

# Histopathological Changes of Gallbladder Mucosa Due to Cholelithiasis

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## *Abstract*

**Objectives:** This work was carried out to study the diverse histopathological changes in the gallbladder mucosa as a result of cholelithiasis.

**Patients and methods:** The study included 25 of gallbladder specimens, which were resected. They were collected from Al-Ramadi General Hospital. Stones were found in each specimen of gallbladder. Gross examination for length and width of gallbladder was calculated and the samples were fixed in 10% formalin for histological study. The relation of age and gender with cholelithiasis was studied in this work.

**Results:** In gross examination, We found increase in length (Mean=4.64cm) and width (Mean=2cm). Also our observation recorded increase of cholelithiasis in females compared with males 1:24(4:96%) and increase of cholelithiasis with aged (Mean=44) and also gallstones were calculated. Histological changes in mucosa of gallbladder by using heamatoxylin and eosin stains were observed and calculated the percentage as following: hyperplasia was observed in 14(46%), antral metaplasia 8(32%), intestinal metaplasia in 3(8) and dysplasia in 1(4%)

**Conclusion:** We found that cholelithiasis and even silent gallstones can Produce 56% in the gallbladder mucosa, which could be a precursor lesion gallbladder carcinoma.

**Key word:** Cholelithiasis, dysplasia, hyperplasia, metaplasia.

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## *Introduction*

Cholelithiasis is defined as presence of stones within the lumen of the gallbladder or in the extra hepatic biliary tree.<sup>4</sup>

The gall bladder is small, hollow, and pear-shaped organ.<sup>1</sup> Absorption of water, as well as emptying of bile, are important functions of the gallbladder<sup>2</sup>. The gallbladder pathologies are very common<sup>3</sup> from these troubles that the gallbladder undergoes to functional and histological changes due to accumulation of gallstones called cholelithiasis.

Gall stones are crystal-like particles that are formed in the gall bladder when certain substances are separated out of bile. There are two types of stones: cholesterol stones and pigment stones which are formed from bilirubin and calcium so we may find stones which differ in size, number, shape, colour and degree which they lead to problems.<sup>5</sup>

## *Patients and Methods*

Our study consisted of 25(24 females and only 1 male) gall bladder cholecystectomies for patients of different ages. The age of the patients ranged from (27-60) years with mean of 44 year.

In gross examination, length and width of gall bladder were calculated. Stones that found in all specimens were also calculated. Resected specimens were fixed with formalin and embedded in paraffin wax. Serial sections 4µm in thickness Slices were Obtained stained with haematoxylin and eosin and examined microscopically. These sections including entire wall thickness were obtained from the fundus, body and neck of gall bladder.

The following microscopic histopathological changes in Gall Bladder Mucosa were Recorded Hyperplasia, antral metaplasia, intestinal metaplasia and dysplasia in the gallbladder mucosa.

The results were obtained and calculated by percentage.

## *Results:*

The mean of length is (4.64), width(2), age (44). Number of stones was recorded in table(1). Histological changes in mucosa of gall bladder were recorded as following: Hyperplasia is 14 (56%), antral metaplasia 8 (32%),intestinal metaplasia 2 (8%) and dysplasia 1(4%), as shown in table( 2). Fig (1) shows the gross view of gallbladder, Fig (2) shows multiple stones.

**Table 1: Patient characteristics**

Age	Mean:44 year (27-60)
Male: female ratio	1:24 – (4:96%)
Length of gall bladder	Mean:4.64 cm
Width of gall bladder	Mean:2.0 cm
Single stone	N (2)-(8%)
Multiple stones	N (23)-(92%)

**Table 2: Lesions found in the mucosa of gallbladder (n=25)**

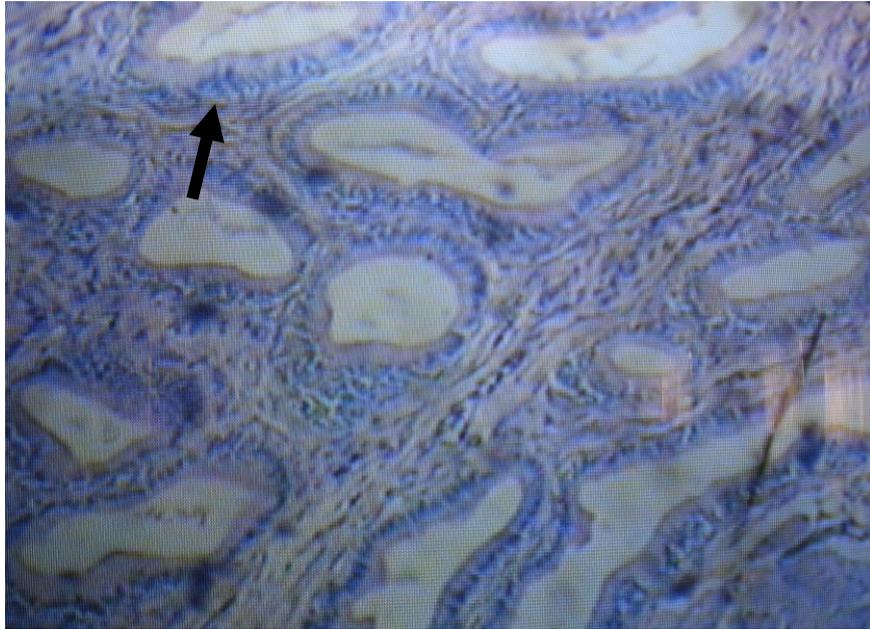
Lesion	Number of cases(25)	Percentage
Hyperplasia	14	56
Antral metaplasia	8	32
Intestinal metaplasia	2	8
Dysplasia	1	4



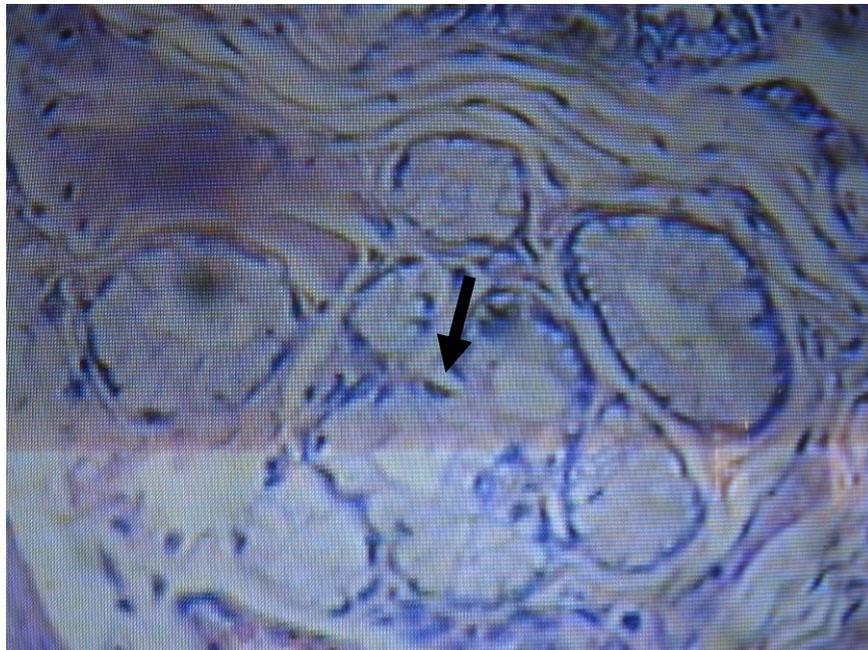
**Fig-1 View of gall bladder**



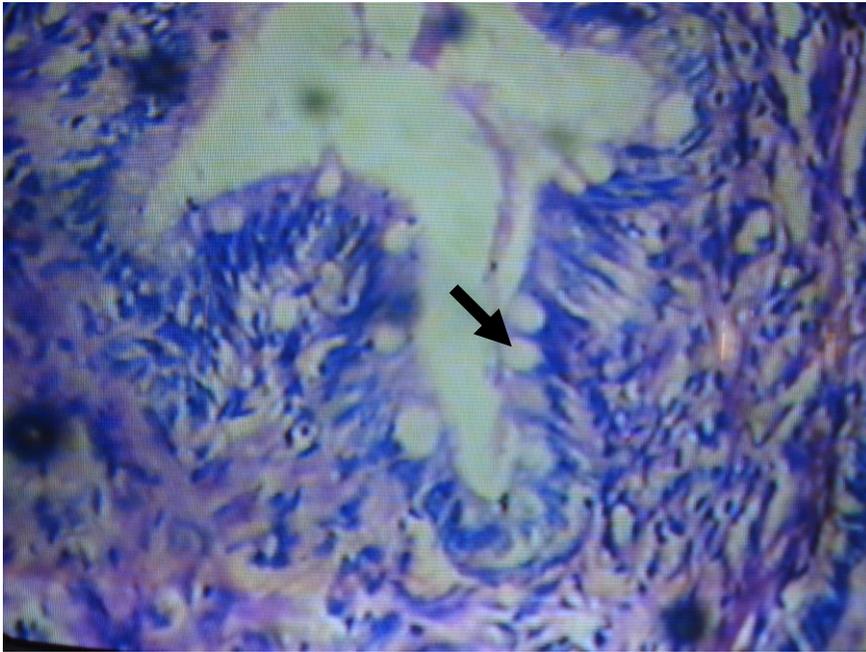
**Fig-2 View of multiple gall stones**



**Fig.-3: Section shows hyperplasia of gall bladder Mucosa ( 150x)**



**Fig-4: Section shows Antral metaplasia H&E( 200x)**



**Fig 5: Section shows intestinal metaplasia with numerous goblet cells. H&E(200x)**



**Fig6: Section shows mild dysplasia  
H&E( 150x)**

## **Discussion:**

The presence of gallstones is a well established risk factor for gallbladder carcinoma, and risk seems to be correlated with stone size<sup>7</sup>.

Cholecystectomy is one of the most common surgical procedures. Chronic cholecystitis was seen in 75% of cases with epithelial metaplasia and 73% with regenerative epithelium<sup>6</sup>.

Hyperplasia Constitutes an increase in the number of cells in organ or tissue and physiological hyperplasia is divided into hormonal hyperplasia and compensatory hyperplasia<sup>8</sup>. In our study, epithelial hyperplasia is the most frequent change and was found in 56% of our gallbladder specimens with stone disease as shown in Table(2), Fig (3). Saavedra et al<sup>9</sup> suggested that a small number of hyperplasia of the gall bladder evolves towards atypical hyperplasia and that this may progress to carcinoma. Jeffery et al<sup>10</sup> showed that mild to moderate degree of epithelial hyperplasia is accompanied with chronic cholecystitis.

Metaplasia is a reversible change in which we have one adult cell type (Epithelial or mesenchymal) is replaced by another adult cell type. Metaplasia of the antral and intestinal variety is frequently seen in gallbladders containing stone<sup>11</sup>. Antral metaplasia is branched tortuous glands in lamina propria, while intestinal metaplasia is present in goblet cell<sup>12</sup>. We found about 32% antral metaplasia and 8% intestinal metaplasia in our specimens, see Table(1), Figs(2,3), while others reported that the incidence of antral Metaplasia in 50 to 100% of their cases with Lithiasis<sup>13,14</sup>. Yamamoto et al and Ajiki et al<sup>15,16</sup> proposed that there might be two histogenic pathways for gall bladder cancer, one path derived from normal epithelium and the other from metaplastic epithelium.

Dysplasia was found in 4% of gall bladder specimens Table(1), Fig(4). Others have reported the incidence of dysplasia in 2.2% of cholelithiasis specimens and 42% in the mucosa adjacent to invasive carcinoma.

The intestinal metaplasia, dysplasia and carcinoma sequence have been considered the main route of carcinogenesis in the gallbladder<sup>17</sup>.

Csendes et al., observed 33% abnormal histological finds, mainly chronic cholecystitis, which increased with age and was frequently seen among women<sup>18</sup>. The frequency and severity of mucous gland hyperplasia and metaplasia were also found to be increased with age and were more commonly observed in patients above 40 years of age<sup>19</sup>. Impaired gallbladder function was more frequently observed in older patients ( $\geq 65$  years old) than in younger patients ( $\leq 65$  years old)<sup>20</sup>. Our study recorded an increase of cholelithiasis in older ages than smaller ones and it also revealed among women than men; in addition to accumulation of multiple stones. This mostly may be due to the nature of food.

Obese people also have a higher risk factor of gall stones. Diet in high cholesterol seems to be linked to gall stone and some researchers believed that high cholesterol must be accompanied by genetic predisposition toward gall stone<sup>21</sup>.

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