

## Original Research Article

# Cholelithiasis: causative factors, clinical manifestations and management

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### ABSTRACT

**Background:** Cholelithiasis is a common gastrointestinal disorder with an overall prevalence of 2-29%. This study aims to evaluate the evolution of demographic and etiological factors, the clinical manifestations of Cholelithiasis, the surgical management with its post-operative complications and the histopathological findings of the post-cholecystectomy specimen of gallbladder, in central India.

**Methods:** Patients symptomatic or asymptomatic diagnosed ultrasonically as cholelithiasis were included in the study and patients with primary choledocholithiasis were excluded.

**Results:** A total of 92 patients were enrolled, of which 62 (68.89%) were female, with mean age of 45.03yrs ± 13.59. Fifty four patients (58.69%) were having BMI >25. Pain was most common complaint seen in all patients. Jaundice was observed in 13 patients (14.13%) who had associated CBD calculus. Sickling was positive in 8.69% of patients. Lap cholecystectomy was done in 71 (77.17%) patients with a conversion rate of 6.57%. Nineteen (20.65%) were open cholecystectomy with or without CBD exploration and 2 underwent Lap cholecystostomy. Post operatively, surgical site infection was seen in 3 patients (4.22%) of laparoscopic cholecystectomy, 5 patients (26.31%) of open cholecystectomy and biliary leak was seen in 3 patients (15.78%) of open cholecystectomy. Histopathology of gallbladder was chronic cholecystitis in 70 patients (77.77%), malignancy was detected in 5 patients (5.55%) and Xanthogranulomatous cholecystitis in 2 patients (2.22%).

**Conclusions:** Cholelithiasis is commonly seen in females in 4th and 5th decade mainly presenting with abdominal pain and dyspepsia. Laparoscopic cholecystectomy offers best surgical management with lesser complications.

**Keywords:** Cholecystectomy, Cholelithiasis, Gallstones, Laparoscopy

### INTRODUCTION

Cholelithiasis is one of the most frequently encountered disease and one of the major causes of abdominal morbidity throughout world.<sup>1</sup> Incidence of gall stone disease is on a rise globally due to the vast changes in the dietary habits, life style changes associated with high junk diet consumption and increased sedentary life style.<sup>2</sup> Its prevalence in India is estimated to be around 2 to 29%, where it is most commonly prevalent in northern

states as compared to southern states.<sup>3,4</sup> Changing scenario in India is mainly attributed to availability of investigation such as ultrasound in urban as well as rural areas and also because of increasing affordability.

The present study aims to evaluate the demographic and etiological factors, the clinical manifestations of Cholelithiasis and its surgical management with its post-operative complications. Also, it will study the

histopathological findings of the post-cholecystectomy specimen of gallbladder.

## METHODS

The present study was done at NKPSIMS & RC, Lata Mangeshkar hospital, Hingna, Nagpur, a tertiary care hospital. It was an observational study carried out in an academic hospital over a period of 2 years from October 2016 to October 2018.

All patients above 18 years of age presenting with upper abdominal pain, dyspepsia with or without jaundice diagnosed ultrasonically as cholelithiasis and choledocholithiasis with cholelithiasis were included in the study and patients managed conservatively, patients with primary choledocholithiasis and with asymptomatic gallstones were excluded from the study.

Using a proforma following study factors were studied and data recorded was entered into an excel sheet and analyzed using standard statistical methods. Descriptive statistics like mean and standard deviation were calculated to summarize continuous variable. Percentages were used to summarize categorical variables. Inferential statistics included tests of significance. Fischer's exact test was used for small sample size. P value <0.05 was considered statistically significant.

Demographic and etiological factors like age, gender, body mass index (Based on WHO classification) and dietary factors (vegetarian diet and mixed diet) were included. Clinical factors based on history of pain, dyspepsia, nausea, vomiting, fever and jaundice were studied. Baseline investigations of patients were done [haemogram, random blood sugar, liver function test, coagulation profile and sickling profile (immediate/delayed)]. Imaging studies like ultrasonography and MRCP (Magnetic resonance cholangiopancreatography) (Cholelithiasis with dilated CBD >7 mm; Raised alkaline phosphatase) were done. Endoscopic retrograde cholangiopancreatography (ERCP) as per indications were done (suspected cases of CBD calculus, suspected cases of periampullary malignancy, for therapeutic stenting or stone removal in obstructive jaundice prior to surgical intervention, removal of retained stones after laparoscopic/open cholecystectomy).

All patients underwent surgery depending on surgeon's decision and available resources. Open cholecystectomy, laparoscopic cholecystectomy, CBD exploration and cholecystostomy were the operations that were performed. All cholecystectomy specimens were sent for histopathological examination and their results were studied. Post operative complications like the surgical site infections and bile leak (as per Strasberg classification) were compared in the open and laparoscopic cholecystectomy group.

## RESULTS

A total of 92 patients of gallstones were enrolled with the mean age of 45.03±13.59 years in a range from 19 to 80 years with peak incidence in 4<sup>th</sup> and 5<sup>th</sup> decade, accounting for more than half of all cases (51.08%). If we divide the age groups into 3 groups as ≤30, >30-50 and >50 years, the number of patients in the age group >30-50 are significantly more than the other two groups (p value- 0.0106). The decade of peak incidence of cholelithiasis is same for both the genders. Female preponderance was seen with 62 patients (68.89%) being females and 30 patients (31.11%) males and Male: Female ratio is of 1:2.06 which is statistically a significant difference (p value- 0.0165).

On studying the etiological factors, 54 patients (58.69%) had BMI of >25 out of which 52 patients (56.52%) were overweight (25-29.99) and 2 patients were obese (2.17%), while rest of the 38 patients (41.30%) had a normal BMI (19-24.99). This is not statistically significant (p value- 0.2370). Fifty two patients (56.52%) consumed a mixed diet, which included both vegetarian and non-vegetarian food, while the remaining forty patients (43.48%) consumed purely vegetarian diet. This was not statistically significant (p value- 0.3753).

Associated symptoms with cholelithiasis were pain in abdomen, which was observed in all the patients (100%). Of these, 68 patients (73.91%) presented with chronic upper abdominal pain and 24 patients (26.09%) presented with acute upper abdominal pain. Other presentations were of dyspepsia, observed in 61 patients, followed by presentation of GI symptoms like nausea in 51 patients and vomiting in 40 patients. Fever was seen in 19 patients (20.65%), of which 4 patients had acute cholecystitis and 2 patients had empyema gall bladder. Jaundice was noticed in 16 patients (17.40%) of which 6 patients (6.52%) had pruritus and 13 patients had CBD calculus on ultrasonography (Table 1).

**Table 1: Clinical presentation in patients of cholelithiasis.**

Clinical presentation	N	Percentage (%)
<b>Abdominal pain</b>	92	100
<b>Dyspepsia</b>	61	66.30
<b>Nausea</b>	51	54.34
<b>Vomiting</b>	40	43.47
<b>Fever</b>	19	20.65
<b>Jaundice</b>	16	17.40
<b>Pruritus</b>	6	6.52

On investigating these patients for haematological disorder sickling was found to be positive in 8 patients (8.69%), out of the 92 patients. Out of these, 2 patients were in the age group of 20-30 years and 6 patients were in age group of 30-40 years. Out of the total 8 sicklers, 6

were female and 2 were male (Male: female ratio 1:3) showing female preponderance.

Abdominal ultrasound was the investigation of choice for diagnosing cholelithiasis and out of the 92 patients, solitary stone was seen in 7 patients (7.60%) and multiple calculi in 85 patients (92.40%). Ultrasound detected thickened gall bladder wall in 22 patients (23.91%), out of which 5 patients had carcinoma gall bladder, 2 had xanthogranulomatous cholecystitis, 1 had cholesterolosis, 9 had acute cholecystitis and 4 patients turned out to be chronic cholecystitis on histopathological examination.

Out of the 24 patients presenting with acute abdominal pain, 2 had solitary stones, 22 had multiple gallstones 6 had CBD calculus with gallstones and 11 had thickened gall bladder wall on ultrasonography. Whereas, out of the 68 patients presenting with chronic abdominal pain, 5 had solitary stones, 63 had multiple gallstones, 7 had CBD calculus with gallbladder calculus and 11 had thickened gall bladder wall on ultrasound examination.

All the 92 patients (100%) underwent surgery. Seventy one patients (77.17%) underwent laparoscopic cholecystectomy, 19 (20.65%) open cholecystectomy and 2 cholecystostomy for empyema gall bladder. CBD calculus was seen in 13 patients of which 6 had CBD exploration with open cholecystectomy and 6 had ERCP guided stone removal followed by open or lap

cholecystectomy and in one patient no stone was found on exploration. Of the 2 patients who underwent cholecystostomy, 1 died due to sepsis and another underwent an open cholecystectomy (Table 2).

**Table 2: Operative management in patients of cholelithiasis.**

Surgery	N	Percentage (%)
Laparoscopic cholecystectomy	71	77.17
Open cholecystectomy	19	20.65
Laparoscopic cholecystostomy	2	2.17

On comparing the post operative complications in laparoscopic and open cholecystectomy, 8 (8.69%) out of 92 patients had surgical site infection (Grade A, CDC guidelines), of which 3 patients (4.22%) were in laparoscopic cholecystectomy group and 5 (26.31%) in open cholecystectomy group. Bile leak was seen in 3 patients of open cholecystectomy group which were minor leaks that healed spontaneously while none were seen in lap cholecystectomy group. This difference of post operative complications observed in the laparoscopic and open approach was found to be statistically significant (Table 3).

**Table 3: Comparison of postoperative complications in laparoscopic and open cholecystectomy patients.**

Complications	N	Laparoscopic	Open	P value (Chi square test)
Post operative fever	16	7/73 (9.85%)	9/19 (47.36%)	0.0004
Surgical site infection	8	3/73 (4.22%)	5/19 (26.31%)	0.0092
Biliary leak	3	0/73 (0)	3/19 (15.78%)	0.0154 (Fischer's exact test)

Histopathological evaluation was done in 90 patients (97.82%) of the 92 patients. 2 patients underwent cholecystostomy. Of the 90 patients 70 patients (77.78%) patient had chronic cholecystitis, 12 patients (13.33%) had acute cholecystitis, 5 patients (5.55%) had carcinoma gall bladder, 2 (2.22%) had xanthogranulomatous cholecystitis and 1(1.11%) had cholesterolosis of gallbladder.

Of the 5 patients diagnosed of carcinoma gallbladder, 2 patients had carcinoma confined to muscularis mucosa with negative margins and no metastasis, hence no further surgical management was advised and the rest of the 3 patients had either metastasis or positive margins which were managed as per standard guidelines.

Of the 24 patients, presenting with acute abdominal pain 12 were found to be acute cholecystitis on histopathological examination, 6 were chronic cholecystitis, 3 were carcinoma gall bladder, 1 was xanthogranulomatous cholecystitis and 2 patients underwent Laparoscopic cholecystostomy. Whereas, out

of the 68 patient presenting with chronic abdominal pain, 64 were found to be chronic cholecystitis, 2 were carcinoma gall bladder, 1 was xanthogranulomatous cholecystitis and 1 was cholesterolosis on histopathological examination.

## DISCUSSION

Cholelithiasis is most commonly prevalent in northern states as compared to southern states. It is 7 times higher in northern states.<sup>4</sup> There are very few studies for prevalence in central India. This study aims to study the causative factors, clinical manifestation and management of gallstones in central India.

The mean age in present study was 45.03±13.59 years. This is consistent with the study of Muthalaisamy.<sup>6</sup> (Trichy) with mean age in the study of 43.56±13.18 years and other studies in literature like Shukrya Kamil Khalaf (Iraq) and Adam Gyedu (Ghana).<sup>9,10</sup>

Maximum patients were observed in 4<sup>th</sup> and 5<sup>th</sup> decade in present study, which is suggestive of early occurrence of

gallstone disease in Indian population that is consistent with study done by Bhatti in Lahore Pakistan and Muthalaisamy in Trichy but Veerbhadrappa in Madhya Pradesh found an increased incidence in 5<sup>th</sup> and 6<sup>th</sup> decade in India.<sup>5-7</sup>

The decade of peak incidence in the present study is same for both genders but Selvi et al found the decade for peak incidence of cholelithiasis in females was 5<sup>th</sup> decade and 6<sup>th</sup> decade for males.<sup>8</sup> This difference indicates geographical variation with incidence of cholelithiasis. The present study observed the female preponderance with 68.88%. A study by Cirillo et al suggested a causal association between estrogen and gallstone disease indicating the cause of preponderance.<sup>11</sup> This finding is consistent with the literature like Alghaythi et al and Sun et al with male: female ratio of 1:1.5 and 1:1.27 respectively.<sup>12,13</sup>

In the present study, although the number of patients with BMI >25 were 58.70% as compared to 41.30% of patients with normal BMI (<25), this difference was not statistically significant. A study by Shukrya Kamil Khalaf in 2016 stated that an increased BMI was independently associated with a higher risk of gallstones.<sup>9</sup> Similar findings were seen in the studies by Talseth, in Sweden, in 2016 and Stender in 2013 in which a causal association between elevated BMI and increased risk of symptomatic gallstone disease was seen.<sup>14,15</sup> But a study by Hui Sun et al. in 2009 (China) stated that the causal association is gender specific and obese women are more significantly associated with gallstone disease compared to obese men.<sup>13</sup>

In the present study, 56.52% patients had mixed diet as compared to 43.48% patients with vegetarian diet but this association was not statistically significant. Similar finding was seen in a study by Shabanzadeh in which it was stated that there is no significant association of clinical gallstone events and diet.<sup>16</sup> But this association is variable in literature like a study by Verma and by McConnell are of exactly contrast opinion in relation to association with vegetarian and non vegetarian diet.<sup>17,18</sup>

Pain in abdomen is the most common presentation of cholelithiasis. In the present study all patients (100%) had pain, as it was an inclusion criterion. This finding is well documented in the literature.<sup>18-21</sup> Dyspepsia was seen in 66.30% patients in the present study which were similar to the findings of Lokesh et al.<sup>19</sup> In the present study jaundice was seen in 17.40% and fever was seen in 20.65% which was more than that seen in the literature this difference may be due to small sample size.<sup>7,21</sup>

In the present study the total patients with sickle cell disease were 8 (8.69%) of which 2 were <30 years of age and 6 were in the age group of 30-40 years of age. A study by Martins et al in Germany states that the vast majority of the patients are diagnosed before 30 years of age, with an average age at diagnosis of 16 years and a

prevalence of 25.2% and the prevalence in a study by Gumi et al was 45%.<sup>22,23</sup> This difference could be due to the exclusion criteria of the present study being patients less than 18 years of age and the geographical variation.

Ultrasound revealed 7.60% of patients with solitary stones and 92.40% with multiple stones in the present study which was similar to the study of Verma et al and other studies in literature.<sup>18</sup> The CBD calculus in present study was 14.13% which was consistent with the literature.<sup>21</sup>

All patients (100%) in the study underwent surgery. The percentage of patients undergoing laparoscopic cholecystectomy was 77.17%, open cholecystectomy were 20.65%. The percentage of patients who underwent CBD exploration with open cholecystectomy was 6.52% which was similar to that found in literature.<sup>6,24</sup> Also the conversion rate found in the present study (6.57%) was similar to that found in literature.<sup>6,25</sup> (Table 4).

**Table 4: Comparison between conversion rate in patients of cholelithiasis.**

Study	n	Year	Conversion rate (%)
Csikesz et al <sup>26</sup>	859,747	2008	9.5
Muthailasamy et al <sup>6</sup>	104	2017	9.6
Kemal Beksacet al <sup>27</sup>	1335	2016	7.7
Present study	92	2018	6.57

Post-operative complications in the laparoscopic group and open cholecystectomy group were compared in the present study, it was observed that the complications like bile leak, surgical site infection and fever were found more after the open cholecystectomy compared to the laparoscopic group and this difference was statistically different. These findings were similar to that found in studies by Barase et al and Rachamalla et al.<sup>24,28</sup>

Most common histopathological finding was chronic cholecystitis (77.78%), followed by acute cholecystitis and carcinoma gall bladder which is quite consistent with the literature except for carcinoma gall bladder which is more than that in literature which may be due to the geographical variation.

## CONCLUSION

Cholelithiasis is commonly seen in females in 4<sup>th</sup> and 5<sup>th</sup> decade mainly presenting with abdominal pain and dyspepsia. Multiple gallstones are common and Laparoscopic cholecystectomy offers best surgical management with 6.57% of conversion rate to open cholecystectomy, with lesser complications.

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