

Observational Study of Gall Bladder Cancer in Patients of Cholelithiasis Study from a Tertiary Care Centre: Rims, Ranchi

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Abstract

Background: Gallstone disease is the most common biliary pathology and is a major health problem worldwide. Gallbladder cancer is the most common malignancy of the biliary tract but extremely variable by geographical region and racial ethnic group.

Material and Methods: A total of 120 resected cholecystectomy specimens with gallstone received during the period of six months were included. Clinical details and other relevant information were collected from the records. Statistical correlation was calculated using chi-square test and p value was calculated. value of $p < 0.05$ was considered statistically significant.

Results: of total 120 cholecystectomy specimens it included 91 females and 29 males. Most of the cases were of age group 41-50 years . Majority of malignant cases occurred in age group 41-50 years and 60-70 years. Most common diagnosis was calculous cholecystitis and more common in females. Multigravida females are more prone to develop gallbladder diseases. The commonest presenting complaints were right hypochondrial pain in 108(90%) cases followed by epigastric pain in 6(5%), nausea in 3(2.5%) and vomiting in 3(2.5%) cases.

Conclusion: Gallbladder stones are more common in females with multiparity and mixed diet being important risk factors. It is recommended that each and every specimen of gallbladder be subjected to histopathological examination.

Key Word: Gallbladder, stones, carcinoma, Histopathology.

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I. Introduction

Gall stones are the most common biliary pathology and is a major health problem worldwide. Its occurrence has been found to be atleast 6% in the adult population of North India.

The rate of gallstones are more common in females. Gallbladder diseases are more common in north and northeastern states of Bihar, Uttar Pradesh, Orissa, West Bengal and Assam.¹ cholelithiasis has become a major cause of abdominal pain and discomfort in developing world. The types of gallstones include-cholesterol stones, pigment stones and mixed stones.

Carcinoma of the Gall bladder is the most common malignancy of the biliary tract but extremely variable by geographical region and racial ethnic groups.

In India, gallbladder cancer is rare(1%). Majority of gallbladder cancer are from northern(the gangetic belt) and central parts of the country.² screening of premalignant lesions of gall bladder is essential to identify suspicious lesions and detect the disease early. An appropriate early measure is important for curative treatment and long term survival of the patients.

II. Aims And Objectives

The study was undertaken with aim of establishing the relationship of carcinoma of gall bladder to age, sex and gall bladder stone(cholelithiasis).

III. Materials And Methods

The study was conducted in DEPARTMENT OF GENERAL SURGERY, RAJENDRA INSTITUTE OF MEDICAL SCIENCES,RANCHI from October 2019 to March 2020. All data were collected from patients admitted in RIMS for treatment of cholelithiasis from OPD and EMERGENCY. The diagnosis was made on

basis of detailed clinical history, thorough clinical examination, radiological investigation followed by details of operative findings and finally confirmed by histological examination.

A total of 120 resected specimens of gall bladder(cholecystectomy done for gall stones) received during the above mentioned period. specimens which were not sent in proper fixative and where morphological details were not discernible were excluded out. Atleast three representative sections were taken, one each from fundus, body and neck. Additional sections were taken whenever an abnormal area was seen. One section was taken from attached lymph node , if present. Microscopic examination was performed on paraffin embedded blocks. Hematoxylin and Eosin stained tissue section were examined and following features were assessed-inflammation, cholesterolosis,granulomas,metaplasia,dysplasia,calcification,benign and malignant neoplasm.

Statistical Analysis

Statistical correlation was calculated using chi-square test and p value was calculated. value of p<0.05 was considered statistically significant.

Results

In the present series a total of 120 cholecystectomy specimens were subjected to histopathologic evaluation. This included 29 males and 91 females. Most of the cases were of age group 41-50 years followed by age group 31-40 years. Most common diagnosis was calculous cholecystitis and was relatively more common in females.

Peak incidence of gallstone disease in the present study was 41-50 years. Majority of patients were female 91(75.83) whereas males were only 29(24.16%).

TABLE 1:

GENDER	NO. OF PATIENTS	%
MALE	29	24.16
FEMALE	91	75.83
TOTAL	120	

Multigravida females were 88(96.38%) in number and are more prone to develop gallbladder stone than nullipara which were only 3(3.29%) in number. Stone characteristics and its association with various benign and malignancy cases are shown in table 2. Most common type of stone was mixed presnt in 96(80%) cases. 4 malignant cases had multiple stones whereas all cases of granulomatous cholecystitis and empyema had multiple stones. A statistically significant relation was found between presence of stones and carcinoma(p=0.01).

TABLE 2:

TYPE OF LESIONS	PIGMENT STONES	%	CHOLESTEROL STONES	%	MIXED STONES	%
NON NEOPLASTIC	10	71.42%	06	60%	83	86.45%
PREMALIGNANT	03	21.42%	01	10%	04	4.16%
MALIGNANT	01	7.14%	03	30%	09	9.37%
TOTAL	14		10		96	

The most common presenting complaint among patients suffering from gallstone were right hypochondrium pain in 108(90%) cases followed by epigastric pain in 6(5%), nausea in 3(2.5%) and vomiting in 3(2.5%) cases

TABLE 3:

SYMPTOMS	NO. OF CASES	%
RHC PAIN	108	90%
EPIGASTRIC PAIN	06	5%
NAUSEA	03	2.5%
VOMITING	03	2.5%

Maximum number of cases of gallbladder lesions were associated with multiple gallstones in 84(70%) cases followed by single calculous in 26(21.66%) and double calculi in 10(8.33%) cases. Mixed stones were more commonly found in 96(80%) patients followed by pigment stones in 14(11.66%) and then cholesterol stones in 10(8.33%) cases.

Among total cases , 8(6.66%) turned out to be pre malignant and 13(10.83%) cases were malignant. it was observed that among malignant category, females in the age group 41-50 were mostly affected followed by age group 51-60 years. And in males both 41-50 and 61-70 years age groups were affected.

TABLE 4: Age and sex wise distribution of Gallstone disease

TOTAL CASE	AGE GROUP IN YEARS	FEMALE	MALE	FEMALE:MALE RATIO
	0-20	01	01	
	21-30	23	01	
	31-40	28	06	
120	41-50	30	14	
	51-60	05	03	
	61-70	03	03	
	>70	01	01	
TOTAL		91	29	3.1:1

TABLE 5: Distribution of carcinoma gallbladder among age and sex

TOTAL CASE	AGE GROUP IN YEARS	NO.OF CASES	MALE	FEMALE	MALE:FEMALE RATIO
	21-30	NIL			
13	31-40	02		02	
	41-50	06	02	04	
	51-60	03		03	
	61-70	02	01	01	
TOTAL		13	03	10	1:3.33

When the lesions were divided as per dietary intake majority of patients 86(71.66%) were observed to consume mixed diet in all the cases. In malignant category mixed diet consumption was the maximum with 11(84.61%) patients.

TABLE 6: Distribution of cases of gallstone according to diet

DIET	NON NEOPLASTIC WITH PREMALIGNANT LESIONS	MALIGNANT
VEG	32	02
MIXED	75	11
TOTAL	107	13

IV. Discussion

Male to female ratio observed was 1:3.1. The result of the present study shows that female are more prone to develop gallstone diseases thus holding true the saying that “ a fatty, fertile, flatulent, female of forty is the classical sufferer from symptomatic gallstones.

In this study, the most common involved age group for cholelithiasis was 41-50 years followed by age group of 31-40 years while Pradhan et al³ reported maximum 32.5% cases belonging to age group 30-39 years with M:F of 1:3.2. similar observations were reported by Idris et al⁴ and Aslam et al³, who observed majority of cases from age group 31-50 years.

The most common physical sign found in the present study was right hypochondrial tenderness. In this study, maximum percentage of cases had mixed type of gallstones followed in decreasing order by pigment stones and then by cholesterol stones. The findings are similar to the findings in the study done by Pradhan et al³. In contrast Idris et al⁴ reported in their study in sudan, maximum 51.1% cases had pigment stones.

Khanna et al⁶ conducted a histopathological study of 140 consecutive gallbladder in which, epithelial hyperplasia was observed in 83(69%), antral metaplasia in 53(16.5%), intestinal metaplasia in 22(15.5%), dysplasia in 12(8.5%) and carcinoma in situ in 1(0.7%) specimen. Cholelithiasis and even silent gallstones, which were asymptomatic, produced a series of epithelial pathological changes in the gallbladder mucosa, which could be the precursor lesion of carcinoma gallbladder. These changes include metaplasia and dysplasia¹⁷. The incidence of gallbladder cancer is approximately 7 times more common in the presence of cholelithiasis and chronic cholecystitis than in the without gallstones. In addition, the risk of developing gallbladder cancer is higher in patients with symptomatic gallstones than in patients with asymptomatic gallstones as reported by Ahrendt and Pitt^{7,8}.

Non vegetarians were found to have cholelithiasis more than vegetarians. Pradhan et al³ reported non vegetarian and vegetarian ratio of 9:1. In malignant category mixed diet consumption was maximum with 11(84.6%) patients affected. Out of total 96 cases of mixed gallstones, maximum 83(86.45%) were present in non neoplastic category, 9(9.37%) were present in malignant and 4(4.16%) were present in premalignant category.

Prophylactic cholecystectomy has been recommended in many high risk populations such as Chile. Mohandas and Patil^{9,10} suggest that preventive cholecystectomy be offered to all young healthy women in northern india when they are diagnosed with asymptomatic gallstones, as incidence and mortality rates of gallbladder cancer in northern Indian women is one of the highest in the world. Khanna et al⁶ also supports the

recommendation the cholecystectomy should be offered to all asymptomatic gallstone patients, especially if they are less than 60 years of age and are living in high incidence area.

Gallbladder disease constitutes a significant health problem in developed societies, affecting 10% to 15% of the adult population¹¹. Gallstones are one of the major causes of morbidity and mortality all over the world affecting 10% of the adult population¹². Risk factors for gallstone disease are non-vegetarian (93.9%), multiparous (90.8%), obesity, and sedentary life style¹².

The most common malignancy of the biliary tract reported is carcinoma of the gallbladder, which is the third most common cancer in the gastrointestinal tract¹³. The highest incidence of carcinoma of the gallbladder in India has been seen along the Ganges delta¹⁴. A significantly higher incidence of carcinoma of the gallbladder has been observed in patients with gallstones for longer duration which progresses from various epithelial lesions¹⁵. Prolonged irritation by gallstones or chronic inflammation causes metaplastic changes in the gallbladder mucosa which leads to development of carcinoma¹⁶.

In the present study, the commonest presenting complaint among patients suffering from cholelithiasis was right hypochondrial pain in 108 (90%) cases. This observation was consistent with the findings of Agarwal et al¹⁰. Mazlum M et al¹⁷ studied specimens of gallbladder in which the rate of cholelithiasis was 89.9%. Vrbcic SM et al¹⁸ studied gallbladder specimens and found 80% were calculous lesions.

In the present study, out of a total of 120 cases, 84 (70%) were having multiple stones. This was consistent with the findings of Mathur SK et al¹⁹ who studied gallbladder specimens and found multiple stones in 170 (51.6%) cases. The observation made by Singh AK et al²⁰ was similar to that of our study.

V. Conclusion

Gallbladder stones are more common in females with a mixed diet and multiparity being important risk factors. The maximum number of gallstones are mixed, followed by pigment and then cholesterol stones. The most common age group affected with gallstones is 41-50 years, followed by 31-50 years, with a majority of cases in females. The age group 41-50 years followed by the age group 51-60 years were having the maximum cases of carcinoma of the gallbladder. The maximum number of cases with multiple gallstones are found in chronic cholecystitis with cholelithiasis, chronic cholecystitis with cholelithiasis and dysplasia, well-differentiated adenocarcinoma with cholelithiasis and intestinal metaplasia. Gallstones mainly injure the mucosal columnar epithelium and thus cause changes like metaplasia, dysplasia and neoplasia.

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