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CLINICOPATHOLOGICAL EVALUATION OF CHOLELITHIASIS AND MANAGEMENT STRATEGIES AT A TERTIARY CAREHOSPITAL

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ABSTRACT

Background: Cholelithiasis is a chronic recurrent disease of the hepatobiliary system. The impaired metabolism of cholesterol, bile acids and bilirubin are characterized by gallstone formation. The prevalence of cholelithiasis varies and has been reported as 2-29% in India, and increased in the recent years. In the present study, apart from studying the epidemiology i.e., demographic factors, dietary habits, clinical presentation, diagnostic tools and management, it also looks at the stone analysis and complications after surgery, in rural population in Southern India.

Material and Methods: A prospective cohort study undertaken at the department of Surgery a from September 2014 to October 2016. 104 patients fulfilling the inclusion criteria selected for the study after an informed consent has been obtained. Clinical symptoms were noted according to clinical history of the patients. An ultrasonography was done as confirmatory study and all patients underwent either open/laparoscopic cholecystectomy. Post operative complications and histopathological analysis of gallbladder along with chemical analysis of gallstones was carried out.

Results: The mean age of the patients was 43.56 years with a male-female ratio of 0.52:1. Pain flatulence and nausea/vomiting are the major clinical presentation of the gall stone. Multiple calculi were most frequently found in mixed type of stone while less in cholesterol while single calculi is more in mixed and less in pigmented type of stone. Wound infection was the commonest complication in open cholecystectomy group, and the mean hospital stay was significantly more in this group.

KEYWORDS : Cholelithiasis, cholecystectomy, gall stones, hepato-biliary, gall bladder

INTRODUCTION

Gallstone disease remains one of the major causes of abdominal morbidity and mortality through the world. Nowadays, gallbladder disease is a frequent problem in developed countries, representing a major health problem. Gallstone disease is a chronic recurrent hepatobiliary disease, the basis for which is the impaired metabolism of cholesterol, bilirubin and bile acids, which is characterized by the formation of gallstones in the hepatic bile duct, common bile duct, or gallbladder. Gallstone disease and cardiovascular disease, common diseases worldwide, are strongly associated and have considerable economical impact.[1]

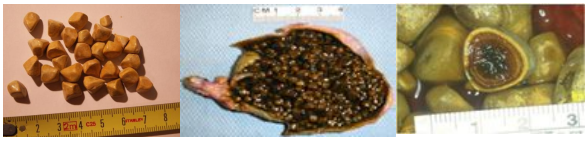
Prevalence of cholelithiasis in India is more in females than men. The prevalence was more common in Northern Indians than Southern Indians followed by Maharashtra particularly form coastal region.[2]

There are many researches on etiology, clinical presentation, management specifically evaluating the modalities of treatment but chemical analysis and bile culture though age old investigations were not given much importance in spite that they could give an insight into pathogenesis and presentation. Incidence in India partially attributed to widespread use of ultrasonography (USG) in the last two decades but changing socio-economic structure and changes in various other epidemiological factors including diet may also be responsible.

AIMS AND OBJECTIVES

- To study the demographics of incidence of gallstones.
- To study the clinical presentation of gallstones
- To correlate the ultrasound findings of the number of gallstones to the chemical analysis of gallstones.
- To assess the laparoscopic and open cholecystectomy for symptomatic gallstone disease.
- To evaluate the post operative complications in laparoscopic and open cholecystectomy.
- To assess the histomorphological features of resected gallbladder specimens.
- To evaluate the post operative complications of laparoscopic and open cholecystectomy

- **Classification of Gallstones.**[3]



MANAGEMENT OF GALLSTONE DISEASE

The therapeutic option of gallstone disease is based on few crucial steps, i.e., presence/absence of typical symptoms (i.e., colicky pain), presence of complications, and gallbladder function, as well as composition and size of gallstones.[4]

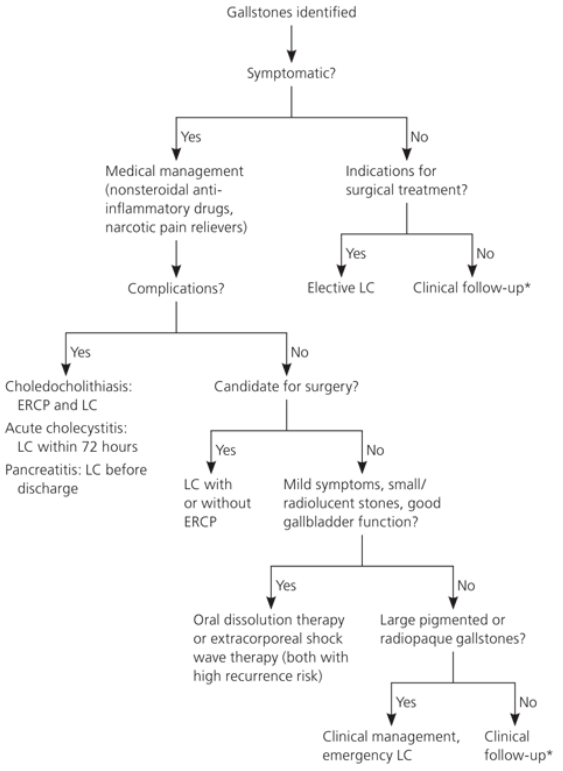
Bearing in mind data on epidemiology and overall costs of both medical and surgical therapies, it is not routinely recommended to treat asymptomatic gallstone patients.

Thus, an expectant management (medical attention) is currently considered the most appropriate choice in patients with gallstones of any type without specific symptoms (i.e., biliary colic).

Indeed, approximately 60%-80% of patients with gallstones are completely asymptomatic and stones are frequently found during routine abdominal ultrasonography. In general, the risk of developing typical biliary pain is low (2.0%- 2.6% per year although microlithiasis or biliary sludge in the gallbladder lumen puts patients at risk for colicky pain or acute pancreatitis. Nevertheless,

the overall risk rate for complications (yearly incidence 0.3%) and gallbladder cancer (0.02%) are very low.[5]

If biliary pain and/or complications are present, cholecystectomy represents the gold standard (see below), as oral litholysis with hydrophilic bile acids have a limited role, and are reserved to symptomatic patients with small radiolucent gallstones in a well functioning gallbladder with a patent cystic duct.[6]



*—Exceptions to expectant management include patients with calcification of the gallbladder, hemolytic anemia, or large gallstones (greater than 3 cm); patients with small gallstones and gallbladder dysmotility; patients who are morbidly obese and undergoing bariatric surgery; patients planning to have a transplant; and Native Americans.

Fig 8: Algorithm for management of gallstone disease[4]

MATERIALS AND METHODS

The study was a hospital based cohort study conducted over a period of two years from October 2014 to September 2016, for patients admitted in **Chennai medical college hospital. Trichy,** South India.

Inclusion Criteria:

All patients with clinical diagnosis later confirmed with ultrasound of having cholelithiasis.

- Patients with acute or chronic cholecystitis.
- Mucocoele of gall bladder
- Empyema of gall bladder
- Gall stone pancreatitis
- Cholangitis
- Patients with combined gall bladder and CBD stones.

Exclusion criteria:

- Patients unwilling to participate in study.
- Isolated CBD stones.
- Gall bladder malignancy.
- Post cholecystectomy gall stones.
- Acalculous cholecystitis.

Methodology:

Informed consent was obtained from all patients willing to participate in the study. All patients presenting with dyspeptic symptoms along with clinical suspicion of gall stones were included in the study. Only those with confirmed radiological diagnosis of cholelithiasis and its complications were included in the final study. A thorough history and clinical examination was carried out on all patients, with particular detail to the duration of symptoms, previous episodes of symptoms, co morbidities. The clinical examination focused on identifying jaundice, tenderness in upper abdomen, identifying a palpable mass per abdomen. Routine hematology and biochemical evaluation including hemogram, liver function tests were carried out for all patients. All the patients were subjected to Ultrasound abdomen as first investigation of choice for confirmation of the diagnosis.

A thorough preoperative assessment was carried out and patients underwent surgery either open cholecystectomy or laparoscopic cholecystectomy, as per the decision made after informed consent was obtained from patient or legal guardian. At the time of surgery, all patients received prophylactic antibiotics 30 minutes before surgery and post operatively intravenous antibiotics for 48 hrs followed by oral antibiotics for further 5 days.

Suture removal was done on the 7th post operative day for all cases except for those with wound infection where sutures removed on 10th day. The gall bladder specimen was sent for routine histopathological evaluation and the stones were subject to chemical analysis. All patients were followed up on 7, 28 post operative days, with a further follow up 3 months post operatively. No patents were lost to follow up in our study. The study findings were documented in the pro forma created for the study.

Discussion

A total of 104 patients were included in the final study. A thorough evaluation was carried out peri operatively, with standard antibiotic prophylaxis according to hospital protocols. Patients were followed up according to the proforma developed at the initiation of the study. There were no patients lost to follow up.

Age and Gender Distribution:

Cholelithiasis was most common in 3rd and 4th decades accounting for more than half of all cases (56%) among whom 41 were female and 18 were male patents. The next common age group was 5th decade (17.3%) with 12 female and 6 male patents. There were a total of 10 patents in the age group of 60- 70 yrs (9.6%) with slight male predominance (6 male patents and 4 female patients).Among the younger age group patients, aged less than 30 yrs, (16.3%), of whom 11 were female and 6 were male patients.The mean age of patients with gallstones was 43.56 years with a standard deviation of 13.18 in a range from 13 to 70 years.

Of the total 104 patents, 36 were male and the rest 68 were females in keeping with female gender predominance of cholelithiasis. The male-female ratio was 1:1.88.

The youngest female patient was 13 yrs old while the youngest male was 19 yrs old. The oldest patients among both genders were 70 yrs each.

Comparing the mean age with reference to gender, the mean age of females was

44.29 years and 41.93 years in males ($p > 0.05$ not significant). The difference was statistically not significant, though it appeared to be more in older male population.

Variable	Present study	Palanivelu C et al	U A Chandak et al
Mean age of patients	44.29 yrs	40.4 yrs	45.77 yrs

Table 14: Comparative analysis of mean age of patients.

In a study by Battacharya showed 71.4% were female; 28.6% were

male.[7] Similar sex preponderance in the favour of females were observed by Tamhankar et al.[8]

A study carried out by Sharma showed that 30% were male and 70% were female[9]

and Thamil Selvi et al. showed 20.5% males and 79.5% females were patients of cholelithiasis.[10]

Variable	Present study	Battacharya et al[46]	Sharma et al[49]	Thamil selvi et al50
Male	34.6%	28.6%	30%	20.5%
Female	65.4 %	71.4%	70%	79.5%

Table 15: Comparative analysis of gender prevalence of cholelithiasis

More than half of our study population (56%) belonged to the age group of 30-50 yrs. Studies by Ghosh SK et al[11] and Shenoy et al[12] showed highest prevalence in 41 to 50 yrs age group. In a further study by Tyagi et al[13] showed higher incidence in 31 to 40 years.

Clinical Features:

All patients presented with pain in the upper abdomen, of which 74 patients (71.1%) presented with chronic upper abdominal pain while 30 patients (28.9%) had acute upper abdominal pain. 72 patients (69.2%) presented with dyspepsia and flatulence, 67 patients (64.4%) with nausea or vomiting, only 7 patients (6.7%) had jaundice. 14 patients had fever, of these 4 patients were diagnosed as CBD calculus and rest were continuations of acute process of cholecystitis.

We observed that 26 patients had acute onset of pain while the remaining patients had chronic pain similar result were found by Ganey et al. and Sharma.

Vomiting was spontaneous and occurred mostly during the attacks of pain this was also seen by Ganey et al. In a study by Wani NA[14] the incidence of jaundice was documented as 8.6% cases.

Abdominal Ultrasound:

All patients underwent routine ultrasound examination of abdomen and pelvis as confirmatory investigation of choice for cholelithiasis. Ultrasound scanning revealed gall bladder calculus only in 99 patients and 5 patients had stones both in gallbladder and common bile duct. On Ultrasound examination solitary calculus was identified in 38 patients (36.5%) and multiple calculi in 66 patients (63.5%). Ultrasound also identified CBD calculus, it was able to identify them in 5 patients, however total of 7 patients had CBD calculi on intra operative correlation. Hence, the accuracy of abdominal ultrasound for diagnosis CBD calculus was 71.4% in this study.

Ultrasound examination also identified evidence of inflammation, i.e cholecystitis (acute or chronic) based on wall thickness of the gall bladder. Among 104 patients, ultrasound examination could identify, thin walled gall bladder in 5 (4.80%) of the patients. A gall bladder thickness in the normal range was seen in 67 (64.43%) of the patents. The rest 32 (30.77%) patients had a thick walled gall bladder.Solitary calculus was found in 38 patients on sonography, but on intra-operative correlation three of these patients were found to have multiple calculi. Thus, the USG percentage of accuracy of solitary calculus is 92.1%.

Pre operative Diagnosis:

Based on history, clinical, biochemical and radiological examinations, patients were diagnosed pre operatively in the following groups. Most common presentation was that of biliary colic with 56 out of 104 patients (53.84%). This was followed by chronic or recurrent cholecystitis among 27 (25.96%) patients. 14 patients (13.46%) had presented with acute cholecystitis. CBD stones were seen in 7 patients of whom 4 patients (3.85%) were diagnosed as Cholangitis, while 3 patients (2.88%) had choledocholthiasis presenting with obstructive jaundice.

Management:

All 104 patients underwent surgery. A total of 56 patients (53.85%) had laparoscopic cholecystectomy and 41 (39.42%) patients underwent open cholecystectomy. A total of 7 patients had CBD calculus, of which 5 (4.81%) patients underwent open cholecystectomy with CBD exploration and 2 (1.92%) patients had ERCP guided stone removal followed by laparoscopic Cholecystectomy.

In our study 56 patients had laparoscopic cholecystectomy and 43 patients underwent open cholecystectomy 7 patients had CBD calculus, of which 5 patients underwent open cholecystectomy with CBD exploration and 2 patients, had ERCP guided stone removal followed by laparoscopic cholecystectomy.

Laparoscopic cholecystectomy is a feasible and safe procedure even in most cases of acute cholecystitis albeit the conversion rate may be as high as 32%. The risk of bile duct injuries is higher and the operation time longer than in elective laparoscopic cholecystectomy.

Factors associated with the need to convert may be male gender, duration of right upper abdominal pain and severity of the inflammatory process.[15]

Several studies demonstrated that the risk of conversion depends mainly on the degree of inflammation, pathology of gallbladder disease (e.g. thickness of gallbladder wall), age, male sex, and CBD diameter.

Conversion rate in elective laparoscopic cholecystectomy may be 0% to 15%, but in cases of gangrenous cholecystitis or empyema it may be 50-83%. Ultrasound may help to predict the risk of conversion. However, the surgeon has to decide intra operatively whether to convert to the open procedure within a short time.

The conversion rate from laparoscopic to open cholecystectomy was about 9.6% of the total attempted laparoscopic cases (6 out of 62). The conversion rate in other studies was 7% in Schlumpf et al. Our results matched with a study of 376 patients by Fajardo et al. for evaluation of cost effectiveness of laparoscopic and cholecystectomy in Colombian population.

Variable	Present study	Schlumpf et al.	Fajardo et al.
Conversion rates from laparoscopic to open cholecystectomy	9.6%	7%	9%

Table 18: Comparative studies for conversion from laparoscopic to open cholecystectomy

Type of Gall Stones:

In our study, the most common type of stone was mixed stone seen in 47 (45.2%) patients. While, cholesterol stones accounted for 28 (26.92%) of cases, pigment stones were identified in 29 (27.88%) patients.

Of the 66 patients identified with multiple stones, majority of them were mixed stones comprising 45.45% (n=30), followed by pigment stones 34.85% (n=23) and cholesterol stones 19.7% (n=13). While, there were 38 patients identified with single stones, mixed single stones formed majority, comprising of 44.74% (n=17), followed in order by cholesterol stones 39.47% (n=15) and pigment stones constituting the remaining 15.79%, (n=6).

Our study showed that 48 (46%) patients had mixed stones, 39

(38%) pigment stones and 17(16%) cholesterol stones out of 104 patients of gallstone. While a study done in Haryana by Chandran et al. showed 26%, 38% and 36%, respectively. In northern India, a study by Pundir et al. showed the prevalence respectively 14.2%, 68.6% and 17.2%.52 Mixed stones are the most commonly encountered stones in North India.

Type of stones	Present study	Narang et al	Goyal et al
Single stone	36.55%	7%	30.6%
Multiple stones	63.45%	93%	69.4%

Table 19: Comparative studies on number of gallstones.

In our study we found that out of 66 multiple stones 31 (46.97%) were mixed, 23 (34.85%) were pigment and 12 (18.18%) were cholesterol stones, and in 38 single calculi 18 (47.3 8%) were mixed, 14 (36.84%) cholesterol and rest 6 (15.78) were pigment calculi.

Gallstones in Tamil Nadu and Pondicherry, South India are probably due to the infection rather than super saturation as evidenced by the predominance of the Pigment stones where as in Sikkim and North Bengal, only cholesterol stones were found. similarly, in a study done by Kamiya T et al in Bolivia, the incidence of cholesterol stone was 56.6%.

Domeyer et al. concluded that the solitary gallstones were the most important predictors for severe inflammation. Khanna et al. could not document any association between the two in their respective studies.

In a recently published series, Narang et al showed the incidence of gallstones as

Cholesterol 7.03%, Mixed 90.8%, Pigment 1.62%, Combined 0.54%. Another recent series by Goyal et al. concluded Cholesterol stones 5.43%, Mixed gallstones 68%, Pigment stones 5.75% and combined stones 20.8%.

Type of stone	Present Study	Chandran et al.	Pundir et $_{al}$	Narang et $_{al}$	Goyal et al	Pradhan et al
Pigment	38%	26%	14.2%	1.62%	5.75%	8.75%
Mixed	46%	38%	68.6%	90.8%	68%	78.75%
Cholesterol	16%	36%	17.2%	7.03%	5.43%	12.5%
Combined	-	-	-	-	20.8%	

Table 20: Studies on incidence of types of gallstones

Correlation between diet and type of stone:

Mixed and pigment stones were the commonest stones observed in patients having pure vegetarian diet while mixed and cholesterol stones were commonly observed in patients having mixed diet. Cholesterol stones were seen approximately 3 times more common in patients consuming mixed diet than patients consuming vegetarian diet. However, statistical analysis using the Chi-square test showed that there was statistically insignificant difference in types of stones in patients with different diets.

Post operative complication:

Five out of 104 patients had surgical site infection which was managed by regular dressings and antibiotics. 5 patients had post-operative biliary leak of which one was classified as Type C biliary leak, as per Strasberg's classification and required re- exploration for biliary tract injury repair. When the post-operative complications between the two modalities of treatment were statistically compared, there was no statistical difference seen in wound infection or biliary tract leak or post- cholecystectomy syndrome.

The wound infection rate in the study of Chung-Mao Lo et al was 11.1%. Harris in his study found similar results of Bile leak of 2% in laparoscopic cholecystectomy and 1% in open cholecystectomy. Peters JH study also showed an incidence of bile leak in 2% and incidence of wound infection in 2% of patients undergoing laparoscopic cholecystectomy.

Post op Complication	Present study	Harris	Peter JH
Bile leak	4.8%	2%	2%

Table 21: Comparative studies on post operative bile leak.

Post-operative length of stay:

Post operative stay was relatively shorter in laparoscopic cholecystectomy with average stay at 4.3 days, where as in open cholecystectomy group, stay was 6.9 days. Patients who underwent open cholecystectomy with CBD exploration, had to stay longer with their average length of stay being 7.2 days. Similarly Hardy et al in their study had a result of post operative stay of 6.5 days for open cholecystectomy and 2 days for laparoscopic cholecystectomy.

Morphology of Gallbladder size:

In our study the size of the gallbladder was small or contracted in 27 (26%) specimens, normal in 57 (55%) specimens and enlarged in 20 (19%) specimens of cholecystectomy sent for histopathological examination.

Tyagi et al in their study observed small or contracted gallbladder in 16.6% of the cases, enlarged gallbladder in 29.8% of the cases and normal in 53.6% of the cases.

Morphological features of gallbladder	Present study	Tyagi et al
Normal	55%	53.6%
Enlarged	19%	29.8%
Contracted	26%	16.6%

Table 22: Comparative studies on morphological features of gallbladder.

Histopathological Examination:

Histopathological examination revealed a normal appearing gall bladder wall in 45 out of 104 patients (43.27%). Acute cholecystitis was seen in 18(17.31%) patients while chronic cholecystitis seen in 41 patients (39.42%).

Summary

This is a prospective observational study of patients with symptomatic cholelithiasis. A total of 104 patients were included in the study. The objective was to evaluate demographics, clinical presentation, correlate the type of stone with diet and body mass index. The post operative complications and histopathological features were also documented. Based on our observations, the study can be summarized as:

- Cholelithiasis was predominant in females with male to female ratio 1:1.88.
- The mean age of presentation was 43.56 ± 13.18 yrs.
- Upper abdominal pain was the most common presenting symptom, seen in all patients, followed by dyspepsia and flatulence in 69%. The incidence of jaundice was 6.7%
- 56 patients (53.85%) underwent laparoscopic cholecystectomy, which was found to have better outcomes in terms of post operative pain and stay, as well as post operative complications, compared to open cholecystectomy.
- Multiple and single calculi most frequently seen in mixed type of stone, while cholesterol calculi are more likely to be single.
- Post operative bile leak seen in 4.8% cases.
- Post operative length of stay was much less in laparoscopic cholecystectomy.
- Biliary colic was the most common final diagnosis (43.27%) followed by chronic cholecystitis (39.4%).

CONCLUSION

From the present study, we conclude that the mean age of the patients was 43.56 years with a male-female ratio of 1:0.52. Cholelithiasis is most prevalent in the 3rd to 5th decade of life.

Multiple calculi were most frequently found in mixed type of stone while less in cholesterol while single calculi is more in mixed and less in pigmented type of stone.

Pain flatulence and nausea/vomiting are the major clinical presentation of the gall stone. The most common clinical and histopathological diagnosis being Biliary colic followed by chronic cholecystitis and acute cholecystitis.

Wound infection and other complication were more predominant in open cholecystectomy group than the laparoscopic procedure. Laparoscopic cholecystectomy yielded better results in terms of less post operative pain, less stay in post operative period, and better cosmetic results, compared to the open cholecystectomy.

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