

## Spectrum of gallbladder diseases- A comparative study in North Vs South Indian population

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### Abstract

**Introduction:** Cholecystectomy specimens are frequently received specimens. The number of cholecystectomy has increased more than 50% in the last decade, a vast majority performed annually for gallstone related diseases. Present study was done to study the morphological features of cholecystectomy specimens & to compare the spectrum of gallbladder diseases in both the populations in North Indian as well as South Indian populations.

**Materials and Methods:** A total 800 cholecystectomy specimens (400 cases each from North India & South India) were studied at Kasturba Medical College, Mangalore and Postgraduate Institute of Medical Sciences & Medical Research and associated Dr. Ram Manohar Lohia Hospital, New Delhi.

**Results:** Gender distribution (M:F) in North India was 1:4.88, whereas in South India it was 1:1.33. Chronic cholecystitis was significantly higher in North Indians (84%) as compared to South (66.75%). Gallbladder carcinoma was more common in North India (2%) as compared to South (1.25%). Dysplasia associated with cholecystitis was more common in North India (2.50%) as compared to South (1.75%). Associated cholesterolosis was significantly seen in North Indian study group (17.75%), whereas no case was seen in South.

**Keywords:** Cholecystitis, Metaplasia, Dysplasia, Carcinoma, Gallbladder, Indian population.

### Introduction

Gallbladder is one of the most commonly encountered specimens in the surgical pathology laboratory. A majority of such specimens show, rather mundane changes associated with chronic cholecystitis, a minority will harbour a highly lethal carcinoma. Often under appreciated, the gallbladder may be affected by a variety of pathological processes that have specific clinical correlates. Reactive changes within cholecystitis may mimic dysplasia. Usual stone associated cholecystitis has only mild inflammation, but variants of cholecystitis may have abundant xanthoma cells, eosinophils or lymphocytes and plasma cells. Metaplasia from normal columnar absorptive epithelium to mucinous epithelium occurs in some cases & a few may progress to dysplasia which is thought to be the main precursor of invasive carcinoma. Most invasive carcinomas present at advanced stage & therefore are highly lethal. Resections of gallbladder performed in such cases must be accurately classified & staged to provide optimal prognostic information.<sup>1,2</sup> This study was thus conducted to compare the spectrum of gallbladder diseases in North Indian & South Indian populations.

### Aims and Objectives

1. To study the morphological features of cholecystectomy specimens in North Indian as well as South Indian population.
2. To ascertain the presence of precursors of dysplasia in gallbladder involved by chronic cholecystitis.
3. To compare the spectrum of gallbladder diseases in both the populations.

### Materials and Methods

In the present study a total 800 cholecystectomy specimens (400 cases each from North & South Indian population) were studied. Initially 400 cases were studied in the departments of Pathology, Kasturba Medical College, Mangalore (South Indian population) over five years (from May 2002 to April 2007) and were compared with 400 cases received at Postgraduate Institute of Medical Education & Research, and associated Dr. Ram Manohar Lohia Hospital, New Delhi (North Indian population), over one year (from January 2009 to December 2009). Detailed history & other investigations were obtained from records available. H&E sections were evaluated for spectrum of various gallbladder lesions including metaplasia, dysplasia & carcinomas, in both the populations.

## Results

Gender distribution (M:F) in North Indian study group was 1:4.88, whereas in South India it was 1:1.33. Mohan et al (2005)<sup>3</sup> reported M:F ratio of 1:6.4, while Khanna et al (2006)<sup>4</sup> found M:F ratio of 1:4.8 and Baig et al (2002),<sup>5</sup> 1:2.63. Khanna et al (2006)<sup>4</sup> reported mean age in North Indian 42.50 years, Mohan et al

(2005)<sup>3</sup> found that most common age group affected was 31-40 years (Table 1).

Spectrum of various gallbladder diseases and associated lesions, in both the populations are described in Table 2 & 3.

**Table 1: Age distribution**

	North Indian population	South Indian population
Common mean age	41.97 yrs. (M-45.35, F-41.35)	45.56 yrs. (M-47.47, F-45.87)
Age range	4 months to 82 yrs	1 ½ to 85 yrs
Mean age for carcinoma	54.50 yrs	51.38 yrs
Maximum case in age group	31-40 yrs (26%) followed by 41-50 yrs (25%)	41-50 yrs (28.25%) followed by 51-60 yrs (17.50%)

**Table 2: Diagnosis of 400 cases each of North Vs South Indian populations**

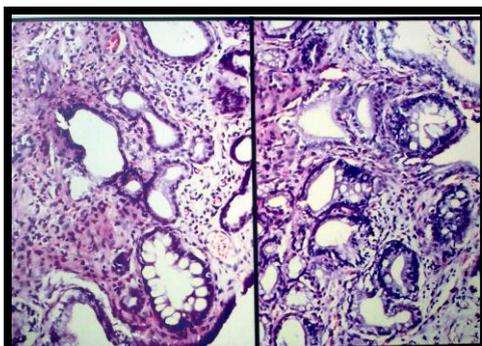
Diagnosis	North Indian population	South Indian population	p-value
Chronic cholecystitis	336 (84.00%)	267 (66.75%)	0.001
Acute cholecystitis	04 (1%)	24 (6%)	0.001
Chronic active cholecystitis	18 (4.50%)	81 (20.25%)	0.001
Gangrenous cholecystitis	01 (0.25%)	09 (2.25%)	0.406
Xanthogranulomatous cholecystitis	29 (7.25%)	02 (0.50%)	0.001
Chronic Follicular cholecystitis	01 (0.25%)	00	0.001
Choledochal cyst	01 (0.25%)	01 (0.25%)	1.00
Adenocarcinoma	8 (2%)	5 (1.25%)	0.080
Bile duct atresia	1 (0.25%)	00	0.001
Empyema	00	4 (2%)	0.0045
Mucocele	1 (0.25%)	1(0.25%)	1.00
Autolysed Gallbladder	00	1(0.25%)	0.001
Normal Gallbladder	00	5 (1.25%)	0.0249
Total	400	400	

**Tab 3: Associated gallbladder lesions**

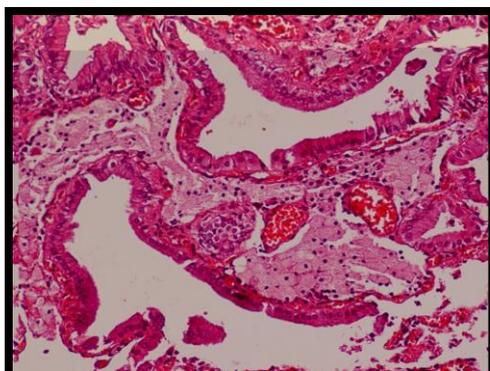
	North Indian population	South India population
<b>Stones</b>	382/400 (95.5%) (M 62, F 320)	321/400 (80.25%) (M172, F 228)
<b>Cholesterolosis</b>	71 (17.75%)	00
<b>Hyperplasia</b>	140/400 (35.00%)	126/400 (31.50%)
<b>Metaplasia-</b>	96/400 (24%)	95/400 (23.75%)
1. Pyloric	87 (21.75%)	79 (19.75%)
2. Intestinal	8 (02%)	11 (2.75%)
3. Combined	0	2 (0.50%)
3. Squamous	0	3 (0.75%)
4. Chondroid	1 (0.25%)	0
<b>Dysplasia ( low Grade)</b>	10 (2.5%)	7 (1.75%)



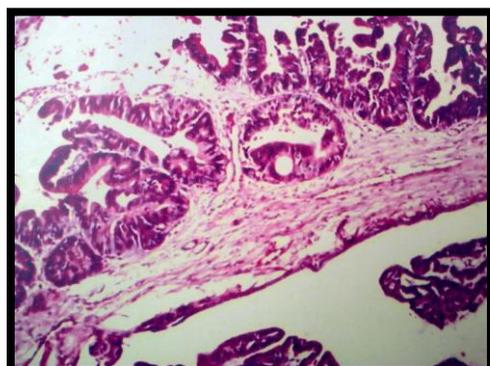
**Fig 1: Specimen of carcinoma gallbladder with intraluminal growth & multiple pigment stones**



**Fig 2: Chronic cholecystitis with intestinal metaplasia (400X, H&E)**



**Fig 3: Cholesterosis (400X, H&E)**



**Fig 4: Invasive adenocarcinoma of gallbladder (100X, H&E)**

## Discussion

Inflammatory diseases of gallbladder are a frequent cause of morbidity in west. The term cholecystitis encompasses a group of disorders that differ in their pathologic, pathogenetic and clinical characteristics. Most inflammatory diseases of gallbladder show nonspecific histologic features in that they elicit non distinctive types of cellular infiltrate. However, characterization of inflammatory patterns helps the pathologist to establish a diagnosis and provides insight into the pathogenesis of a disease.<sup>6</sup>

The 1<sup>st</sup> discussion of gallstones as “dried up humors concreted as stones” is ascribed to the Greek physician, Alexander of Tralles (5<sup>th</sup> century A.D.). The 14<sup>th</sup> century physician, Gentile da Foligno, suggested for the 1<sup>st</sup> time the relationship of cholecystitis & gallstones based on autopsy findings. Gallstones were removed from a living patient for the 1<sup>st</sup> time in 1618 by German surgeon, Wilhelm Fabry. First successful cholecystectomy was done by Carl Langenbuch in 1882.<sup>6,7</sup>

Mohan et al (2005)<sup>3</sup> reported estimated prevalence of gallstones in India as 2% to 29%. In India, this disease is around seven times more common in North India (stone belt) than in South India. Unisa S et al (2011)<sup>8</sup> population-based study to estimate prevalence and determine risk factors of gallbladder diseases in the rural Gangetic basin of North India revealed a prevalence of GBD of 6.20%. In present study, we found a significant difference in prevalence of gallbladder diseases (tab 2) in two studied populations (five times more common in North India). Associated gallbladder lesions including gallstones, hyperplasias, metaplasia, dysplasia & cholesterosis are discussed in Table 3. Dietary differences in the two regions are suspected to be responsible for the difference in prevalence rate. Sex hormones and sedentary habits of most women in India expose them to factors that possibly promote the formation of gallstones. Gender distribution (M:F) in North India was 1:4.88, whereas in South India it was 1:1.33. Mohan et al (2005)<sup>3</sup> reported M:F ratio of 1:6.4, while Khanna et al (2006)<sup>4</sup> found M:F ratio of 1:4.8 and Baig et al (2002)<sup>5</sup>, 1:2.63. Increase in the prevalence of gallstones with the age probably because of decrease in activity of alpha reductase, and an increase in activity of HMG CoA reductase resulting in an increased cholesterol secretion & saturation of bile. Shukla et al<sup>10</sup> and Usha & Gupta<sup>11</sup> reported that, the average age of these patients in India is a decade younger than those in the west. The reported incidence of gallbladder carcinoma (GBC) in India varies from 4.4- 12.4% It is upto 10 times more frequent in North India as compared to South India. Eastern Uttar Pradesh and Indo Gangetic belt is amongst the highest incidence of GBC in the world along with Chile & Bolivia. Dominant lithogenic genes are now suspected based the studies from North

America which had showed that gallstone associated diseases are more common in migrants from Asia. The relationship of gallstones to carcinoma was assumed to be due to chronic stimulation leading to mucosal metaplasia which may occasionally or rarely, eventually lead to development of carcinoma.

### Conclusion

In present study, gallbladder diseases are five times more common in North Indian population as compared to South.<sup>12</sup> M:F ratio was 1:4.88 in North Indians as compared to 1:1.33 in South Indians. Mean age was lower in North Indian population. Acute cholecystitis, acute on chronic cholecystitis & gangrenous cholecystitis were significantly higher in South Indian population as compared to North Indians. Chronic cholecystitis was significantly higher in North Indians (84%) as compared to South (66.75%). Gallbladder carcinoma (Fig 1 & 4) was more common in North Indians (2%) as compared to South (1.25%). Dysplasia associated with cholecystitis (Table 3) was more common in North India (2.50%) as compared to South (1.75%). Associated cholesterolosis (Table 3& Fig 3) was significantly seen in North Indian study group (17.75%), whereas no case was seen in South Indian population studied.

All the patients with symptomatic gallbladder diseases undergoing excision of gallbladder must have the benefit of a thorough histopathological examination of the specimen to confirm a benign diagnosis, if any; to detect precursors to carcinoma in long standing cases & have a thorough assessment of type & extent of disease in case of malignancy. Therefore, care must be taken to ensure adequate and immediate fixation of the specimen by the surgeon accompanied by meticulous gross and microscopic evaluation by the pathologist.

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