Section: Miscellaneous

Original Research Article

PATHOLOGICAL CHANGES OF GALL BLADDER IN RELATION TO COMPOSITION OF GALL STONE: A CROSS SECTIONAL STUDY IN A TERTIARY CARE HOSPITAL

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Received : 11/04/2023
Received in revised form : 10/05/2023
Accepted : 21/05/2023

Keywords:
Gall bladder, gallstone, cholecystitis, hyperplasia, metaplasia, carcinoma.

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DOI: 10.47009/jamp.2023.5.3.256

Source of Support: Nil,
Conflict of Interest: None declared

Int J Acad Med Pharm
2023; 5 (3); 1258-1261

Abstract

Background: Gallstone disease is a common health problem worldwide including India. It is commonly believed that bile stasis is the prime factor for gallstone formation. The function of the gallbladder is not only to store bile, but also to concentrate it during the interdigestive phase by means of salt-dependent water reabsorption. Pathological changes related to gallstone formation are still the focus of intensive research. The hypothesis most widely accepted is the stasis of bile caused by gallbladder dyskinesia, while dyskinesia may be the result of pathologic changes in the gallbladder wall. The aim of this study is to investigate the relation between gallstones and light as well as electron microscopic changes in the gallbladder epithelium. **Materials and Methods:** A cross sectional study was conducted in the Department of Pathology and Department of Surgery at Tertiary Care Teaching Hospital. A total number of 90 specimens were selected from gallbladders after cholecystectomy with clinical and histopathological diagnosis of chronic calculus cholecystitis. Paraffin sections were stained with haematoxylin and eosin to demonstrate the general histology. The gallbladders were divided into groups depending on the type of gallstones found; cholesterol, pigment or mixed stones. **Result:** In the present study, of 90 cases, majority of the patients (30%) were in age group of 40–49 years. Of the total 90 cases studied, 80% were female and 10% were male patients. Male‑to‑female ratio was 1:5.7. Maximum type was of mixed stones (49) and was multiple in number (43). Gallbladder size was normal in 54%, enlarged in 24%, and fibrotic in 12% of the specimens. **Conclusion:** As the weight, volume and size of the stone increases the changes in the gall bladder mucosa changes from cholecystitis, hyperplasia, metaplasia, dysplasia, to carcinoma.

INTRODUCTION

Gallstone disease is a common health problem worldwide including India.[1] It is commonly believed that bile stasis is the prime factor for gallstone formation. The function of the gallbladder is not only to store bile, but also to concentrate it during the interdigestive phase by means of salt-dependent water reabsorption.[2] Epithelium of the gallbladder and biliary tract is exposed to high concentrations of potentially harmful exogenous and endogenous compounds excreted into primary bile.[3]

All columnar epithelial cells are lined by a blanket of mucus, a native physiological gel-like secretion which separates the host mucosal cells from the external milieu.[4] The gallbladder mucus plays a regulatory role in cholelithiasis as it promotes the nucleation of stones.[5] Mucus, calcium and lipids act in concert to form the gallstones.[6] Gallbladder mucin is one of the key factors in gallstone formation. However, there is little information about the diversity of mucin secretion according to the stone composition.[7]

A major causative agent for stasis is gallbladder dyskinesia which in turn may be a consequence of

ISSN (O): 2687-5365; ISSN (P): 2753-6556

gallbladder wall pathology.[8] However, it was observed that gallbladder tension increased, rather than decreased during the early stage of gallstone formation.[9] Cholelithiasis produces diverse histopathological changes in gallbladder mucosa namely acute inflammation, chronic inflammation, glandular hyperplasia, granulomatous inflammation, cholesterosis, dysplasia, and carcinoma.[10]

The aim of this study is to probe the relation of gallstone and histopathological changes in the gallbladder epithelium.

MATERIALS AND METHODS

A cross sectional study was conducted in the Department of Pathology and Department of Surgery at Tertiary care Teaching Hospital. A total number of 90 specimens were selected from gallbladders after cholecystectomy with clinical and histopathological diagnosis of chronic calculus cholecystitis received in the Department of Pathology.

Specimen inclusion criteria was specimens of cholecystectomy with cholecystitis and cholelithiasis, specimens with histopathological confirmation of chronic calculous cholecystitis, specimens from male and female of any age group. Specimens excluded were those without any clinical details, autolysed specimens, specimens of acalculous cholecystitis, specimens with prior diagnosis of malignancy.

Physical characteristics of stones namely cholesterol, pigment or mixed, based on morphology were noted as per the following parameters and clinical reports were reviewed. Yellow and whitish stones were identified as cholesterol stone. Black and dark brown stones were identified as pigment stones. Brownish yellow or green stones were identified as mixed stones.

The gall bladder specimens were collected in 10% formalin. The age range of the patients undergone cholecystectomy varied from 18 to 84 years. The gallbladders were divided into groups depending on the type of gallstones found, cholesterol, pigment or mixed stones. The full thickness tissue block about 1 cm x 0.5 cm was taken from the body part of each gallbladder fixed in 10% formalin. Tissues were subjected to formalin fixation, routine processing and paraffin embedding for histological examination. Paraffin sections was further processed for staining with hematoxylin and eosin (H&E) for studying general histology.

RESULTS

In the present study, of 90 cases, majority of the patients (30%) were in age group of 40–49 years [Table 1].

Table 1: Age group distribution (years)

Age group	Frequency (%)
<30	13 (14.4)
30‑39	20 (22.2)
40-49	27 (30)
50-59	17 (19)
>60	13 (14.4)
Total	90 (100)

Table 2: Gender distribution and gallstones characteristics

Parameter	Observation
Gender distribution (male/female)	10/80
Number of stone (single/two/multiple stones)	35/12/43
Type of stone (mixed/combined/cholesterol/pigment stones)	49/25/07/09
Gallbladder size (normal/enlarged/fibrotic)	54/24/12
Gallbladder wall thickness (<3 mm/>3 mm)	51/39

Of the total 90 cases studied, 80% were female and 10% were male patients. Male‑to‑female ratio was 1:5.7. Maximum type was of mixed stones (49) and was multiple in number (43). Gallbladder size was normal in 54%, enlarged in 24%, and fibrotic in 12% of the specimens. The average gallbladder wall thickness is also shown in [Table 2].

Table 3: Distribution of subjects according to various mucosal responses

Mucosal response on histological examination	Frequency (%)
Chronic cholecystitis with cholelithiasis	75 (83.4)
Chronic cholecystitis with metaplasia and cholelithiasis	6 (6.7)
Adenomatous hyperplasia with cholelithiasis	3 (3.3)
Adenomyomatous hyperplasia with cholelithiasis	2 (2.2)
Acute on chronic cholecystitis with cholelithiasis	1 (1.1)
Xanthogranulomatous cholecystitis with cholelithiasis	1 (1.1)
Papillary carcinoma	1 (1.1)
Intestinal metaplasia and cholelithiasis	1 (1.1)
Total	90 (100)

All 90 cases underwent microscopic evaluation and were categorized histologically. In specimens with more than one mucosal response, the predominant pattern was used for categorization (one condition per case). The majority of cases had chronic inflammation, of which chronic cholecystitis was predominant comprising 83.4%,

ISSN (O): 2687-5365; ISSN (P): 2753-6556

followed by chronic cholecystitis with metaplasia in 6.7% cases. In 1.1% of cases, carcinoma was observed, while intestinal metaplasia was observed in 1.1% of cases. All the patients suffering from carcinoma were female [Table 3].

Table 4: Association of mucosal response with gallstone type

Histological diagnosis	Gallstone type				Total
	Mixed	Combined	Cholesterol	Pigmented	
Cholecystitis	43	22	7	7	79
Hyperplasia	2	1	0	1	4
Cholecystitis with metaplasia	3	1	0	1	5
Carcinoma	1	1	0	0	2
Total	49	25	07	09	90

*P>0.05; not significant, P<0.05; significant

Table 5: Association of mucosal response with gallstone number

Histological diagnosis	Gallstone number			Total
	Single	Double	Multiple	
Cholecystitis	31	8	37	76
Hyperplasia	2	2	1	5
Cholecystitis with metaplasia	1	2	4	7
Carcinoma	1	0	1	2
Total	35	12	43	90

*P>0.05; not significant, P<0.05; significant

Table 6: Association of mucosal response with gallbladder wall thickness

Histological diagnosis	Gallbladder wall thickness		Total
	<3 mm	>3 mm	
Cholecystitis	45	34	79
Hyperplasia	1	2	3
Cholecystitis with metaplasia	5	2	7
Carcinoma	0	1	1
Total	51	39	90

*P>0.05; not significant, P<0.05; significant

Table 7: Association of mucosal response with gallstone size

Histological diagnosis	Mean size of stone±SD (cm)
Cholecystitis	0.75±0.39
Hyperplasia	2.48±2.05
Cholecystitis with metaplasia	0.94±0.55
Carcinoma	5.00±0.34

*P>0.05; not significant, P<0.05; significant. SD: Standard deviation

Association of mucosal response with gallstone type, gallstone number, gallbladder wall thickness, and gallstone size is shown in [Table 4‑7].

DISCUSSION

The estimated prevalence of gallstone disease in India has been reported between 2-29%. In India, this disease is seven times more common in north (stone belt) than in south India.[11] The present study undertook the evaluation of 330 cholecystectomy specimens with cholelithiasis with an aim to correlate various gallstone characteristics with host mucosal response.

The age of the patients ranged from 18 to 80 years. Majority of the patients (22.2%) were in the age group of 30-39 years with a mean age of 44.2 years. No age group was completely free of gallstones. The main sufferers were females; the male to female ratio being 1:6.6, an incidence similar to that reported by others.[12] The age and sex distribution of present as well as previous studies indicates that the incidence of cholelithiasis is higher in older age group and in females. Female sex hormones and sedentary habits of most women in India expose them to factors that possibly promote formation of gallstones.[13]

Mixed stones are the most commonly encountered stones in north India. In contrast to our study where combined stones were the next common type, cholesterol stones were the second most common variety in studies by Mohan and Tyagi.[14,15] There are no specific explanations for this variation. We could not document any specific difference in age of the patients with different types of stone, a finding supported by Jayanthi.[16]

Multiple stones have been found more commonly (35%) than solitary stones (12%) in our study as well as previous reports. This indicates that cases with multiple number of stones are more symptomatic than those with solitary stones. Precancerous changes of the gall bladder mucosa are of particular importance from both clinical and pathological standpoints. Improved diagnostic procedures aid in detection of early and/or resectable invasive carcinoma more frequently.

ISSN (O): 2687-5365; ISSN (P): 2753-6556

Precancerous conditions however, seem to be not infrequently overlooked by pathologists.[17]

We observed cholecystitis with hyperplasia in 8% cases. Cases of both adenomatous and adenomyomatous hyperplasia were included, although cases with simple epithelial hyperplasia including pseudostratification of epithelium were not considered. This led to an apparent decrease in the incidence of hyperplasia in our study when compared with Khanna in which incidence of hyperplasia was found to be 59%.[18] Elfvinget proposed the hypothesis that primary cholelithiasis causes secondary hyperplasia because of mechanical irritation caused by the calculi.[19]

Metaplasia is not an infrequent finding in gall bladder. Chronic cholecystitis with metaplasia was noted in 18% of our cases. Likewise, intestinal metaplasia was noted in 8% and pyloric metaplasia in 10% cases. Our results are comparable to those reported by other studies with almost similar distribution of metaplasia cases.[20]

When association of the four main types of mucosal response (cholecystitis, hyperplasia, metaplasia and carcinoma) was compared with the calculus type using chi-square test, no statistically significant association was found. Our results are in conformity with the findings of Khanna.[18]

During our investigations we categorized our cases on the basis of number of stones we encountered as single, double or multiple. We observed that benign, premalignant and malignant lesions were more frequently associated with multiple gallstones. Amongst all lesions metaplastic changes were relatively more frequent with solitary gallstones. These associations however were relative and no statistical association could be demonstrated between mucosal response and number of gallstones.

CONCLUSION

In conclusion it was seen that the average weight, volume and size of the gall bladder significantly correlated in increasing order with cholecystitis, hyperplasia, metaplasia and carcinoma.

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ISSN (O): 2687-5365; ISSN (P): 2753-6556