Original Article

Anatomy

Histological Changes in Human Gallbladder Mucosa due to Cholelithiasis

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ABSTRACT

Objective: To observe the histological changes in gallbladder mucosa due to Cholelithiasis.
Study Design: Observational study
Place and Duration of Study: This study was carried out at Department of Surgery, Anatomy and Pathology of Isra University Hospital and Institute of Biochemistry Sindh University Jamshoro.
Materials and Methods: Sixty nine cases of Cholelithiasis undergoing surgery were included in this study. After operation the gall bladders were obtained and fixed in 10% formalin. Gall bladder stone were obtained and their analysis was done in the Institute of Biochemistry Sindh University Jamshoro. Gross examination of gall bladders was done and for microscopy after hematoxylin and eosin staining, sections were obtained from the fundus, body and neck of the gallbladder. Additional sections were taken from grossly abnormal looking areas.
Data analysis: Data was analyzed by using SPSS version 16.0. Chi square test was used to determine statistical significance between categorical groups ($p<0.5$)
Results: it was observed that size of gall bladder were normal in 41(59.4%), increased in 20(29.0%) and shrunken in 08(11.6%) cases. The mucosal changes seen in Cholelithiasis include, Cholestrolosis in 18 (26.08%), ulceration 07 (10.1%), atrophy 12 (17.4%) and lymphocytic infiltration in 67 (97%) cases
Conclusion: Cholelithiasis produced a series of histopathological changes in the gallbladder mucosa. These changes have no relation with type of gall stone
Key Words: Gall bladder Mucosa, Cholelithiasis,

INTRODUCTION

Cholelithiasis is one of the most common medical problems leading to surgical intervention and affects approximately 10% of the adult population in the United States. Around 500,000 cholecystectomies are performed in the US every year [(1)]. In Asian population, prevalence of gallstone disease is lower, ranging from 3% to 15%. [(2)]. In Pakistan the incidence of Cholelithiasis is increasing[3,4]. Incidence of Cholelithiasis in Sind is about 9.03% with female to male ratio of females 3.3:1[3]. Cholesterol, bile pigment and calcium are major constituents involved in the formation of human gallstones[5]; majority of gallstones are cholesterol and pigment stones[6]. Cholesterol gallstones constitute around 70% cholesterol and remaining small fraction is composed of pigment residues and trace elements [(7)]**.** Calcium salts of phosphate, mucin, glycoprotein, phospholipids and some metals are other constituents of gall stones. All these substances are normally found in the sera of stone formers[8]. The gallbladder mucus plays a major role in the pathogenesis of Cholelithiasis as it promotes the nucleation of stones[9]. Various histopathological changes in mucosa of gall bladder including acute inflammation, chronic inflammation, glandular hyperplasia, Cholestrolosis, dysplasia and carcinoma[10]. Gross features associated with Cholelithiasis include congestion in serosal surface and thickening of gall bladder wall. Mucosa became hemorrhage, strawberry-like, atrophic and slightly nodular in appearance[11]. Changes in epithelium also depend on the type of stones[12]. In countries like Pakistan where incidence of carcinoma gall bladder is higher than other countries, the knowledge of histological changes in gall bladder mucosa will help us understanding the pathogenesis of the malignant process. Present study is aimed to see the changes in the mucosa of gall bladder and the extent of damage caused by different type of stones.

MATERIALS AND METHODS

This study was carried out at Department of Surgery, Anatomy and Pathology of Isra University Hospital and Institute of Biochemistry Sindh University Jamshoro. Sixty nine cases of Cholelithiasis undergoing surgery were included in this study. The personal and medical data of patients was recorded on specific Performa. After operation the gall bladders were obtained and fixed in 10% formalin. Gall bladder stone were obtained and their analysis was done in the Institute of Biochemistry Sindh University Jamshoro. Gross examination of gall bladders was done to observe the outer surface of gall bladder, wall thickness, and mucosal abnormalities. For microscopy after hematoxylin and eosin staining, sections were obtained from the fundus, body and neck of the gallbladder. An additional section was taken from grossly abnormal looking areas. Data were analyzed on SPSS-version-16.

RESULTS

Sixty nine cases of Cholelithiasis undergoing surgery were included in this study. Mean Age of the patients was 35.81± 8.12 years. 53.63% of the patients belonged to the age group 35-44 years. (Table-1) 71.0% patients were female with a female to male ration of 2.45:1. (Table-2). In the present study, Cholesterol stones were most common (55.07%). (Table-3). Gall bladder size were normal in 41(59.4%), increased in 20(29.0%) and shrunken in 08(11.6%) cases. (Table 4). Gall bladder wall was normal in 47(68.1%) and thickened in 22(31.9%) cases. (Table-5). In our study microscopic changes found in the mucosa of gall bladder with Cholelithiasis included, Cholestrolosis 18 (26.08), Ulceration 07 (10.1%), atrophy 12 (17.4%) and lymphocytic infiltration in 67 (97%) cases.(table-6). Microscopic changes when related to type of gall stone revealed that; Cholestrolosis was present in 13(72.22%) case of cholesterol stones, 03(16.67%) case of pigmented stones and 02(11.11%) cases of mixed type of gall stones. Ulceration was present in 04(57.14%) case of cholesterol stones, 02(28.57%) case of pigmented stones and 01(14.29%) cases of mixed type of gall stones. Atrophic changes was present in 09(75.0%) case of cholesterol stones, 02(16.66%) case of pigmented stones and 01(08.34%) cases of mixed type of gall stones. Lymphocytic infiltration was present in 35(52.23%) case of cholesterol stones, 25(37.33%) case of pigmented stones and 07(10.44%) cases of mixed type of gall stones. (Table-6).

Table No.1: Age distribution of patients

n = 69, Mean age = 35.81± 8.12		
	Frequency	%
15-24	08	11.60
25-34	17	24.64
35-44	37	53.62
45-54	06	8.69
55-64	01	01.45
Total	69	100

Table No.2: Gender distribution of patients

	Frequency	%
Male	20	29.0
Female	49	71.0
Total	69	100.0

Table No.3: Frequencies of different type of gall stones

n = 69		
Gall Stones Type	Frequency	%
Cholesterol	38	55.07
Pigmented	20	28.99
Mixed	11	15.94
Total	69	100

Table No.4: Gall Bladder size

	Frequency	%
Normal	41	59.4
Increased	20	29.0
Shrunken	8	11.6
Total	69	100.0

Table No.-5: Wall thickness of gall bladder

	Frequency	Percent
Normal	47	68.1
Thickened	22	31.9
Total	69	100.0

Table No.-6: Microscopic mucosal changes in gall bladder

Microscopic Mucosal Changes		Type of Gallstone			Total
		Cholesterol	Pigmented	Mixed	
Cholestrolosis	Frequency (%)	13 (72.22%)	03 (16.67)	02 (11.11%)	18 (100%)
Ulceration	Frequency (%)	04 (57.14%)	02 (28.57%)	01 (14.29%)	07 (100%)
Atrophic Change	Frequency (%)	09 (75.0%)	02 (16.66%)	01 (8.34%)	12 (100%)

DISCUSSION

Gallstones remain a serious health concern affecting millions of people throughout the world. It exhibits prevalence rates of about 25% in industrialized societies but are uncommon in underdeveloped or developing societies [13]. The present study shows that in Hyderabad, the cholesterol stones are most common type. Our results are in agreement with the studies carried out in Riyadh[14]. This finding is also in agreement with a study in the western region of Saudi Arabia, where 90.4% of the gallstones contained cholesterol[15]. Reports from western countries, such as Germany and some Scandinavian countries also showed cholesterol as the primary component of the gallstones[16, 17]. Another study conducted by Channa et al also shows that 67.9% of gall stones are cholesterol stones[18]. Formation of cholesterol calculi have been related to high carbohydrate diet, which leads to cholesterol super saturation in the bile[19]. When cholesterol concentration becomes more than bile acids and salts with in bile then it results in the nucleation of cholesterol and thus results in gall stone formation. The reason for this super saturation of cholesterol is believed to be abnormal production of bile from liver. Such type of cholesterol nucleation in the absence of bile acids and salts is only true for cholesterol stones, which are composed of mainly cholesterol[20]. Our results showed that females were more affected with Cholelithiasis than males, with a female to male ratio of 1.6:1. According to the Central Department of Statistics, Saudi Arabia, female to male ratio of the total

Saudi population was 100:102 in 2005[21]**.** One study carried out at different hospitals at Hyderabad by Channa et al shows that among gall bladder disease patients, 70.63% were females[20]. This might be due to basic hormonal differences between males and females, together with the differences that might exist due to co-expression of sex hormone receptors in the gallbladder of both sexes[21]. The medical records of the patients of the present study showed that most of the female patients had parity. This is also in agreement with other studies, which concluded that fertility and multiple pregnancies appeared to be a risk factor for gallstones among Saudi women[22]. In our study, the mean gallbladder wall thickness in patients with gall stones was higher in 22(31.9%) cases. These observed differences might be due to the fact that the presence of gall stones in the gallbladder causes irritation of the gallbladder wall thereby resulting in thickening of the gallbladder wall[23]. The healthy gallbladder absorbs cholesterol and desaturates bile. This protective function is lost in chronic cholecystitis resulting from inflammation of the gallbladder wall. The inflamed gallbladder, with its thickened wall, encourages super-saturation of gallbladder bile and subsequent gallstone formation[24]. Portincasa *et al* working in Italy found a significant increase in gallbladder wall thickness amongst Italians with gall stones compared to those without gall stones[25]. In our study, mucosal changes were present in 52 (75.36%) in gall bladder with stones, our result is in agreement with the results of Khanna et al, which shows that mucosal changes are present in 90(64.5%) cases[6,12]. In our study microscopic changes in the mucosa of gall bladder with Cholelithiasis includes, Cholestrolosis 18 (26.08), Ulceration 07 (10.1%), and atrophy 12 (17.4%), Cholestrolosis 18 (26.08). Another study conducted by Zahrani and Mansoor, showed 11% specimens with Cholestrolosis[26]**.** In literature, Cholestrolosis is reported in approximately 20% of cholecystectomy specimens. This is characterized by the accumulation of cholesterol esters and triglyceride in aggregates of sub epithelial macrophages and, to a lesser extent, in the gallbladder epithelium itself[27]. Although the origin of Cholestrolosis is unknown, most theories stress that either super saturation of the bile with cholesterol, which is found in many but not all cases, or abnormal lipid transport across the mucosa leads to the formation of the lipid deposits. Bile cholesterol super saturation is also seen with cholesterol gallstones[28]. In the present study, Cholestrolosis was present in 13 (72.22%) case of cholesterol stones, 03(16.67%) case of pigmented stones and 02(11.11%) cases of mixed type of gall stones. Our results are in agreement with the results of Mohan et al. According to their study, Cholestrolosis was present in 26.3% of cases with cholesterol stones[29].

CONCLUSION

Cholelithiasis produced a series of histopathological changes in the gallbladder mucosa. These changes have no relation with type of gall stone.

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