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A Cross-Sectional Study on Correlation between Gallstone Morphological Characteristics and Mucosal Changes in Gall Bladder.

[1]Thiyam Santosh Singh, [2]Ranjita Achom, [3]Y.Sanatomba, [4]L.Sushila
[1]PGT, [2,3] Associate Professor, [4]Professor & HOD
[1,2,3] Department of Surgery, [4]Department of Pathology
Jawaharlal Nehru Institute of Medical Sciences (JNIMS) Imphal.
Corresponding Author: Ranjita Achom

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ABSTRACT: Cholelithiasis is defined as the formation of stone inside the Gallbladder. It has been described as a disease of civilization. Gallbladder is an accessory organ of the digestive tract. It lies on the underside of the liver in the main liver scissura at the right and left lobes of the liver. The function of gallbladder is not only to store bile, but also to concentrate it during the inter-digestive phase by mean of salt dependent water re-absorption.Cholelithiasis is the most prevalent disorder of the biliary tract Bile stasis secondary to dyskinesia is the prime factor for gallstone formation. The most common complication of the presence of gallstone is cholecystitis whether acute or chronic. It may be associated with appearance of hyperplasia, metaplasia and even carcinoma of the gallbladder.The study plans to evaluate various gallstone morphological characteristics and to assess the mucosal changes in gallbladder in relation to gallstone morphological characteristics.The study was conducted on 80 patients of aged 18 and above, whom undergoing open cholecystectomies for cholelithiasis in JNIMS, Imphal during October 2020 to September 2021. Patients undergoing Laparoscopic cholecystectomy, patients diagnosed as cholelithiasis with preoperative confirmed case of gallbladder carcinoma were excluded. Gallstones were assessed for various parameter i.e. number, weight, shape, size and morphological type. Gallbladder mucosa was subjected to histopathological examination. All the observations were recorded on excel sheet and were evaluated with SPSS software.Out of 80 cases, maximum type was Cholesterol (81.2%) and was multiple in numbers (71.2%). However, gallstone size, shape and number are non-significant variable to produce precancerous lesions. Statistically significant results were obtained while comparing the mucosal response with gallstone types (P=0.010).The changes in gallbladder mucosa ranging from hyperplasia, dysplasia, metaplasia to carcinoma in situ are related to gallstone type. Other morphological characteristics were not found related with precancerous lesions of gallbladder mucosa.

KEYWORDS: Cholelithiasis, Cholecystitis, Cholesterol, Metaplasia, SPSS, Dyskinesia.

I.INTRODUCTION

Gallbladder is an accessory organ of the digestive tract, it lies on the underside of the liver in the main liver scissura at the junction of the right and left lobes of the liver. Cholelithiasis is defined as the formation of stone inside the gallbladder.[1] It has been described as a disease of civilization. They have been observed in Egyptian mummies dating as far back as 3400 BC. It appears likely that Charaka (two centuries B.C.) and Sushruta (six centuries B.C.) from India were also familiar with this disease of the biliary tract.[2] Cholelithiasis is the most prevalent disorder of the biliary tract , it produces a series of epithelial pathological changes which might be precursor lesion of gallbladder cancer. The function of gallbladder is not only to store bile, but also to concentrate it during the inter-digestive phase by means of salt dependent water reabsorption.[3] Epithelium of the gallbladder and biliary tract is exposed to high concentration of potentially harmful exogenous and endogenous compound excreted into the primary bile. The bilestasis caused by gallbladder dyskinesia is the prime factor for gallstone formation.[4] Bile-stasis secondary to dyskinesia which may be the result of gallbladder pathology is the most widely accepted theory for stone formation. Other studies related to gallstone formation to alternation in the bile composition resulting from oxidative stress and the effect of

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oxygen free radical in the gallbladder mucosa, such condition might lead to an altered adsorption and concentration of bile with resultant saturation followed eventually by stone formation.[5,6] It is a world wide medical problem but the rate show substantial geographical variation with the lowest rate report in African population group.

The prevalence varies with age, sex and ethnic group.[7] Most people are unaware of disease and remain asymptomatic for life.[8] Twenty million people in the united state are estimated to have gall stone disease and one half million cholecystectomies are performed each year.[9] The most common complication of the presence of gallstone is cholecystitis (inflammation of gallbladder) whether acute or chronic. It may be association with appearance of hyperplasia,metaplasia and even carcinoma of the gallbladder.[10,11] A significant higher incidence of carcinoma gallbladder has been observed in patient population with a traditionally high incidence of gallbladder or in persons harboring gallstone for longer duration.[12]

II.MATERIALS AND METHODS

The study was conducted on 80 patients of aged 18 yrs and above, whom undergoing open cholecystectomies for cholelithiasis in JNIMS, Imphal during October 2020 to September 2021. Patients undergoing Laparoscopic cholecystectomy, patients diagnosed as cholelithiasis with preoperative confirmed case of gallbladder carcinoma were excluded.Morphorlogical characteristics of the gallstones were assessed for various parameters:1) number, 2) weight, 3) shape, 4) size and 5) morphological type. Gallbladder mucosa was subjected to histopathological examination.

The pattern of response in the gallbladder mucosa was studied with regard to number, size, shape, weight and morphological type of the gallstones.The various morphological responses were then categorized into five broad categories-cholecystitis, Reactive atypia, Xanthochromatosis, Dysplasia and Adenocarcinoma.The data thus collected were systemically compiled and analysis of variance for averages and Chi-square test for contingency tables and proportions. All the observations were recorded on excel sheet and were evaluated with SPSS software.Statistical significance was considered when P< 0.010.

III.RESULTS

In the present study, of 80 cases, majority of the patients were in age group of 40-50 years. Mean age of the participants was 42.81yrs and mean BMI was 28.77kg/m^2. Of the total 80 cases, 85% were female and 15% were male patients, male to female ratio was 1:5.7.Out of 80 cases, maximum type was Cholesterol (81.2%) and was multiple in numbers (71.2%). However, gallstone size, shape and number are non-significant variable to produce precancerous lesions. Statistically significant results were obtained while comparing the mucosal response with gallstone types. Descriptive statistic of variables are showing in TABLE-1(a) & 1(b) and association of mucosal response with gallstone number, size, weight, shape and type are showing in TABLE-2 to 6. p< 0.05 is considered as statistically significant.

TABLE-1(a): SHOWING DESCRIPTIVE STATISTICS OF VARIABLES

VARIABLES		FREQUENCY	PERCENTAGE
GENDER	MALE	12	15%
	FEMALE	68	85%
NUMBER	SINGLE	23	28.80%
	MUTLIPLE	57	71.20%
SHAPE	MULTIFACETED	50	62.50%
	ELLIPSOID	21	26.30%
	SPHERICAL	6	7.50%
	SLUDGE	3	3.80%
SIZE	</= 12 mm	61	76.30%
	> 12 mm	19	23.70%
TYPE OF STONE	CHOLESTEROL	73	91.25%
	PIGMENTS	1	1.30%

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	MIXED	6	7.45%

TABLE-1(b): SHOWING DESCRIPTIVE STATISTICS OF VARIABLES

VARIABLES		FREQUENCY	PERCENTAGE
HISTOPATHOLOGICAL	CHR. CHOLECYSTITIS	74	92.40%
FINDING	CHR. CHOLECYSTITIS WITH REACTIVE ATYPIA	2	2.20%
	CHR. CHOLECYSTITIS WITH DYSPLASIA	1	1.30%
	XANTHOCHROMATOUS CHOLECYSTITIS	2	2.50%
	ADENOCARCINOMA	1	1.30%

TABLE-2: ASSOCIATION OF MUCOSAL RESPONSE WITH GALLSTONE NUMBER

HISTOLOGICAL DIAGNOSIS	GALLSTONE NUMBER		TOTAL	P- VALUE
	SINGLE	MULTIPLE		
CHR. CHOLECYSTITIS	20	54	74	0.424
CHR. CHOLECYSTITIS WITH REACTIVE ATYPIA	1	1	2	
CHR. CHOLECYSTITIS WITH DYSPLASIA	1	1	2	
XANTHOCHROMATOUS CHOLECYSTITIS	0	1	1	
ADENOCARCINOMA	1	0	1	
TOTAL	23	57	80	

TABLE-3: ASSOCIATION OF MUCOSAL RESPONSE WITH GALLSTONE SIZE

HISTOLOGICAL DIAGNOSIS	GALLSYTONE SIZE		TOTAL	P-VALUE
	≤ 12	> 12		
CHR. CHOLECYSTITIS	57	17	74	0.29
CHR. CHOLECYSTITIS WITH REACTIVE ATYPIA	2	0	2	
CHR. CHOLECYSTITIS WITH DYSPLASIA	1	1	2	
XANTHOCHROMATOUS CHOLECYSTITIS	0	1	1	
ADENOCARCINOMA	1	0	1	
TOTAL	61	19	80	

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TABLE-4: ASSOCIATION OF MUCOSAL RESPONSE WITH GALLSTONE WEIGHT

HISTOLOGICAL DIAGNOSIS	GALLSTONE WEIGHT		TOTAL	P-VALUE
	<10 gram	>10 gram		
CHR. CHOLECYSTITIS	71	3	74	0.99
CHR. CHOLECYSTITIS WITH REACTIVE ATYPIA	2	0	2	
CHR. CHOLECYSTITIS WITH DYSPLASIA	1	0	1	
XANTHOCHROMATOUS CHOLECYSTITIS	2	0	2	
ADENOCARCINOMA	1	0	1	
TOTAL	77	3	80	

TABLE-5: ASSOCIATION OF MUCOSAL RESPONSE WITH GALLSTONE SHAPE

HISTOLOGICAL DIAGNOSIS	GALLSTONE SHAPE				TOTAL	P-VALUE
	MULTIFACETED	ELLIPTICAL	SPHERICAL	SLUDGE		
CHR. CHOLECYSTITIS	48	18	5	3	74	0.15
CHR. CHOLECYSTITIS WITH REACTIVE ATYPIA	1	1	0	0	2	
CHR. CHOLECYSTITIS WITH DYSPLASIA	0	1	0	0	1	
XANTHOCHROMATOUS CHOLECYSTITIS	1	1	0	0	2	
ADENOCARCINOMA	0	0	1	0	1	
TOTAL	50	21	6	3	80	

TABLE-6: ASSOCIATION OF MUCOSAL RESPONSE WITH GALLSTONE TYPE

HISTOLOGICAL DIAGNOSIS	GALLSTONE TYPE			TOTAL	P-VALUE
	CHOLESTEROL	PIGMENTS	MIXED		
CHR. CHOLECYSTITIS	69	0	6	75	0.01

CHR. CHOLECYSTITIS WITH REACTIVE ATYPIA	2	0		0	2	
CHR. CHOLECYSTITIS WITH DYSPLASIA	1	0		0	1	
XANTHOCHROMATOUS CHOLECYSTITIS	1	0		0	1	
ADENOCARCINOMA	0	1		0	1	
TOTAL	73	1		6	80	

IV.DISCUSSION

The estimated prevalence of cholelithiasis in India has been reported between 2% and 29%. In India, this disease is seven times more common in North than South India.[13] The present study was conducted to evaluate 80 patients with cholelithiasis undergoing open cholecystectomy with an aim to correlate various gallstone characteristics with morphological mucosal responses in the gallbladder.

In our study, the majority of the patients were between 40 and 50 yrs, with a mean age of 42.18 yrs. Our study results were in concordance with the results obtained by khurana et al[14], Tyagi et al[15] and Singh et al[16], who reported the mean age of 42.5, 43.6 and 45.3yrs respectively. 85% of patients we studied were female, similar results have been reported in the studies of Mathur et al[17] and Mohan et al[18], who reported that 86.97% and 86.54% of patients were female respectively. We also observed that multiple stones (71.2%) were more common than solitary or two stones, similar results reported in the study of Tyagi et al[19].

In our study, the number of stone with size of more than 12mm was 76.2%. However, the correlation between size of stone and precancerous mucosal changes was found statistically insignificant(P= 0.29). Similarly, in case-control studies of Roa et al[9] and Moerman at al[20] found no relationship between size of stone and gallbladder cancer. In this study, we observed that correlation between the mucosal changes and gallstone type was statistically significant(P=0.01).Similarly, Goyal S et al[21.] correlate the various types of mucosal response to gallstone type and number.

V.CONCLUSION

The changes in gallbladder mucosa ranging from hyperplasia, dysplasia, metaplasia to carcinoma in situ are related to gallstone type. Other morphological characteristics were not found related with precancerous lesions of gallbladder mucosa.

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THANK YOU