

# A Prospective Observational Study of Histopathological Changes in Gallbladder Mucosa Associated with Cholelithiasis

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Conflict of interest: Nil

## Abstract

**Introduction:** Gallstones are responsible to produce various histopathological changes in the gall bladder. Our aim of this study was to correlate various gallstone characteristics with the type of mucosal response in gall bladder.

**Materials and Methods:** The observational study was conducted on 72 cholecystectomy specimens with complete gallstones. The stones were assessed for various parameters. For microscopy, sections were obtained from the fundus, body and neck of the gallbladder. Additional sections were taken from abnormal looking areas.

**Results:** Morphological types of gallstones among the 72 cases found were as follows: 64% had mixed stones, 20% combined, 9% pigment stones, and 7% cholesterol stones. Number of stones varied from a single calculus in 30%. Majority (52 specimens) of HPE shows chronic cholecystitis. Pigment stones appear to correlate with severity of inflammation (6/16 in Grade I inflammation, 18/22 in Grade III inflammation).

**Conclusion:** We conclude that pigment gallstones are associated with severe inflammation and higher degree of fibrosis. Gall stone also leads to the gallbladder mucosa changes from cholecystitis, hyperplasia, and metaplasia to carcinoma.

**Keywords:** Cholelithiasis, Gallbladder Mucosa, Histopathology.

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## Introduction

Cholelithiasis is a major cause of morbidity throughout India, which requires hospitalization and cholecystectomy.

Gallbladder is prone to the formation of gallstones. Various factors which interact with gall bladder mucosa play an important role in pathogenesis of gall stone formation.

Lithogenic bile which includes saturated cholesterol is considered an important factor in gallstone formation in healthy individuals. Other factors are bile with calcium,

gallbladder mucus, prostaglandins and functional failure of electrolyte absorption by mucosa also may interact with gallstone formation [1]. Biliary calcium can reduce the solubility of cholesterol. Gallbladder mucus has long been recognized as an important factor contributing to gall stone development [2].

In this study we are correlating the interaction between gallbladder mucosa and bile in pathogenesis of gallstone disease.

### Aim of study

Aim to correlate various gallstone characteristics with the type of mucosal response in gall bladder.

### Method and Materials

This prospective study was conducted in department of pathology, Shri Shankara Institute of Medical Sciences from March 2018 to December 2022. Total 100 patients were selected for this study.

### Inclusion criteria:

1. Histopathological confirmation of chronic calculous cholecystitis.
2. Presence of calculi accompanying the specimen.
3. Well preserved mucosa lining epithelium in sections.
4. Availability of corresponding paraffin blocks.

Total 72 patients out of 100 were fulfilled these criteria rest excluded from study.

### Methods

After proper sampling of tissue and the specimen was processed by routine histological techniques for paraffin embedding and sectioning at slandered thickness. Histopathological diagnosis was established on hematoxylin and eosin

staining of the sections. Four sections including entire wall were obtained: two from body and one each from fundus and neck of the gallbladder. Additional sections if deemed necessary were taken from abnormal mucosa. The pattern of response in the gallbladder mucosa was studied with regard to number, size, and morphological type of the stone.

All collected data were systematically compiled and analyzed using analysis of variance for averages and Chi-square test for contingency tables and proportions. Statistical significance was considered when  $P < 0.05$ .

### Results

Out of 72 cases, majority of the patients (32%) were in age group of 40–49 years. Of the total 72 cases studied, 81% were female and 19% were male patients. Male-to-female ratio was 1:5.7. Gallbladder size was normal in 49%, enlarged in 37%, and fibrotic in 14% of the specimens.

Morphological types of gallstones among the 72 cases found were as follows: 64% had mixed stones, 20% combined, 9% pigment stones, and 7% cholesterol stones. Number of stones varied from a single calculus in 30%, double in 24%, and multiple in the remaining 46% cases.

**Table 1: Distribution of mucosal responses with gallstone**

HPE of mucosa with cholelithiasis	Number
Chronic cholecystitis	52
Acute on chronic cholecystitis	08
Chronic cholecystitis with metaplasia	06
Adenomatous hyperplasia	04
Papillary carcinoma	02
Total	72

Out of 72 patients on HPE shows Chronic cholecystitis in 52 patients, Acute on chronic cholecystitis in 8 patients, Chronic cholecystitis with metaplasia in 06 patients, Adenomatous hyperplasia in 4 patients and Papillary carcinoma in 2 patients.

**Table 2: Composition of Calculi and grade of inflammation**

Grade Of Inflammation	Pigment Stone	Cholesterol Stone
I (16 cases)	6	10
II (28 cases)	16	12
III (22 cases)	18	4
<b>Total</b>	<b>40</b>	<b>26</b>

Out of the 72 cases with inflammation 3 did not have calculi suitable for biochemical analysis. The results tabulated in table VII are on the remaining 66 cases. There were 26 cases with cholesterol calculi and 40 with pigment calculi. Distribution of the two types of calculi among the three grades of inflammation is shown. The presence of pigment stones appears to correlate with severity of inflammation (6/16 in Grade I inflammation, 18/22 in Grade III inflammation) as against cholesterol stones (10/16 in Grade I inflammation, 4/22 in Grade III inflammation).

### Discussion

The estimated prevalence of cholelithiasis in India has been reported between 2% and 29%. In India, this disease is seven times more common in North than in South India [3]. The present study was conducted to evaluate 72 patients with cholelithiasis undergoing cholecystectomy with an aim to correlate various gallstone characteristics with morphological mucosal responses in the gallbladder.

The majority of the patients in this study were between the age group of 40 and 49 years, with a mean age of 41.3 years. 81% percent of the patients we studied were female. The age and gender distribution of present as well as previous studies indicate that the incidence of cholelithiasis is higher in adult females. This may be due to decrease in activity of cholesterol reductase and increase in activity of HMG-CoA reductase with age, resulting in increased cholesterol secretion and saturation of bile. The female sex hormones may also

expose them to factors that possibly promote the formation of gallstones [4].

Cholelithiasis represents one of the most frequent medical situations requiring surgical intervention. Frequently, chronic cholecystitis presents a large range of associated lesions such as cholesterosis, muscle hypertrophy, adenomatous proliferation of the mucous glands, metaplasia, hyperplasia, and dysplasia. The last three lesions are unanimously recognized as precursor lesions with cancerous potential [5].

We found chronic changes in the form of chronic cholecystitis and chronic cholecystitis with metaplasia being more common histological finding than other changes. Similar findings have been reported in the past who reported preponderance of chronic cholecystitis in gallstone patients in their studies [6,7].

In our study we trying to associate mucosal response with the type of gallstone, it was found that precancerous lesions (hyperplasia and metaplasia) although clinically seem to be more common in mixed and combined type of stones as compared to cholesterol stone, this association could not reach statistical significance ( $P > 0.05$ ) on statistical analysis. Khanna *et al* [8]. and Mathur *et al* [9]. also reported similar findings in their studies.

Another interesting finding was that cholecystitis, hyperplasia, metaplasia, and carcinoma, i.e., all the lesions, were more common with multiple gallstones [Table 1]. However, on statistical analysis, nonsignificant results were obtained ( $P$

=0.570). Mathur *et al.* also could not demonstrate any significant association between mucosal response and number of gallstones ( $P > 0.05$ ).

Basu *et al* [10]. studied the morphological changes in chronic calculous cholecystitis in relation to the type of stones. They found that inflammation was more severe with pigment calculi while fibrosis and related complications were more frequent with cholesterol calculi.

The present study supports the association between pigment stones and severe inflammation. Fibrosis also was more in cases with pigment calculi in our study. Mucins have been shown to be a structural component of gallstones. Histochemical studies carried out on calculi have demonstrated presence of sulphomucins in them, especially in pigment stones [11]. However no correlation between mucin histochemistry of mucosal epithelium and the type of stone has been recorded in literature. In the present study, pigment stones were found more often in association with severe inflammation, gastric metaplasia and increased expression of sialomucins, as against cholesterol stones.

### Conclusion

We conclude that pigment gallstones are association with severe inflammation and higher degree of fibrosis.

Gall stone also leads to the gallbladder mucosa changes from cholecystitis, hyperplasia, and metaplasia to carcinoma.

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