

**Evaluation of Morphological Changes in Gall Bladder Mucosa Correlation with Various Types of Cholelithiasis**Anita Kumari<sup>1</sup>, Shweta Kumari<sup>2</sup>, Pradeep Kumar Singh<sup>3</sup><sup>1</sup>Tutor, Department of Pathology, Govt. Medical College (GMC), Bettiah, West Champaran, Bihar<sup>2</sup>Tutor, Department of Pathology, Sri Krishna Medical College (SKMC), Muzaffarpur, Bihar<sup>3</sup>Associate Professor, Department of Pathology, Govt. Medical College (GMC), Bettiah, West Champaran, Bihar

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Conflict of interest: Nil

**Abstract:****Background:** Around the world, gallstones are a common source of illness. Gallstones in the gallbladder cause a variety of histopathological alterations. A portion of them might be precancerous lesions. The purpose of this study was to establish a relationship between the different histological alterations in the gallbladder and the chemical makeup of gallstones, specifically the cholesterol, mixed, or pigment kind.**Method:** We analysed gallbladders of 100 patients who underwent cholecystectomy for gall stones. The age, sex distribution and the incidence of different types of gallstones were studied. The histological changes in the gallbladders were observed and correlation with the type of gallstones was evaluated.**Result:** Gallstones were more common in the 40-49 age group with increased incidence in females. Many histological changes including hyperplasia, lymphoid follicles, prominent Rokitansky Aschoff sinuses, muscular hypertrophy, metaplasia and carcinoma were observed. Most of these histological changes were seen in the gallbladders with cholesterol stones. Hyperplasia was observed in 31.5%, lymphoid follicles in 31.5%, Rokitansky Ashoff sinus in 36.8%, muscular hypertrophy in 47.3%, pyloric metaplasia in 26% of gallbladders with cholesterol stones. Intestinal metaplasia was commonly associated with pigment stones(11%) and carcinoma was seen in gallbladders with mixed stones (6.7%).**Conclusion:** Gallstones are common in the adult population with a female predominance. Mixed stones were the common stones encountered. Correlation of histological changes with the chemical composition of gallstones showed increased incidence of changes in gallbladders with cholesterol stones. This could be due to the larger size of the cholesterol stones leading to more irritation and chemical injury produced by lithogenic bile.**Keywords:** Cholesterol Stone, Mixed Stones, Hyperplasia, Lymphoid Follicles.

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**Introduction**

Gallstone disease is a common health problem throughout the world affecting 10% to 20% of adult population.[1] Majority of the gallstones are asymptomatic. Gallstones are classified into cholesterol stones containing more than 80% crystalline cholesterol monohydrate, pigment stones composed predominantly of bilirubin calcium salts and mixed stones with components of both types.[2]

Cholesterol stones are more common in the West whereas pigment stone is the predominant type in non-western population. Hypomotility of gallbladder, accumulation of lipids in bile and mucus hypersecretion contribute to the formation of cholesterol stones.[3] Pigment stones occur in disorders associated with elevated unconjugated bilirubin in bile.[4] Gallstones produce a spectrum of morphological changes in gallbladder that ranges

from inflammation, hyperplasia, metaplasia and carcinoma. The aim of this study is to evaluate the various histological changes in gallbladder in correlation with the chemical composition of gallstones.

**Materials and Methods**

This study was conducted in Department of Pathology, Govt. Medical College, Bettiah, West Champaran, Bihar from November 2020 to July 2021. Gallbladder of 100 patients who underwent cholecystectomy for gallstone disease between November 2020 and August 2021 were included in this study.

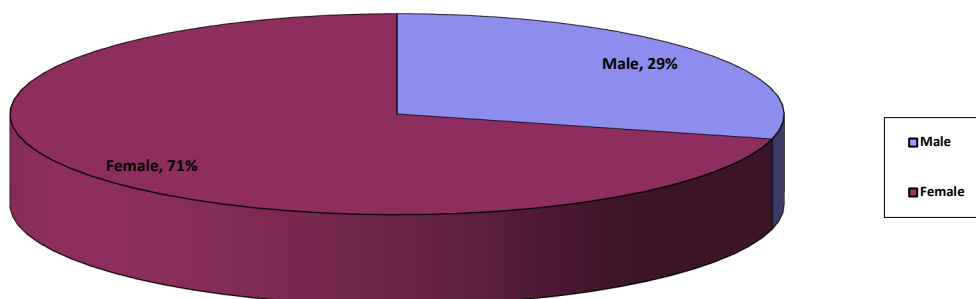
Each gallbladder was serially sectioned from neck to fundus. The sections obtained were fixed in 10% formalin, processed and cut into 5 microns thickness and stained in H and E. The histological

changes in all the layers of the gallbladder such as hyperplasia, lymphoid follicles, Rokitansky Aschoff sinuses, muscular hypertrophy, pyloric gland metaplasia and intestinal metaplasia were observed and noted. Biochemical analysis of the gallstones was done. The various histological changes observed in the gallbladder were analysed in correlation with the type of gallstones.

**Result**

Out of the 100 cholecystectomy specimens studied, 29 were from males and 71 from females with a male to female ratio of 1:2.4. [Pie Chart1 ]. The age ranged from 20 to 75 years. Maximum number of patients belonged to the age group of 40 – 49 years. [Table 1 ]. Most of the patients had mixed gallstones (45%) followed by pigment stones (36%) and cholesterol stones (19%). Among the many histological changes observed in the present study, mucosal hyperplasia was seen in 21 cases. [Table 2]. It occurred in 31.5 % of gallbladder with cholesterol stones followed by those with pigment stones (19.44%) and mixed stones (17.7%).

Lymphoid follicles in the lamina propria and muscle layer were seen in 31.57% of gallbladder with cholesterol stones. It was less obvious in gallbladders with mixed stones(22.22%) and pigment stones (19.44%). Rokitansky Aschoff sinuses were seen in 36.8% of gallbladders with cholesterol stones, 31% in mixed stones and 27.7% in pigment stones. Muscle hypertrophy was common in gallbladders with cholesterol stones(47.36%) followed by mixed stones (35.55%) and pigment stones (22.2%). Metaplastic changes were seen in 18% of the cases. Pyloric gland metaplasia was observed commonly in gallbladders with cholesterol stones (26%), 13% of gallbladders with pigment stones and 6.6% of those with mixed stones. Intestinal metaplasia was common in gallbladders with pigment stones (11%) followed by those with mixed stones (6.6%) and cholesterol stones (5.2%). Adenocarcinoma was observed in three cases. All the three were elderly females and had mixed stones.(6.7%). Associated intestinal metaplastic changes were observed in all the gallbladders with carcinomatous change.



**Pie Chart 1: Sex Ratio in This Study**

**Table 1: Age and Sex wise Distribution**

Age (yrs)	Pigment Stone		Mixed Stone		Cholesterol Stone		Total		
	M	F	M	F	M	F	M	F	
20-29	1	6	1	-	-	3	2	9	11
30-39	2	8	-	7	-	3	2	17	20
40-49	2	6	7	9	1	5	10	19	30
50-59	5	3	3	6	2	3	10	13	22
60-69	2	-	2	7	-	1	4	9	12
70-79	-	1	1	2	-	1	1	4	5
Total	12	24	14	31	3	16	29	71	100
	36		45		19				

**Table 2: Frequency of Histological Changes in Each Stones**

Histological Changes	Cholesterol Stone	Pigment Stone	Mixed Stone
Mucosal Hyperplasia	31.5%	19.4%	17.7%
Lymphoid Follicle	31.5%	19.4%	22.2%
Rokitansky Aschoff Sinuses	36.8%	27.7%	31.0%
Muscular Hypertrophy	47.3%	22.2%	35.5%

Pyloric Metaplasia	26.0%	13.0%	6.7%
Intestinal Metaplasia	5.2%	11.0%	6.7%
Carcinoma	-	-	6.7%

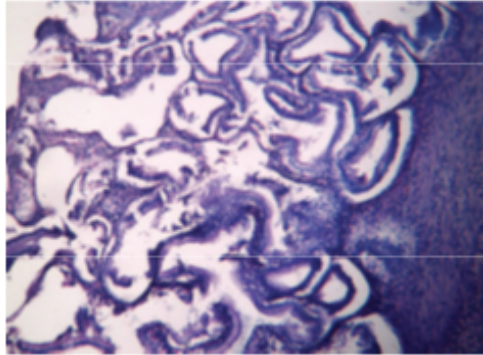


Figure 1: Photomicrograph of gallbladder mucosa showing hyperplasia. (H & E - 10X)

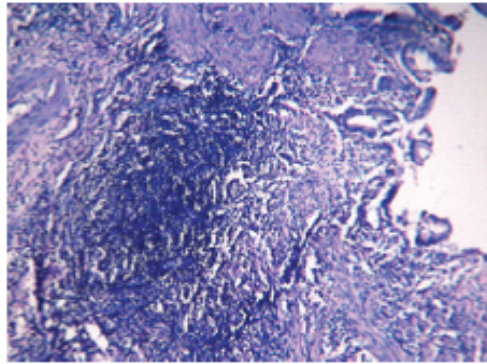


Figure 2: Photomicrograph of gallbladder wall showing lymphoid follicles. (H & E - 10X)

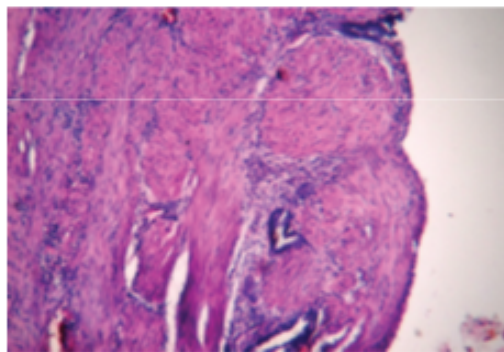


Figure 3: Photomicrograph of gallbladder wall showing muscle hypertrophy. (H & E -10X)

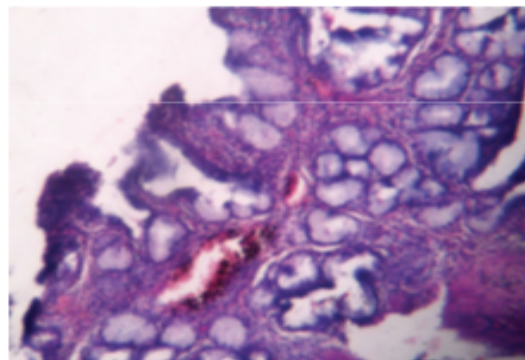


Figure 4: Photomicrograph of gallbladder mucosa showing pyloric metaplasia. (H & E-10X)

## Discussion

Gall stones are a common cause of morbidity throughout the world. The prevalence of gallstones disease in India ranges from 2 to 29%. [5,6] It is seven times more common in North India (stone belt) than in South. [7] This may be attributed to the dietary differences in the two regions. [8]

In our study, majority of the patients belonged to the 40 – 49 years age group. This correlated with other studies. [9,10] In the present study, gallstones were more common in females with a male to female ratio of 1:2.4. Such female preponderance was noted in many other studies. [10] This increased incidence may be attributed to the female sex hormones and sedentary habits. [11]

Gallstones are of three types: cholesterol, pigment and mixed stones. Factors that increase hepatic secretion of cholesterol like pregnancy, oral contraceptives and rapid weight loss enhance cholesterol stone formation. Conditions like chronic haemolytic anaemia and bacterial contamination of biliary tree increase the risk of pigment stones. In the present study. Mixed stone was the most common variety encountered. This correlated with the study by Mathur et.al. [10,20]

Gallstones produce a series of histological changes in gallbladder and some could be precursor lesions for gallbladder carcinoma. In the present study, epithelial hyperplasia with disruption was observed in 21 cases. Putz and Willens suggests cholelithiasis induces active proliferation of the epithelium in response to chronic irritation. [12] According to Albores –Saavedra et al, a small number of hyperplasia evolves into atypical hyperplasia progressing into insitu carcinoma and finally into invasive carcinoma. [13] In our study epithelial hyperplasia was more common in gallbladder with cholesterol stones (31.57 %) as in the study by Muna Zahir et.al. [14]

Prominent Rokitansky Achoff sinuses which are outpunching are of the mucosal epithelium through the wall was observed in 31 cases. As in the study by Muna Zahir et.al, it was commonly associated with cholesterol stones (36.84%). This could be due to the fact that cholesterol is a more potent stimulus leading to its formation. [14] Lymphoid follicles in the lamina propria and muscular layer were seen in 23 cases. It was found mainly in the gallbladder with cholesterol stones (31.57%) as in the study by Muna Zahir et.al. [14].

Muscular hypertrophy was found in 33 cases. It was more common in gallbladders with cholesterol stones (47.36%). But in the study by Muna Zahir et.al, it was found mainly associated with pigment stones. [14] However no specific explanation can be given for this variation. In the present study, metaplastic changes were observed in 18 % of the

cases. Chang HG in his study stated mucous hypersecretion enhance stone formation and then the stone itself would produce metaplastic changes along with inflammation and physical injury to the epithelium. [15] In our study pyloric gland metaplasia was commonly observed in gallbladders with cholesterol stones (26%). This is in correlation with the study by Mathur et.al and Chang HG. [10,15].

Intestinal metaplasia was observed in 8 cases which correlated with the study by Mathuret.al. [10]. In the present study, intestinal metaplasia was common in gallbladders with pigment stones (11%) followed by mixed stones (6.7%). Intestinal metaplasia is considered as a precancerous lesion in contrast to pyloric gland metaplasia which is considered a benign lesion. [16] In our study too, intestinal metaplasia was observed in gallbladders harbouring malignancy.

Carcinoma of gallbladder is the most common malignancy of the biliary tract. [17]. The incidence is more in women when compared to men. [18]. Cholelithiasis is one of the most important risk factor for gallbladder cancer. The relationship of gallstones to carcinoma is attributed to the chronic stimulation leading to metaplasia and carcinoma. [19] In the present study, carcinomatous changes were seen in three cases. During the period of this study only four cases of carcinoma gallbladder were reported in our centre. Out of the four cases, three were associated with gallstones indicating its significance. All the three cases were elderly females which is comparable to other studies. [10,20] The increased risk of gallbladder carcinoma in females might be due to the higher incidence of gallstones in females and to female sex hormones. [20] All the three cases in the present study had mixed stones as in the retrospective study of 313 cases by Sunder Goyal et.al. [20]

## Conclusion

Gallstones produce diverse histopathological changes in the gallbladder including hyperplasia, metaplasia and carcinoma. In the present study most of the changes were associated with cholesterol stones. Cholesterol stones which are usually larger in size may lead to more irritation. Moreover the toxic effect of lithogenic bile produces chemical injury to the mucosa. But carcinomatous changes were observed in mixed stones, the pathogenesis of this needs further studies. Moreover various preventable risk factors are attributed to gallstones. Proper counselling regarding dietary modification, weight reduction and obesity management goes a long way in preventing gallstone formation and its complications.

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