

Study of clinical features of cholelithiasis and its correlation with histopathological findings

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Abstract

Background: Gall stone disease is one of the most prevalent gastrointestinal diseases with a substantial burden to health care system. Incomplete and infrequent emptying of the gallbladder may cause the bile to become concentrated and contributes to gallstone formation. In present study, we aimed to study clinical features of cholelithiasis and its correlation with histopathological findings. **Material and Methods:** Present study was hospital based, prospective, observational study, conducted in gall bladder specimens of patients with prior clinical diagnosis of cholelithiasis. **Results:** Total numbers of specimens studied were 100. Maximum number of cases were in the 4th decade. Our study had 68 (68%) females and 32 (32%) males. Females outnumbered the males with a male to female ratio of 1:2.1. Non vegetarians were affected more than vegetarians with a ratio of 5.6:1. Obesity was seen in 35% of cases in our study with a BMI >30 kg/m². Pain in the right hypochondrium was the most common symptom seen in 55 cases (55%). Multiple stones were the commonest stones seen in 80% of the cases. On gross- examination, thickness of Gall bladder was increased in 57% of cases. Size of the gallstone varied from 0.2 to 3 cm with maximum number of stones measuring 0.2cm (25%) in our study. Chronic nonspecific cholecystitis was the commonest lesion encountered in our study seen in 80% of cases. Mixed stones (71%) were the commonest stones associated with chronic nonspecific cholecystitis. Pigment stones (8%) were seen in follicular cholecystitis, xanthogranulomatous cholecystitis had both pigment (1%) and cholesterol stone (1%). **Conclusion:** Cholelithiasis has an increased prevalence in females and non-vegetarians. Multiple stones were present in majority of the cases and biochemical analysis showed most of the stones to be of mixed variety.

Keywords: cholelithiasis, multiple stones, biochemical analysis, cholecystectomy, histopathological diagnosis

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INTRODUCTION

The epidemiology of gallstones is both exciting and frustrating, exciting because epidemiology holds the key to etiology, when we know exactly who gets the disease, we are a long way to defining why they got it, frustrating because accurate information on who got the disease is so hard to come by. Gall stone disease is one of the most

prevalent gastrointestinal diseases with a substantial burden to health care system. Cholelithiasis common with the incidence ranging from 10% to 20% of world population, 11% of general population of USA.¹ The estimated prevalence of gall stone disease in India has been reported as 2% to 9%.² It is 10 times more frequent in North than South India. Dietary deficiencies in the two regions are suspected to be responsible for the difference in the prevalence rate. It is now commonly agreed that cholelithiasis is an important risk factor for facilitating development of gall bladder cancer despite it being adenocarcinoma. Cholelithiasis is a common digestive surgical disorder characterized by abdominal pain, nausea, vomiting and jaundice. Incomplete and infrequent emptying of the gallbladder may cause the bile to become concentrated and contributes to gallstone formation.¹ The second factor is the presence of proteins in the liver and bile that either promote or inhibit cholesterol crystallization into gallstones. Increased levels of the

hormone estrogen as a result of pregnancy, hormone therapy, or the use of birth control pills, may increase cholesterol levels in bile and also decrease gallbladder movement resulting in gallstone formation.³ In present study, we aimed to study clinical features of cholelithiasis and its correlation with histopathological findings.

MATERIAL AND METHODS

Present study was hospital based, prospective, observational study, conducted in Tertiary Care Hospital, India. Study duration was of 2 years (July 2014 to June 2016). Study was approved by institutional ethical committee.

Inclusion criteria: Patients with prior clinical diagnosis of cholelithiasis

Exclusion criteria: Specimens sent as acalculous cholecystitis and with prior diagnosis of malignancy

Demographic data, clinical details, surgery details were collected for patients selected for study. Cholecystectomy specimens sent were cut open fresh, gallstones removed, labeled with corresponding histopathology number and biochemical analysis of gallstones was done. The specimens were fixed in 10% buffered formalin, minimum of three sections were taken from fundus, body and neck of gall bladder. Tissue was processed by routine histological technique with paraffin embedding and sectioning at 4-micron thickness and stained with hematoxylin and eosin. Biochemical analysis of gallstones was done for cholesterol (Lieberman’s Buchard reaction), calcium, oxalates, phosphates and carbonates by standard methods.

Statistical analysis was done using descriptive statistics.

RESULTS

Total numbers of specimens studied were 100. Age range in our study was between 18 years to 90 years. The youngest patient reported was 18 years and the oldest was 90 years. Maximum number of cases were in the 4th decade. Our study had 68 (68%) females and 32 (32%) males. Females outnumbered the males with a male to female ratio of 1:2.1. Non vegetarians were affected more than vegetarians with a ratio of 5.6:1. Obesity was seen in 35% of cases in our study with a BMI >30 kg/m².

Table 1: General characteristics

General characteristics	No. of cases	Percentage of cases
Age in years		
18 – 30	24	24%
31 – 40	36	36%
41 – 50	21	21%
51 – 60	13	13%
61 – 70	4	4%
>70	2	2%
Gender		
males		68%
females		32%
BMI kg/m ²		
>30	35	35%
<30	65	65%
Diet		
Mixed diet	85	85%
Vegetarian	15	15%

Pain in the right hypochondrium was the most common symptom seen in 55 cases (55%).

Table 2: Clinical features

Clinical features	No. of cases	Percentage of cases
Pain right hypochondrium	55	55 %
pain epigastric region	30	30 %
Jaundice	15	15 %

Multiple stones were the commonest stones seen in 80% of the cases. On gross- examination, thickness of Gall bladder was increased in 57% of cases. Size of the gallstone varied from 0.2 to 3 cm with maximum number of stones measuring 0.2cm (25%) in our study.

Table 3: Gallstones characteristics

Characteristics	No. of cases	Percentage of cases
Number of gallstones		
Multiple stones	80	80%
Single stones	20	20%
thickness of gallbladder		
>3mm	57	57%
<3mm	43	43%
Size of the gallstones		
0.2mm	25	25%
0.3mm	10	10%
0.4mm	5	5%
0.5mm	20	20%
1.0mm	10	10%
1.5mm	5	5%
2.0mm	10	10%
3.0mm	15	15%

Chronic nonspecific cholecystitis was the commonest lesion encountered in our study seen in 80% of cases

Table 4: Spectrum of lesions of the gall bladder

Spectrum of lesions of the gall bladder	No. of cases	Percentage of cases
Chronic nonspecific cholecystitis	80%	
Follicular cholecystitis	8%	24%
Xanthogranulomatous	2%	36%
Acute on chronic cholecystitis	4%	21%
Well differentiated adenocarcinoma	4%	13%
Infiltrating papillary carcinoma	1%	4%
Adenosquamous carcinoma	1%	2%

Mixed stones (71%) were the commonest stones associated with chronic nonspecific cholecystitis. Pigment stones (8%) were seen in follicular cholecystitis, xanthogranulomatous cholecystitis had both pigment (1%) and cholesterol stone (1%). Acute on chronic cholecystitis was associated with mixed stones in 4% of cases. Out of 6 cases of adenocarcinoma, both mixed and pigment stones were seen in 3% of cases each respectively.

Table 5: Correlation of types of gallstones and lesions of gall bladder

Diagnosis	Mixed	Pigment stones	Cholesterol stones
Chronic nonspecific cholecystitis	71 %		
Follicular			8%
Xanthogranulomatous	2%	1 %	1 %
Acute on chronic	4%		
Carcinoma(n=6)	3 %	3 %	

DISCUSSION

Cholelithiasis is the most common biliary pathology. Gall stones have an incidence ranging from 10% to 20% worldwide.² The prevalence of gallstone varies widely in different parts of the world. In India it is estimated to be around 4%. An epidemiological study restricted to rail road workers showed that north Indians have 7 times higher occurrence of gallstones as compared to south Indians.⁴ Gallstones are categorized as cholesterol, mixed, black pigment, or brown pigment stones.⁴ Cholesterol and mixed gallstones are formed from biliary sludge, while pigment

stones are composed of calcium salts of unconjugated bilirubin, with varying amounts of cholesterol and protein. Complications of gall stones include gallstone pancreatitis, gallstone ileus, biliary cirrhosis and gallbladder cancer.³ Maximum numbers of cases in our study were in the range of 31–40 years (36%) which is similar to Mohan *et al.*,⁵ in which maximum number of cases were in the 4th decade. Thamil selvi *et al.*,² SK Mathur *et al.*,⁶ had a peak incidence in 5th decade. Pain in the right hypochondrium was the most common symptom in our study which is similar to Thamil selvi *et al.*,² and Kamran *et al.*,⁷. Pain in

the epigastric region is seen in 30% of cases in our study whereas Tamil selvi *et al.*,² had only 15.3% cases. Jaundice was seen in 15% of cases in our study whereas Tamil selvi *et al.*,² observed jaundice as presenting feature only in 3.8% of cases. In our study patients presented late with symptoms of obstruction thereby presenting with jaundice. In India, 97% cases of cholelithiasis were found in non-vegetarians. Most of the patients in our study were mixed diet (80%) compared to vegetarians (20%) with a ratio of 4:1 similar to Tamil selvi *et al.*,² in which nonvegetarians were preponderant with a ratio of 6:1. Obesity is defined as body mass index >30 kg/m² which in our study was seen in 35% of cases as compared to Tamil selvi *et al.*,² who had 39% of obese cases. cholelithiasis is seen in overweight patients because bile salts in bile is reduced leading to increase in cholesterol. Multiple stones are more common (80%) than solitary stones (20%) in our study which is similar to Tamil selvi *et al.*,² and SK Mathur *et al.*,⁶ who also had increased number of multiple stones. This indicates that cholecystitis with multiple stones are more symptomatic than those with solitary stones. A size of stones in our study varied from 0.2 to 3.0 cm. Stone of the largest size was a solitary cholesterol stone. In study by Tamil selvi *et al.*,² size of stone varied from 0.3 to 2.0 cm. On biochemical analysis, mixed stones (78%) were the commonest stones seen in our study similar to Tamil selvi *et al.*,² Chandran *et al.*,⁸ which were studies done in south India. However, a study by Taher *et al.*,⁹ which was conducted in Baghdad, found cholesterol stones as the commonest stones which again emphasizes the regional variation due to ethnicity and dietary habits. On gross examination, increased thickness of gall bladder (>3 mm) due to chronic inflammation was seen in 57% of cases which is similar to SK Mathur *et al.*,⁶ On histopathology, majority of cases in our study had chronic nonspecific cholecystitis (80%) comprising of lymphocytes, plasma cells, histiocytes and occasional eosinophils which is similar to study by Mustafa mazlum *et al.*,¹⁰ SK mathur *et al.*,⁶ and Tamil selvi *et al.*,² In our study, follicular cholecystitis and xanthogranulomatous cholecystitis were seen in 8% and 2% of the cases each respectively whereas in study by SK mathur *et al.* [6], follicular and xanthogranulomatous cholecystitis were seen in 5% and 3% of cases respectively. Follicular cholecystitis occurs in gram-negative bacterial infection and may be associated with stones. Xanthogranulomatous cholecystitis occurs due to penetration of bile into the gall bladder wall from mucosal ulcers or ruptured rokitansky aschoff sinuses along with outflow obstruction by calculi and infection. Eosinophilic cholecystitis was not seen in our study since it is usually associated with acalculous cholecystitis which were excluded from our study. Acute on chronic cholecystitis

was seen in 4% of the cases in our study whereas SK Mathur *et al.*,⁶ had 12% of the cases. Carcinoma of the gall bladder was seen in 6% of cases in our study. All the cases were sent with a prior clinical diagnosis of chronic cholecystitis. In contrast to our study, Tamil selvi *et al.*,² and Mustafa mazlum *et al.*,¹⁰ has a lower incidence of carcinoma. Chronic nonspecific cholecystitis seen in 80% of cases was most commonly associated with mixed stones which is similar to Mohan *et al.*,⁵ Adenocarcinoma seen in 6 % of the cases in our study was associated with mixed and pigment stones equally whereas in study by Mohan *et al.*,⁵, carcinoma seen in only 1.09% cases is associated only with pigment stones.

CONCLUSION

Cholelithiasis has an increased prevalence in females and non-vegetarians. Efforts should be taken to reduce all variable risk factors which lead to cholelithiasis, especially among females. Multiple stones were present in majority of the cases and biochemical analysis showed most of the stones to be of mixed variety. Upper abdominal ultrasound helps in early screening and detection. Early cholecystectomy is the treatment of choice.

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