n=102) years have difficulty in operation with >40mins of duration of operation with P value <0.001 and the difference is statistically highly significant by Fisher's exact probability test.

Table 9: Analyzing different HPE findings with ultrasound final report (pre- operative parameters n=200)

HPF(Histopathological findings)															
USGF	AC		AGC		CAGB		CC		GBP		MGB		Total		p- value
	count	%	count	%	Count	%	count	%	count	%	Count	%	N	%	
AC	46	23%	5	2.5%	1	0.5%	0	0%	0	0%	4	2%	56	28%	<0.001*
CC	0	0%	0	0%	0	0%	136	68%	1	0.5%	1	0.5%	138	69%	<0.001*
MGB	0	0%	0	0%	0	0%	0	0%	0	0%	6	3%	6	3%	<0.001*
Total	46	23%	5	2.5%	1	0.5%	136	68%	1	0.5%	11	5.5%	200	100%	

Table 10: Sensitivity, Specificity, PPV, NPV and DA of Ultrasound in detecting AC, CC, MGB

Ultra sound gallbladder final	HPE (Histopathological finding)		
	AC (acute cholecystisis)	CC (chronic cholecystisis)	MGB (mucocele of gallbladder)
Sensitivity	100%	100%	54.54%
Specificity	92.3%	96.88%	100%
PPV	82.14%	98.55%	100%
NPV	100%	100%	97.42%
DA	95%	99%	97.5%

Incidental Carcinoma of gallbladder in 1 (0.5%), Gallbladder polyp in 1 (0.5%),CC in 136 (68%), AC in 46 (23%), AGC in 5 (2.5%) & MGB in 11 (5.5%).

Discussion

In our study, patients who had palpable gallbladder (7.5%) on clinical examination had more difficulties in operation when compared to non-palpable gallbladder. similar finding were observed in study done by Agarwal D[8]12% palpable.

When stone becomes impacted in cystic duct and persistently obstructs it, acute inflammation results, bile stasis triggers release of liver enzymes. Liver Function Test (LFT) has been used as a routine pre-operative work up for Laparoscopic cholecystectomy.

In our study, liver enzymes ALP (Alkaline Phosphatase), AST (Aspartate aminotransferase) and GGPT (Gamma Glutamyl transpeptidase) levels are raised and their P value is 0.001 which is highly significant and acts as a good predictor of difficulties in operation. Similar

findings were noted in studies done by Sharma NK[70](increased AST & ALP), Agarwal D[8](increased AST, ALT & ALP) and Bansal SK[9](abnormal LFT values with P value <0.05) had difficulties in operation.

In our study, total bilirubin (P=0.004) along with direct bilirubin (p=0.004), indirect bilirubin (P=0.004) and ALT (P=0.003) are also good predictive factors for difficulties in laparoscopic cholecystectomy. Similar findings observed in studies done by Sharma NK[10] (increased serum bilirubin) and Agarwal D[8](increased total bilirubin) had difficulties in operation.

Ultrasonography is the primary choice of investigation in cholelithiasis, advantages being non-invasive, free of ionizing radiation, economical and portable.

In our study, parameters in ultrasound of gallbladder such as wall thickness greater than 3mm and single stone in gallbladder with P=0.001 are good predictors of difficulties in Laparoscopic cholecystectomy. Similar findings were observed in studies conducted by Nayak G[11](>3mm) and Lonare R[12]had difficulties in operation with thickened gallbladder wall in ultrasound.

In our study, diameter of CBD is not good predictor of difficulty, but studies done by Lonare R[12] (>6mm) and Lal P[13]had difficulty in operation with CBD dilated.

All specimen of laparoscopic cholecystectomy were sent to histopathological examination as a routine investigation.

In our study most common finding in HPE for both males and females is chronic cholecystitis (68%) followed by acute cholecystitis (23%), mucocele of gallbladder (5.5%), gallbladder polyp (0.50%) and adenocarcinoma of gallbladder (0.50%) which was incidental finding. Our findings are comparable to studies done by Sangwan MK[14](chronic cholecystitis 69.81%, acute cholecystitis 11.7% and carcinoma of gall bladder 1.9%), Nayak G[11](chronic cholecystitis 84.28%, acute cholecystitis 14.28%).

In our study, conversion to open-cholecystectomy is 2%, in literature conversion rate is 2.6-14%. In our study, incidental Adenocarcinoma of gallbladder is 0.5%(female) in HPE and which is comparable to percentage mentioned in literature (incidental CaGB is 0.3%-1.5%) and study done by Sanwang MK[14](1.9% female).

Conclusion

- Serum markers like TB, DB, IB, AST, ALT, ALP and GGPT are good predictors of difficulty if they are increased than normal values.
- Ultrasound parameters like contracted gallbladder, wall thickness >3mm and single stones are good factors to predict difficulty in operation.
- Ultrasound is choice of investigation for detection of stone in gallbladder but it cannot show the anatomical abnormalities and adhesions around the gallbladder.
- Ultrasonograph can detect acute or chronic cholecystitis but failed to detect carcinoma of gallbladder in cholelithiasis, where incidental carcinoma of gallbladder is not very rare which has poor survival rate.
- Chronic cholecystitis is the most common finding in the histopathological examination.
- All specimens after LC/OC should be sent for HPE as a routine to enhance the rate of detection of Carcinoma gallbladder in early stage.

References

1. Stanisic V, Milicevic M, Kocev N, Stojanovic M, Vlaovic D, Babic I, *et al*. Prediction of difficulties in laparoscopic cholecystectomy on the base of routinely available parameters in a smaller regional hospital. Eur. Rev Med Pharmacol. Sci.2014;18(8):1204-1211.
2. Ulreich S, Foster KW, Stier SA. Acutecholecystitis: comparison of ultrasound and intravenous cholangiography. Arch Surg.1980;115:158-160.
3. Davis CK, Schoffstall RO. Correlation of ultrasonic gallbladder studies with operative findings. South Med J.1981;74:781-784.
4. Golea A, Badea R, Suteu T. Role of ultrasonography for acute cholecystic conditions in the emergency room. Med Ultrason. 2010;12:271-9.
5. Van RA, Laméris W, Van EHW. A comparison of the accuracy of ultrasound and

computed tomography in common diagnoses causing acute abdominal pain. EurRadiol. 2011; 21:1535-1545.

6. Bingener J, Schwesinger WH, Chopra S. Does the correlation of acute cholecystitis on ultrasound and at surgery reflect a mirror image? Am J Surg. 2004;188:703-707.
7. Pradhan SB, Joshi MR, Vaidya A.Prevalence of different types of gallstone in the patients with cholelithiasis. KUMJ. 2009;7(3):268-271.
8. Agarwal D, Arora D, Avasthi A, Kothari A, Danagayach KK. Study of 292 patients for prediction of difficult laparoscopic cholecystectomy using detailed history, clinical and radiological parameters. Int. Surg. J.2016;3(1):349-353.
9. Bansal SK, Chhabra UK, Goyal SK, Singal G, Goyal PK. Factors influencing the conversion of Laparoscopic to Open Cholecystectomy. IJBAMR. 2011;1(1):3-99.
10. Sharma NK, Barolia DK, Sukhadia M. Preoperative findings predict difficulty during cholecystectomy. Int. J Med Res Rev. 2015;3(10):1133-1139.
11. Nayak G. A Clinicopathological Study of Cholelithiasis in an EasternIndian Population. Int. J Pharm Bio Sci. 2016;7(3):6-11.
12. Lonare R, Singh R, Nirpex T, Singh K. The Present Scenario of Cholecystectomy. IOSR-JDMS. 2016;15(5):71-75.
13. Lal P, Agarwal PN, Malik VK, Chakravarti AL. A Difficult Laparoscopic Cholecystectomy That Requires Conversion to Open Procedure Can Be Predicted by Preoperative Ultrasonography. JSLS. 2002;6:59-63.
14. Sangwan MK, Sangwan V, Garg MK, Singla D, Malik P, Duhan A. Incidental carcinoma of gallbladder in north India: is routine histopathology of all cholecystectomy specimens justified? Int. Surg. J. 2015;2(4):456-470.