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A cross-sectional Study of Pathological Findings in Cholecystectomy Specimens

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Abstract
Introduction: *Gall bladder diseases are one of the common diseases across the globe including India. These comprise the various congenital malformations, inflammatory lesions, lithiasis and malignant conditions. Inflammatory gall bladder lesions are a frequent cause of morbidity and are almost always associated with gall stones. Gall bladder carcinoma represents 20% of all gastrointestinal cancers and has a very dismal outlook. The present study was conducted to study the incidence, age and sex distribution of different gall bladder lesions including malignancy. It also studied the gross and histopathological findings of these conditions with particular reference to malignancy.*
Material and Methods: *A cross-sectional study was carried out in the Department of Pathology, SMS Medical College, Jaipur from June 2017 to December 2017. Approval from institutional ethics committee was taken and all the eligible specimens received to the Department of Pathology during study period were included in the study. Socio-demographic informations like, age, sex, religion and socio-economic status were taken from history sheets received with histopathological specimens.*
Results: *In the present study, chronic cholecystitis with lithiasis was the most common gall bladder lesion (73.33%). Benign lesions comprised 96.33% among all gall bladder lesions while malignant lesions were only 3.67%. Majority of gall bladder lesions were observed in age group 21-50 years with female predominance. All lesions were associated with gall stones except adenoma. Well differentiated adenocarcinoma was the most common carcinomatous lesion.*
Conclusion: *The gall bladder lesions are very common among females which are almost always associated with gall stones. So, in the presence of gall stones cholecystectomy should be indicated in women over 50 years of age to prevent gall bladder carcinoma.*
Keywords: *Cholecystitis, lithiasis, metaplasia, malformations, malignancy.*

Introduction

Gall bladder diseases are very important among gastrointestinal diseases due to their frequent occurrence and pathologic potential. These may be in the form of congenital malformations, inflammatory lesions, lithiasis, metaplastic,

benign and malignant conditions.[1] Inflammatory gall bladder diseases may present as an acute episode (acute cholecystitis) or with vague chronic symptoms (chronic cholecystitis). Many cases of acute cholecystitis and almost all cases of chroniccholecystitis are associated with gall stones. Depending on their composition gall stones are of two types cholesterol stones and pigment stones. [2]

A variety of metaplastic changes have been described in the gall bladder mucosa in association with inflammatory diseases. The most common type of metaplasia is of the antral (pyloric) type. [3] Adenomas are benign epithelial tumors of the gall bladder and are more common in women. Carcinoma of gall bladder has been claimed to represent almost 20% of all gastrointestinal cancers. These are more common in women with a peak incidence in the 70-75 year age group and have a very dismal outlook. [1-3] Incidental carcinoma may be diagnosed only after the gall bladder removed for presumed benign disease and are subjected to histopathological examination. Therefore microscopic examination of every excised gall bladder is mandatory for the detection of intraepithelial malignancy. Therefore the present study was planned to study the various pathological patterns of gall bladder diseases noted at a leading tertiary care centre of Rajasthan including age & sex distribution, gross & histopathological features of cholecystectomy specimens, occurrence of malignancy with underlying gall bladder diseases.

Materials and Methods

A laboratory based cross sectional observational study was carried out in Department of Pathology, SMS Medical College, Jaipur (Rajasthan) from June 2017 to December 2017. After taking approval from institutional ethics committee, total 300 consecutive cholecystectomy specimens received during study period were included. Clinical data like age, sex, clinical history and gross features of surgical pathology specimens of gall bladder were noted in a predesigned and semi-structured proforma. Poorly preserved samples were excluded from the study. The blocks of eligible specimens were made and 4 micron thick sections were studied after staining with haematoxylin and eosin. Wherever necessary, special histochemical stains (Mucicarmine, PAS, D-PAS, Masson's Trichrome, Van Geisson stain) were used to supplement the diagnosis. Data were entered in Microsoft Excel 2010 and analyzed using chi square test of significance. P-value < 0.05 was considered significant.

Results

In the present study, total 300 cholecystectomy specimens received in the Department of Pathology were examined. Chronic cholecystitis with lithiasis was the most common (73.33%) gall bladder lesion followed chronic cholecystitis without lithiasis (6.67%), Adenomyomatosis or diverticular disease (5.67%), carcinomas (3.67%) and acute or chronic cholecystitis with lithiasis (3.33%). Benign lesions comprised 96.33% among all gall bladder lesions (Table-1). Age range of gall bladder lesions was quite large ranging from 17 days to 80 years. Maximum lesions 89 (29.67%) were observed in 31-40 years age group followed by 41-50 years 72(24%) and 21-30 years 61 (20.33%) while lesions were infrequent below 20 years and after 70 years of age (Table-2). It was observed in present study that all gall bladder diseases had female predominance (Figure-1).

Gall stones were found in all the gall bladder lesions except adenoma. Gall stones were present in 100% cases of acute cholecystitis, acute or chronic cholecystitis, adenomyomatosis and mucocele followed by 91.67% in chronic cholecystitis, 83.33% in cholesterolosis and xanthogranulomatous cholecystitis and 81.8% in carcinomas (Table-3).

Out of 300 cases metaplasia was found in 62 cases (20.67%). 61 cases (98.39%) were pyloric gland metaplasia and one case (1.61%) was intestinal metaplasia while mucosal hyperplasia was found in total 44 cases (14.67%). Out of these 44 cases,

2 (4.55%) were of adenomatous hyperplasia and 42 (95.45%) were of villous hyperplasia. Adenomyomatosis was seen in 17 cases (5.67%), 10 cases (58.82%) were localized and 7 cases (41.18%) were in diffuse form.

Out of 11 cases of gall bladder carcinoma, most common histologic type was well differentiated adenocarcinoma (54.55%) followed by moderately differentiated adenocarcinoma (27.27%). One case of each mucinous adenocarcinoma and adenosquamous carcinoma were found (Table-4). Maximum proportion of carcinoma was found in the age group 61-70 years and in female sex (Table-5).

Table-1: Occurrence of different types of gall bladder lesions

S. No.	Type of lesions	No. of cases n (%)
1.	Acute calculouscholecystitis	04 (1.33)
2.	Chronic cholecystitis with lithiasis	220 (73.33)
3.	Chronic cholecystitis without lithiasis	20 (6.67)
4.	Acute on chronic cholecystitis with lithiasis	10 (3.33)
5.	Cholesterolosis	06 (2.00)
6.	Xanthogranulomatouscholecystitis	06 (2.00)
7.	Granulomatous cholcystitis	02 (0.67)
8.	Adenomyomatosis / diverticular disease	17 (5.67)
9.	Mucocele	03 (1.00)
10.	Adenoma	01 (0.33)
11.	Carcinoma	11 (3.67)
	Total	**300 (100)**

Table-2: Age distribution of different types of gall bladder lesions

S. No.	Type of lesion	Age in years						
		11-20	21-30	31-40	41-50	51-60	61-70	> 70
1.	Acute calculouscholecystitis	0	0	1	1	2	0	0
2.	Chronic cholecystitis with lithiasis	6	47	64	51	31	17	4
3.	Chronic cholecystitis without lithiasis	2	1	8	7	1	1	0
4.	Acute on chronic cholecystitis with lithiasis	0	4	3	2	1	0	0
5.	Cholesterolosis	0	0	1	3	2	0	0
6.	Xanthogranulomatous cholecystitis	0	1	1	3	1	0	0
7.	Granulomatous cholcystitis	0	0	2	0	0	0	0
8.	Adenomyomatosis / diverticular disease	0	6	7	4	0	0	0
9.	Mucocele	0	1	2	0	0	0	0
10.	Adenoma	0	1	0	0	0	0	0
11.	Carcinoma	0	0	0	1	3	4	3
	Total	**8**	**61**	**89**	**72**	**41**	**22**	**7**

Table-3: Presence of lithiasis with various gall bladder lesions

S. No.	Type of lesion	Total no. of cases	Presence of lithiasis	
			n	Percentage
1.	Acute cholecystitis	4	4	100
2.	Acute on chronic cholecystitis	10	10	100
3.	Chronic cholecystitis	240	220	91.67
4.	Cholesterolosis	6	5	83.33
5.	Xanthogranulomatouscholecystitis	6	5	83.33
6.	Granulomatouscholcystitis	2	1	50
7.	Adenomyomatosis	17	17	100
8.	Mucocele	3	3	100
9	Adenoma	1	0	0
10.	Carcinomas	11	9	81.81
	Total	**300**	**274**	**91.33**

Table-4: Histological types of carcinoma of gall bladder (n=11)

S. No.	Type	No. of cases	Percentage
1.	Well differentiated adenocarcinoma	6	54.55
2.	Moderately differentiated adenocarcinoma	3	27.27
3.	Mucinous adenocarcinoma	1	9.09
4.	Adenosquamous carcinoma	1	9.09
	Total	**11**	**100**

Table-5: Age and sex distribution of gall bladder carcinoma (n=11)

S. No.	Type	Age in years				Sex	
		41-50	51-60	61-70	> 70	Male	Female
1.	Well differentiated adenocarcinoma	1	2	1	2	1	5
2.	Moderately differentiated adenocarcinoma	0	1	2	0	1	2
3.	Mucinous adenocarcinoma	0	0	1	0	0	1
4.	Adenosquamous	0	0	0	1	0	1

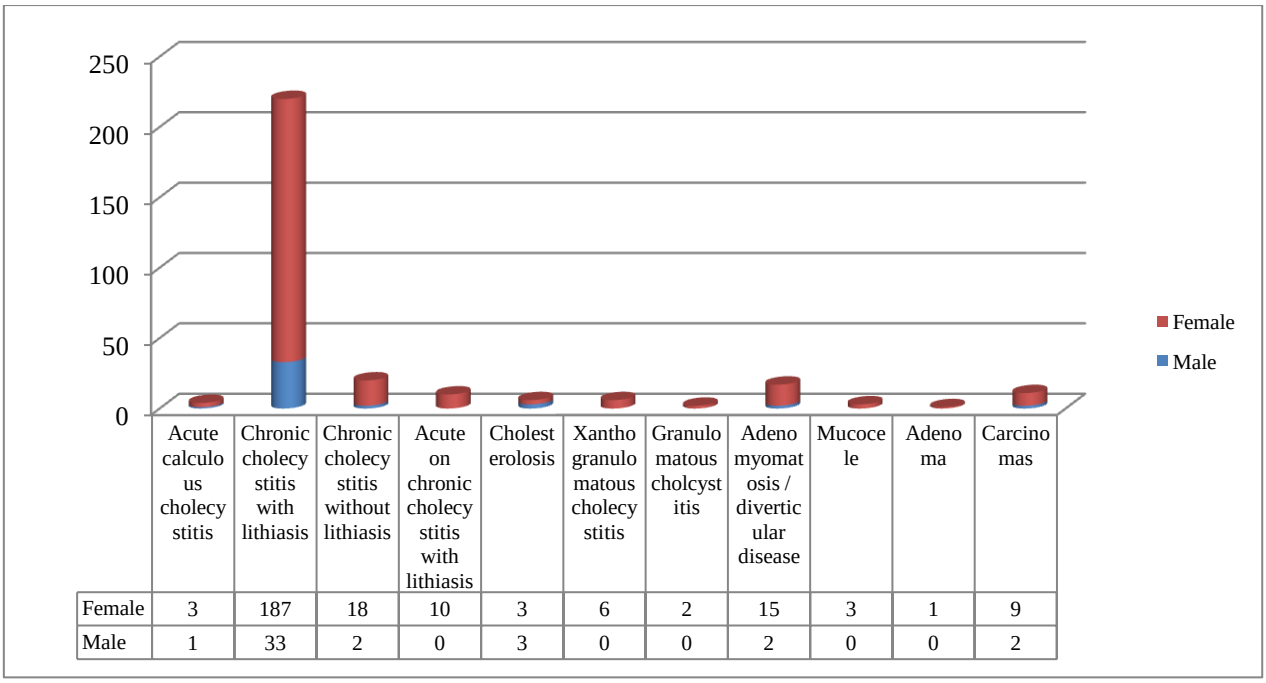

Figure-1: Sex distribution of different types of gall bladder lesions

Discussion

The present study deals with the clinico-pathological aspects of gall bladder diseases at a tertiary care set up.The age range of the patients with gall bladder diseases was 17-80 years which was consistent with previous study by Gupta (2000) [4] where the age range varied from 8-91 years. The maximum number of cases were in the fourth decade (89 cases out of 300) amounting to 29.67%. Similar findings were observed by Adams (1947)[5], Colcock and Manus (1955)[6], Colcock (1964)[7].No case was found in the first decade and 8 cases were found in the second decade in the present study.The present study reveals that females suffer more than males with male to female ratio of 1:5.98 which was similar to ratio of 1:5.2 reported by Kala (1977)[8]. Zaharaniand Mansoor (2001)[9] reported the male to female ratio 1:4.6 in his study. Male to female ratio ranges from 1:1.5 to 1:3 in previous studies by Colcock (1964)[7], Friedman (1966), Essenhigh (1966), Daniel (1978).

Out of the various gall bladder diseases, benign lesions comprised 96.33% and carcinomas 3.67%. 4 cases of acute cholecystitis were found which all were associated with gall stones. This agrees with Matolo et al (1981)[10] who stated that more than 95% cases of acute cholecystitis were associated

with gall stones. Chronic cholecystitis comprised 80% of total cases. Zaharani and Mansoor (2001)[9] studied 740 cholecystectomy specimens and noticed that benign lesions comprised 99% (mostly chronic cholecystitis 97%). 220 cases (out of 240) of chronic cholecystitis were associated with cholelithiasis. Among these 85% (187 out of 220 cases) were females and 15% (33 out of 220 cases) were males. Present study showed2% cases of cholesterolosis which greatly varies from previous studies by Salemenkivi (1964) and Jacyna et al (1987), who reported a prevalence of 12% and 9-26% in autopsy and surgical studies respectively. Xanthogranulomatous cholecystitis comprised 2% of total cases which was in concordance with Fligiel and Lewin (0.5-1.8%), Robert and Parsons (1.8%), Takahashi et al[11] (1.2%) and Karabulnt et al[12](1.3%).

Granulomatous cholecystitis was found in 2 (0.67%) cases. It can occur in known cases of Crohn's disease of the small intestines (McClure John et al, 1984)[13]. Adenomyomatosis or diverticular disease was observed in 17 cases (5.67%) which was close to the findings of Jutras (1960) who reported 8.7% of adenomyomatosis cases. In the present study, one case (0.3%) of adenoma was found which was solitary, pedunculated, 4 mm in diameter and situated in the fundus. The finding agreed with that reported by Albores-Saavedra et al (1986) of 0.3-0.5% [15].

Total 62 cases (20.67%) of metaplasia were found,out of which 58 (93.55%) were associated with chronic cholecystitis with lithiasis and 4 cases (6.45%) were associated with chronic cholecystitis without lithiasis. Mucosal hyperplasia was seen in 44 cases (14.67%), out of which 34 cases (77.27%) were associated with chronic cholecystitis with lithiasis, 6 cases (13.64%) with cholesterolosis and 4 cases (9.09%) with adenomyomatosis.

In the present study, the incidence of carcinoma of gall bladder was found to be 3.67% which was similar to that reported by Vitetta et al (2000)[16] as 3.2%. Martenz-Guzman (1998)[17] reported an incidence of 2.6% from 1367 cases[20]. The present study showed an increased incidence of carcinoma in females than males (i.e.81.82% females against 18.18% males) giving a female to male ratio of 4.5:1. Preponderance of carcinoma of gall bladder in women correlates with their higher incidence of gall stones. This was similar to Brandt-Rauf et al (1982) who in a review of 43 cases of gall bladder carcinoma, stated that overall 79% of cases were in females, Maria Perpetuo et al (1978) who stated that 84% of cases were females while 16% were males. Vitetta et al (2000)[16] also had similar findings who observed gall bladder carcinoma in 14 patients consisting of 11 women (78%) and 3 men (21.4%). Presence of stones were associated in 9 out of 11 cases i.e. 81.82% which was similar to Marcial Rojas (1961) who reported the association of stones in 84%, Martenz-Guzman (1998)[17] reported in 80% and Roa et al (1999)[18] who reported the association of stones in 85%.

Maximum cases of carcinomas were found in 7th decade (36.36%). Youngest case was 45 year old female and oldest was 80 year old female. This agreed with Nakayama (1991) who stated maximum incidence in seventh decade and also with Cunningham et al (2002)[19] who stated that 96% patients in their study were age 50 or greater at diagnosis.

Out of 11 cases, 7 cases were diagnosed incidentally on microscopic examination. The distribution of histological types was shown in table-4. No case of squamous cell carcinoma or poorly differentiated carcinoma was found in the present study. The distribution of various histological types agreed with different authors, Vadheim et al (1944) who studied 75 cases of surgical cases of carcinoma of gall bladder for pathologic examination and found the various histological types as 85.3% adenocarcinomas, 2.7% squamous cell carcinomas and 12% adenosquamous carcinomas. Henson et al (1992)[20] did a study on 3038 patients of gall bladder diseases and found the distribution of histological types as 75.8% adenocarcinomas, 3.6% adenosquamous, 1.7% squamous cell carcinoma,

5.8% papillary adenocarcinoma, 4.8% mucinous carcinoma, 0.5% small cell carcinoma and 7.6% carcinoma not otherwise specified (NOS).

Conclusion

Although the proportion of gall bladder carcinoma in the present study was found to be only 3.67% but its association was observed with gall stones in 81.82% cases. Gall bladder carcinoma being a highly fatal condition needs timely diagnosis and treatment. At present the best hope for reducing the mortality from this disease lies in earlier cholecystectomy in benign gall bladder diseases. In the presence of gall stones cholecystectomy should be indicated in women over 50 years of age.

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