International Journal of Science and Research (IJSR)
ISSN: 2319-7064
Impact Factor (2018): 7.426

Impact of Morphology of Gallstones on Histopathological Changes in Gallbladder Mucosa: A Study

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Abstract: ***Coexistence of gallstones with cholecystitis, hyperplasia, intestinal metaplasia, and carcinoma is well-known in literature. Gallstones may be cholesterol, pigment or mixed type. To study the impact of morphology of gallstones on histopathological changes in gallbladder mucosa was planned. The study was conducted on 50 patients of cholelithiasis, who underwent cholecystectomy. Physical characteristics of gallstones were examined and the gallbladder specimen were sent for histopathological examination. Mixed type of stones were most commonly observed in 52% of patients and 96.1% of patients were having multiple stones. Mural inflammation was the most common histopathological finding significantly associated with mixed type of stones. Metaplasia, dysplasia and carcinoma were found in 6%, 2% and 2% of patients respectively. Present study highlights the importance of careful gross and histopathologic evaluation of gallbladders as cholelithiasis may be associated with hyperplasia, metaplasia or dysplasia; even leading to gallbladder carcinoma in certain cases.***

Keywords: Cholelithiasis, gallstones, hyperplasia, metaplsia

1. Introduction

Gallstone (GS) disease is a very common health problem that affects millions throughout the world [1]. Coexistence of gallstones with cholecystitis, hyperplasia, intestinal metaplasia and carcinoma is well-known in literature. Incidental gallbladder (GB) carcinoma is revealed in 0.3-2% of all cholecystectomies done for benign conditions [2]. Gallstone occurs in various shapes (round, angular, oval and so on), sizes (from few millimeters to 6 cm), color (creamy white, yellow, black and brown) and can be cholesterol, pigment or mixed type [3]. The most common complications of the presence of gallstones are cholecystitis (inflammation of the gallbladder) whether acute or chronic. It may be associated with the appearance of hyperplasia, metaplasia and even carcinoma of the gallbladder. It has been suggested that the metaplastic epithelium is more susceptible to malignant transformation than the normal mucosa and the intestinal metaplasia-dysplasia - carcinoma sequence exists in the gallbladder [4]. Hence the present study was done to study histopathological changes in gallbladder mucosa in patients of cholelithiasis and their correlation with type of gallstones.

2. Methods

The study was conducted on 50 patients of cholelithiasis, aged between 20 to 75 years, who underwent cholecystectomy (open or laproscopic) for gallstones in our institute. After cholecystectomy gallbladder specimen was cut open. Physical characteristics of gallstones were examined regarding number, colour, size, shape and type of stone. Resected gallbladder specimen was sent for histopathological examination. The data was collected, tabulated and analysed using Chi Square test. The p- value <0.05 was considered as significant.

3. Result

In our study, the age of patients varied between 20 to 75 years with mean age of 40.4 years. Forty five patients (90%) were females with male to female ratio of 1:9. Mixed type of stones were most commonly observed in 52% of patients and 96.1% (25/26) of such patients were having multiple stones (p value <0.05). Cholesterol stones were seen in 26% of patients which were predominantly single in 84.6% (11/13) of patients (p value <0.05). Pigment stones were present in 22% which were mostly multiple in 81.8% (9/11) of patients (p value <0.05). Overall, 72% of patients were having multiple stones. (Table I)

Table I: Morphological types and number of stones

Type of Stone	*Single Stone*	*Multiple Stones*	*Total*
Cholesterol	11	2	13 (26%)
Pigment	2	9	11 (22%)
Mixed	1	25	26 (52%)
Total	14 (28%)	36 (72%)	50 (100%)

It was found that mural inflammation (72%) was most common histopathological finding followed by, muscular hypertrophy (70%), fibrosis (56%) rokitansky-aschoff sinuses (24%) and papillary mucosal hyperplasia seen in

24% cases. Increase in mucus secretory cells was seen in 18% and acute cholecystitis was seen in 16% cases. Xanthogranulomatous change was seen in 4% and metaplasia in 6% cases. Calcification, dysplasia and carcinoma was found in one case (2%) each. Gallbladder polyp was also seen in one patient (2%). While considering the type of stone, it was observed that mural inflammation was more commonly associated with mixed stones and was statistically significant (p value <0.05). Fibrosis, rokitansky-aschoff sinuses, muscular hypertrophy were also associated with mixed type of stones. Increases in mucus secretory cells, papillary mucosal hyperplasia were associated more commonly with pigment stones. Metaplasia was associated with cholesterol stones in 2 cases and in 1 case with mixed type stones. Xanthogranulomatous change, calcification, dysplasia and carcinoma were found in patients having mixed type of stone (Table – II).

Table 2: Histopathological changes and their relationship with type of stones

Histopathological Changes	*Cholesterol Stone*	*Pigment Stone*	*Mixed Stone*	*Total*
Mural Inflammation	8	7	20	35
Fibrosis	9	7	12	28
Rokitansky-Aschoff sinuses	2	3	7	12
Muscular hypertrophy	8	9	18	35
Increase in Mucus Secretory Cells	1	5	3	9
Papillary Mucosal Hyperplasia	4	5	3	12
Calcification	0	0	1	1
Xanthogranulomatous change	0	1	1	2
Metaplasia	2	0	1	3
Dysplasia	0	0	1	1
Carcinoma	0	0	1	1

While correlating the mucosal changes with number of stone s, it was found that the association of multiple stones with mural inflammation, fibrosis and muscular hypertrophy was statistically significant (p value <0.05). Other changes like Rokitansky-aschoff sinuses, increase in mucus secretory cells, papillary mucosal hyperplasia, xanthogranulomatous change, dysplasia and carcinoma were also more commonly associated with multiple stones. Metaplasia was observed more in patients having single stone. (Table - III).

Table 3: Histopathological changes in relation to number of stones

Histopathological Changes	*Single Stone*	*Multiple Stones*	*Total*
Mural Inflammation	8	27	35
Fibrosis	8	20	28
Rokitansky_Aschoff sinuses	0	12	12
Muscular hypertrophy	9	26	35
Increase in Mucus Secretory Cells	2	7	9
Papillary Mucosal Hyperplasia	3	9	12
Calcification	0	1	1
Xanthogranulomatous change	0	2	2
Metaplasia	2	1	3
Dysplasia	0	1	1
Carcinoma	0	1	1

4. Discussion

Cholelithiasis is the most prevalent disorder of the biliary tract. It produces a series of epithelial pathological changes, which might be precursor lesions of gallbladder cancer, including hyperplasia and metaplasia [5]. The pathogenesis of all these changes were mainly due to the chronic irritation and chemical injury of the gallbladder mucosa and such changes in the wall of the gallbladder may start before the formation of the stones. In the present work we evaluated the histological changes in the gallbladder mucosa in gallstone patients, and correlated those changes with the type of the stone.

In the present study, mixed stones were the most common type, in 52% of patients. Overall, 72% were having multiple stones. Similar observation was documented by Mathur et al in their study [6]. In the present study, mixed type of stones were predominantly multiple (96.1%), cholesterol type of stones were predominantly single (84.6%) and Pigment stones were predominantly (81.8%) multiple in numbers. These results were also seen in study by Goyal et al [7].

Of all the histopathological changes, mural inflammation was significantly associated with mixed type of stones as well as multiple stones. The association of multiple stones with fibrosis and muscular hypertrophy was also statistically significant (p value <0.05). In our study, metaplasia, dysplasia and carcinoma were found in 6%, 2% and 2% of patients respectively. Other studies by Mathur et al, Goyal et al and Dattal et al have also reported similar results [6]-[8].

Present study highlights the importance of careful gross and histopathologic evaluation of gallbladders as cholelithiasis, even leading to gallbladder carcinoma in certain cases. Routine cholecystectomy performed for a common condition like gallstone disease can result in detection of diverse and wide spectrum of histopathological lesions ranging from chronic cholecystitis to carcinoma.

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