



Morphological spectrum of gallstone disease in 1100 cholecystectomies in North India

H. Mohan, R. P. S. Punia, S. B. Dhawan, S. Ahal, M. S. Sekhon¹

Departments of Pathology and ¹Surgery, Government Medical College and Hospital, Chandigarh, India

For correspondence:

H Mohan, Department of Pathology, Government Medical College, Sector 32-A Chandigarh – 160030, India,

E-mail: drharshmohan@yahoo.com

ABSTRACT

Background: Gallstones are a major cause of morbidity and mortality throughout the world. In India, they are seven times more common in the North as compared to the South. **Aims:** To study the morphological spectrum of gallstone disease in the stone-belt of India, and to understand its probable etiopathogenesis. **Materials and Methods:** Morphological spectrum of gallstone disease was studied in 1100 cholecystectomies over a period of 3 years in the past. **Results:** There was a preponderance of females (M : F ratio 1 : 6.4). The age of the patients varied from 10 to 90 years with maximum number of cases between 31 and 40 years of age. On morphological analysis, gallstones were of mixed type in 686 cases (62.3%), pigment type in 34 cases (3.2%), cholesterol type in 182 cases (17.3%), and combined type in 148 cases (14%). Other lesions associated with chronic cholecystitis were cholesterolosis in 112 cases (10.1%), xanthogranulomatous cholecystitis in 26 cases (2.3%), follicular cholecystitis in 26 cases (2.3%), ceroid granulomas in ten cases (0.9%), eosinophilic cholecystitis in six cases (0.5%), and carcinoma in 12 cases (1.09%). Maximum number of carcinomas were associated with pigment stones, that is, 7 out of 12 cases (58.3%). **Conclusions:** The morphological spectrum of gallstone disease in this stone-belt of India will certainly contribute to understand its etiopathogenesis, and hence prevention. However, further studies on the biochemical composition of stones and their association with morphological changes are required to clarify the etiopathogenesis.

Key words: Carcinoma, cholecystitis, cholelithiasis, cholesterolosis, gallstones

How to cite this article:

Mohan H, Punia RPS, Dhawan SB, Ahal S, Sekhon MS. Morphological spectrum of gallstone disease in 1100 cholecystectomies in North India. *Indian J Surg* 2005;67:140-2.

Gallstones are a major cause of morbidity and mortality throughout the world.^[1] At least 10% adults have gallstones.^{[2],[3]} The prevalence varies with age, sex, and ethnic group.^[1] Most patients are unaware of the disease and remain asymptomatic for life. Only a small percentage develop symptoms necessitating treatment.^[4] Nowadays, laparoscopic cholecystectomy is the treatment of choice in most patients.^[5] Gallstones vary in their composition, a majority being cholesterol stones (80%), and the remaining being mixed, combined, and pigmented.^[6] The diseased gallbladder, in as-

sociation with gallstones show variety of morphologic changes ranging from inflammation to malignancy. The present study is aimed at clinicopathologic analysis of gallstone disease in this part of the country.

MATERIALS AND METHODS

The retrospective study was conducted on 1100 cholecystectomies performed at our hospital over a period of 3 years in the past. Clinical details and pathological data were retrieved from the records. The cholecystectomy specimens that were received were fixed in 10% formalin. The findings on gross examination were noted, and the stones recovered from the gallbladder were classified on the basis of their morphology [Table 1]; however, stones were not analyzed by chemical examination. Two sections were taken from

Paper Received: May 2005. **Paper Accepted:** June 2005.

Source of Support: Nil.



each gallbladder for paraffin blocks and were examined after staining with hematoxylin and eosin staining. Microscopic examination was done to assess the type of inflammatory infiltrate, presence of fibrosis, cholesterosis, metaplasia, tumor, or tumor-like lesion.

Statistical analysis

Chi-square test was applied to find out the association of the type of gallstones and associated microscopic changes.

RESULTS

The age of patients varied from 10 to 90 years with maximum number of patients (316/1100, 28.7%) being between 31 and 40 years. There were 148 males and 952 females with M : F ratio of 1 : 6.4. On the basis of morphological analysis it was found that a maximum percentage of cases had mixed type of gallstones (686 cases, 62.3%), followed in decreasing frequency by cholesterol (182 cases, 17.3%), combined (148 cases, 14%), and pigment type (34 cases, 3.2%) [Table 1]. In our study, there were two children and both had cholesterol stones.

In 50 cases (4.5%), there were no gallstones, but on histological examination all these cases too showed changes of chronic cholecystitis. In addition, histological examination of gallbladder showed other variants of cholecystitis [Table 2]. Association of the type of gallstones with cholesterosis, xanthogranulomatous change, and carcinoma showed that cholesterosis was associated not only with cholesterol stones but also with mixed stones. Xanthogranulomatous change was associated most often with mixed gallstones (19/26 cases, 73%). In two patients, there was adenoma with gallstones. In one patient, the gallbladder wall showed lymphomatous infiltration diagnosed incidentally. Carcinoma of the gallbladder was seen in 12 cases (1.09%) and it was associated most often with pigment stones (7/12 cases, 58.3%) [Table 3].

Statistical analysis revealed significant association of cholesterosis with cholesterol stones ($P < 0.01$).

Table 2: Other lesions associated with cholecystitis

Type of lesion	No. of cases	Percentage
Cholesterosis	112	10.1
Xanthogranulomatous change	26	2.3
Follicular cholecystitis	26	2.3
Ceroid granulomas	10	0.9
Eosinophilic cholecystitis	6	0.5
Cholesterol polyp	2	0.18
Adenomatous hyperplasia	1	0.09
Adenoma	2	0.18
Non-Hodgkin's lymphoma	1	0.09
Carcinoma (all types)	12	1.09

However, association of cholesterosis with mixed and combined stones was significantly low. There was no significant association of xanthogranulomatous cholecystitis with type of stone. Carcinoma gallbladder showed significant association with pigment stones ($P < 0.01$).

DISCUSSION

Gallstones are frequently found at autopsy in subjects who have apparently gone through life without symptoms of their gallstone disease, indicating that many people have gallstones without ever becoming aware of them. The estimated prevalence of gallstone disease in India has been reported as 2% to 29%.^{[7],[8]} In India, this disease is seven times more common in the North (stone belt) than in South India.^[9] Dietary differences in the two regions are suspected to be responsible for the difference in the prevalence rate.^[10] The average age of these patients in India, is a decade younger than those in the West.^[11] The maximum number of patients in this study were in the third decade of their life (316 cases, 28.7%). Studies have shown an increase in the prevalence of gallstones with age probably because of decrease in activity of cholesterol α reductase, and increase in activity of HMG CoA reductase resulting in increased cholesterol secretion and saturation of bile.^[12]

Male to female ratio in this study was 1 : 6.4. Other studies have also shown predominance of females among patients with gallstone disease. In fact, female sex hormones and sedentary habits of most women in

Table 1: Classification of gallstones on the basis of their morphology

Type of stone	Morphology	No. of cases
Pure		
Cholesterol	Solitary, oval, large, granular surface, yellow white. Cut section- radiating glistening crystals	182 (65.3%)
Pigment	Multiple, small, jet-black, mulberry shaped. Cut section - soft and black	34(3.2%)
Calcium carbonate	Multiple small, faceted. Cut section - gray white and hard	0
Mixed	Multiple, multifaceted, variable size. Cut section-laminated alternating dark pigment layer and pale white layer	686(62.3%)
Combined	Usually solitary, large smooth. Cut section - central nucleus of pure gallstone with mixed outer shell or vice versa	148(14.0%)
No stones	-	50(4.5%)

Table 3: Association of the type of gallstones with other changes

Type of gallstone (total no. of cases)	No. of cases Cholesterolosis	Xanthogranulomatous cholecystitis	Carcinoma
Mixed (686)	47 (6.8)	19 (2.7)	3 (0.4)
Cholesterol (182)	48 (26.3)	2 (1.0)	2 (1.0)
Combined (148)	8 (23.5)	4 (2.7)	–
Pure pigment (34)	1 (2.9)	1 (2.9)	7 (20.5)
No stones (50)	8 (16.0)	–	–

India exposes them to factors that possibly promote the formation of gallstones.^{[11],[13],[14]}

In our series, 62.3%, 17.3%, 14.1%, and 3.2% were mixed, cholesterol, combined, and pigment stones, respectively. Other studies have also reported similar incidence of the type of gallstones; however, literature reports, from Chennai were in contrast to our study where majority of gallstones are pigment stones and the remaining are mixed and cholesterol type.^{[5],[9],[15]}

In the pathological findings, cholesterolosis was the commonest change noted (112 cases, 10.1%). Cholesterolosis was present in 26.3% of cases with cholesterol cholelithiasis, and 6.8% of cases with mixed cholelithiasis. Chronic xanthogranulomatous cholecystitis was observed in 26 cases (2.3%). These cases usually present with increased wall thickness and mimic carcinoma on gross. Awareness of this entity and careful microscopic examination helps in diagnosis. Chronic follicular cholecystitis was noted in 26 cases (2.3%). This entity is considered as variant of chronic cholecystitis and represent lymphoid hyperplasia in wall of gallbladder. Other morphological lesions were rare.

Carcinoma of gallbladder is a rare but lethal disease. In the present study, there were only 12 cases (1.09%). Different studies have reported different incidences ranging from 1% to 12.4%.^{[16],[17]} This difference is because carcinoma gallbladder usually presents as an inoperable stage as a result of infiltration into the liver and therefore surgery is not undertaken. In our study, 100% patients with cancer had gallstones. Maximum number of patients with cancer had pigment stones.

Laparoscopic cholecystectomy, introduced in 1987 by Mouret, and then used in 1988 by Du Bois *et al.*, is the treatment of choice.^[6] However, major challenge is medical prevention of gallstone formation in susceptible individuals, although cholecystectomy remains the cornerstone of treatment. Studying the morphological spectrum of gallstone disease in this stone-belt of India will certainly contribute to understand its etiopathogenesis and hence prevention. However, further studies on biochemical composition of stones and their

association with morphological changes are required to clarify the etiopathogenesis.

REFERENCES

1. Johnson DE, Kaplan MM. Pathogenesis and treatment of gallstones. *New Engl J Med* 1993;328:412-21.
2. Diehl AK. Epidemiology and natural history of gallstone disease. *Gastroenterol Clin North Am* 1991;20:1-19.
3. Heaton KW, Braddon FEM, Mountford RA, Hughes AO, Emmett PM. Symptomatic and silent gallstones in the community. *Gut* 1991;32:316-20.
4. Wenckert A, Robertson B. The natural course of gallstone disease-11 year review of 781 non-operated cases. *Gastroenterol* 1966;50:376-81.
5. Dubois F, Berthelots G, Levrad H. Cholecystectomy par coelioscopie. *Presse Med* 1989;18:980.
6. Bowen JC, Brenner HI, Ferrante WA, Maule WF. Gallstone disease-Pathophysiology, epidemiology, natural history and treatment options. *Med Clin North Am* 1992;76:1143-57.
7. Prakash A. Chronic cholecystitis and cholelithiasis in India. *Int Surg* 1968;49:79-85.
8. Khurro MS, Mahajan R, Zargar SA, Javid G. Prevalence of biliary tract disease in India: a sonographic study in adult population in Kashmir. *Gut* 1989;30:201-05.
9. Jayanthi V, Palanivelu C, Prasanthi R, Methew S, Srinivasan V. Composition of gallstones in Coimbatore district of Tamil Nadu State. *Ind J Gastroenterol* 1998;17:134-35.
10. Malhotra SL. Epidemiological study of cholelithiasis among railroad workers in India with special reference to causation. *Gut* 1968;9:290-95.
11. Tandon RK. Pathogenesis of gallstones in India. *Trop Gastroenterol* 1988;9:83-91.
12. Jayanthi V. Pattern of gallstone disease in Madras city, South India: a hospital based survey. *J Assoc Phys Ind* 1996;44:461-64.
13. Baig SJ, Biswas S, Das S, Basu K, Chattopadhyay G. Histopathological changes in gallbladder mucosa in cholelithiasis: correlation with chemical composition of gallstones. *Tropical Gastroenterol* 2002;23:25-7.
14. Dhar SC, Ansari S, Saha M, Ahmad MM, Rahman MT, Hasan M, *et al.* Gallstone disease in a rural Bangladesh community. *Ind J Gastroenterol* 2001;20:223-6.
15. Tyagi SP, Tyagi N, Maheshwari V, Ashraf SM, Sahoo P. Morphological changes in diseased gall bladder: a study of 415 cholecystectomies at Aligarh. *J Ind Med Assoc* 1992;90:178-81.
16. Russel PW, Brown CH. Primary carcinoma of gallbladder. *Ann Surg* 1949;132:121-8.
17. Gupta SC, Misra V, Singh PA, Roy A, Misra SP, Gupta AK. Gallstones and carcinoma gallbladder. *Indian J Pathol Microbiol* 2000;43:147-54.