



## Incidence of malignancy in ultra sonographically normal looking gall bladder with gall stones.

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**Abstract;** a retrospective study was done through 3 years February 2015 till February 2018 on 458 patients with ultra sonographically normal locking gall bladder wall with gall stones in different ages, different sex and different durations of gall stones, after exclusion of acute and chronic cholecystitis or any abnormal locking by ultrasound of gall bladder wall, all these removal gall bladder by laparoscopic and open procedure were send for histopathological study to find any malignancy. our results there were no any case of malignancy were detected. Sub acute cholecystitis were 15.9%, acute cholecystitis 0.87, chronic cholecystitis 9.17%, and normal gall bladder wall 74.01%

**Key word;** gall bladder wall, carcinoma of gall blaader

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### I. INTRODUCTION;

Gallbladder carcinoma is the most common cancer of the biliary tract and is the fifth most common neoplasm of the digestive tract and has an overall incidence of 3 per 100000 people. [1]. The majority of symptomatic patients with malignant gallbladder disease have an incurable tumor. The outcome of gallbladder carcinoma is poor, and the overall 5-year survival rate is less than 5%. In early-stage disease, a 5-year survival rate of 75% can be achieved if stage-adjusted therapy is performed[2]. Gallbladder carcinoma is described in up to 3.4% of autopsies conducted on cholelithiasis patients over 60 years of age[3]. The risk of gallbladder carcinoma increases with age. There are 2 peaks observed in gallbladder tumor incidence. The first peak occurs at 50-60 years of age. The second peak occurs at 70-80 years of age and has a higher prevalence among women[4-5]. There is a wide geographic variance in the frequency of gallbladder carcinoma. The incidence rates are extraordinarily high in Mapuche Indians in Chile, South America. This population exhibits the highest rate of gallbladder cancer: 12.3/100000 for males and 27.3/100000 for females[6]. The women of north India have an incidence of 22/100000. In North American Indians (New Mexico) and Pakistan, the incidence is 11/100000. Europe has a low overall incidence of 0-4/100000. There are also relatively high rates observed in several Eastern European countries such as Poland, which has an incidence of 14/100000. The literature reports Japan as having a high incidence rate at 7/100000, though this value is low compared with that of Poland[7]. There is an inverse relationship regarding the cholecystectomy rate and incidence of gallbladder carcinoma. Thus, countries with a higher rate of cholecystectomy have a lower rate of gallbladder carcinomas because the patients with risk factors have their gallbladders removed before carcinoma develops. Therefore, a survey of disease risk factors is important. Gallstones represent an important risk factor in the formation of gallbladder malignancies. Concrements are present in up to 85% of patients with gallbladder carcinomas[8]. Furthermore, gallbladder cancer rates are correlated with the prevalence of gallstone disease[8]. Increasing stone size elevates the risk of developing gallbladder cancer. Gallstones larger than 3 cm are associated with a greater than tenfold increased risk of cancer compared with that of small gallstones[9,10]. The type of concrement also matters. Cholesterol gallstones resulting from a distinct local mucosal irritation and chronic inflammation are associated with a higher risk of cancer. Chronic inflammation is strongly associated with the malignant transformation of cells. Chronic inflammation causes DNA damage, which provokes repeated tissue proliferation and restoration attempts. This response involves the release of cytokines and growth factors and, thus, predisposes

cells to oncogenic transformation[11]. Porcelain gallbladder is a rare type of chronic inflammation that occurs in approximately 0.8% of all cholecystectomies and is associated with an increased carcinogenic risk. Porcelain gallbladder is a form of diffuse transmural calcification. Several authors have reported a 62% carcinogenic risk, which appears to be an overestimation[12]. Primary sclerosing cholangitis (PSC) is a chronic inflammatory syndrome with a neoplastic “field effect” that further supports the role of chronic inflammation of the gallbladder and consecutive carcinogenesis as there is an increased rate of gallbladder tumors that occur *via* a metaplasia-dysplasia-carcinoma sequence[13]. Gallstones are one of the most important risk factors for developing cancer. The genetic alterations that occur in the gallbladder wall are important for understanding cancer development. The gallbladder wall is altered by gallstones. The molecular pathogenesis results in an accumulation of mutations that may lead to malignancy. The common genetic mutations responsible for carcinogenesis include the activation of oncogenes, deactivation of tumor suppressor genes, microsatellite instability, and methylation of gene promoter regions[14].

Approximately 80%-97% of gallbladder carcinomas are adenocarcinomas. The remaining 3%-20% of tumor types include squamous-cell, adenosquamous-cell carcinomas, or papillary carcinomas. Additionally, gallstones and sludge are coexistent in 96% of cases. There are gallstones present in nearly 100% of squamous-cell and adenosquamous-cell carcinomas. In particular, large (> 1.5 cm) cholesterol, composite, or combination gallstones were found more frequently in gallbladders with squamous-cell and adenosquamous-cell carcinomas. In nearly 88% of gallbladder adenocarcinoma cases, there are also gallstones present. In particular, large, cholesterol, composite, or combination gallstones (> 1.5 cm) have been found in 68.2% of adenocarcinomas. Furthermore, small cholesterol, mixed, or pigmented gallstones and biliary sludge are found in 31.8% of adenocarcinomas[15]. The association between gallstones and carcinoma in cases of SCC requires longer periods of time. Thus, the patients with SCC are often older. SCC is more locally aggressive and is less sensitive to chemotherapeutics. In locally advanced stages, the prognosis of SCC is worse than adenocarcinomas. However, it has also been shown that R0 resection of an intramucosal pure squamous-cell carcinoma has a comparable prognosis to adenocarcinomas[15]. Approximately one-third of gallbladder carcinomas are known preoperatively despite understanding the theoretic risk factors. In the majority of cases, the tumor is diagnosed by the pathologist after a routine cholecystectomy for a benign disease[16-17], and these tumors are termed “incidental or occult gallbladder carcinomas”.

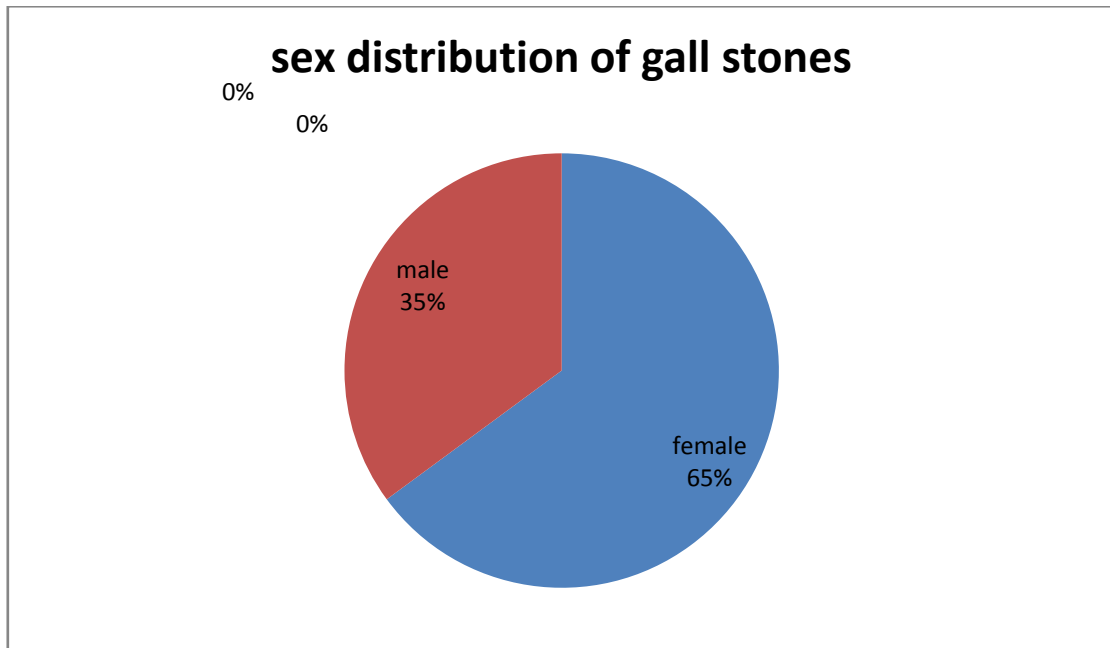
Conflict-of-interest statement: No conflict of interest.

## **II. PATIENTS AND METHODS:**

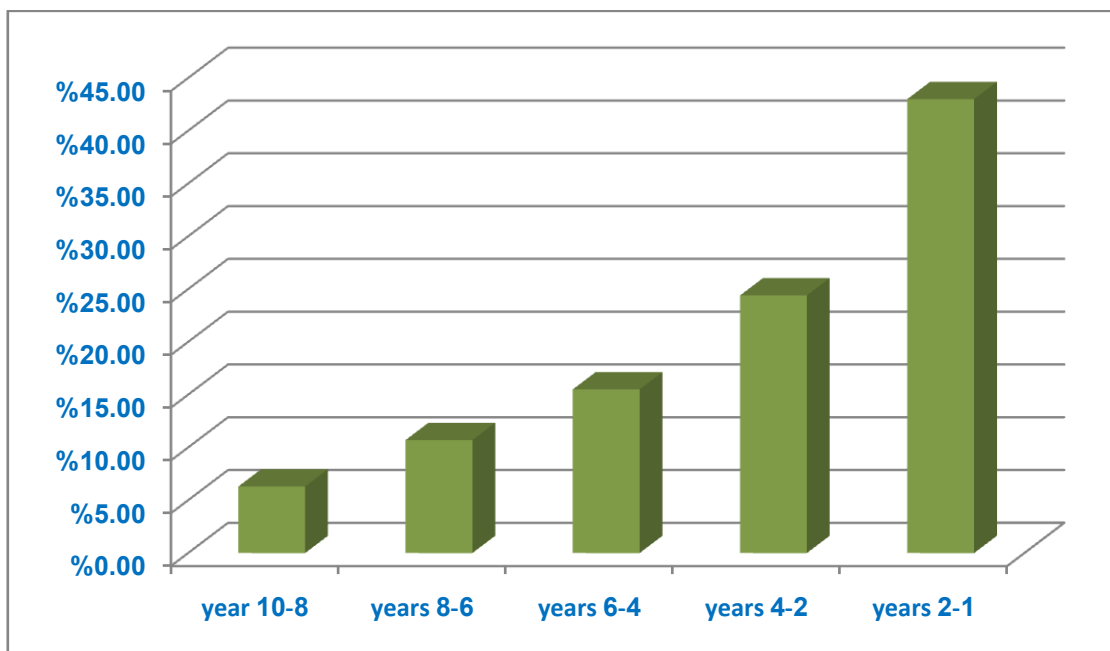
This a retrospective study were done through 3 years from first February 2015 till first of February 2018 on 458 patients were did for them laparoscopic open cholecystectomy in al-hussen teaching hospital in al nassiryia city for normal locking gall bladder wall with gall stones who are diagnosed by ultrasonic radiography .after removal of gall bladder sent it for histopathological study to exclude any malignancy in the wall.usually results appear after 20 to 30 days. we were take inform consent after we explain to the patients why where ,when and who to do the operation ,intra and post operative complications that may occur,completeinformation's from the patients as name sex age durations of gall stones and main complain of the patient , important investigations as complete blood count ,blood group, blood urea, serum creatinine liver function test ,virology test, general urine examination, and r.b.s. chest x ray, ecg, and eco, all patients checked by anesthetic doctors pre operatively, we did the operation under general anesthesia most of cases were done by laparoscopic surgery, most of cases we discharge them at night then we wait the histopathological result .

## **III. RESULTS;**

458 patients were done for them laparoscopic and open cholecystcoy 299 female ( 65.3 %) and 159 male ( 34.7%) (figure 1).duration of gall stones according to the age as in figure 2 most have prolong durations were 1 to 2 years in about 43% while less duration between 8 to 10 years 6.3%. while distributions of gall stones according to the age as in figure 3 most common gall stones occur in age between 40—49 years while lest gall stones occur in ages less than 20 years 1.52% then fallowed 5.67% in ages between 20—30 years then at ages more than 60 years 10.86%.all gall bladder were sent for histopathological examination ,the results as in figure 4 wereNon of these number of a normal locking gall bladder wall with gall stones had positive result of any malignant cells , while 73 patients (15.9%) of cases are subacute inflammations, 4 cases ( 0.87%) gave acute cholecystitis while 42 cases (9.17%) the results was chronic inflammations and 339 cases (74.01%) the results is no signs of inflammation (silent gall stones) those cases the patients prefer to do the prophylactic operation .

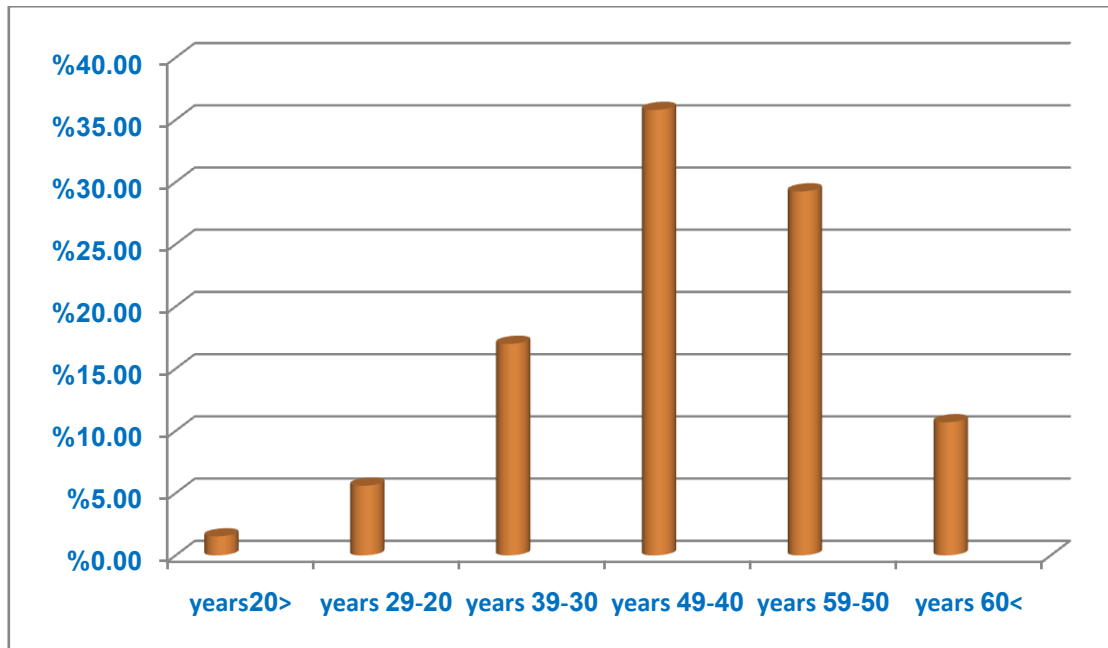


**Figure 1**

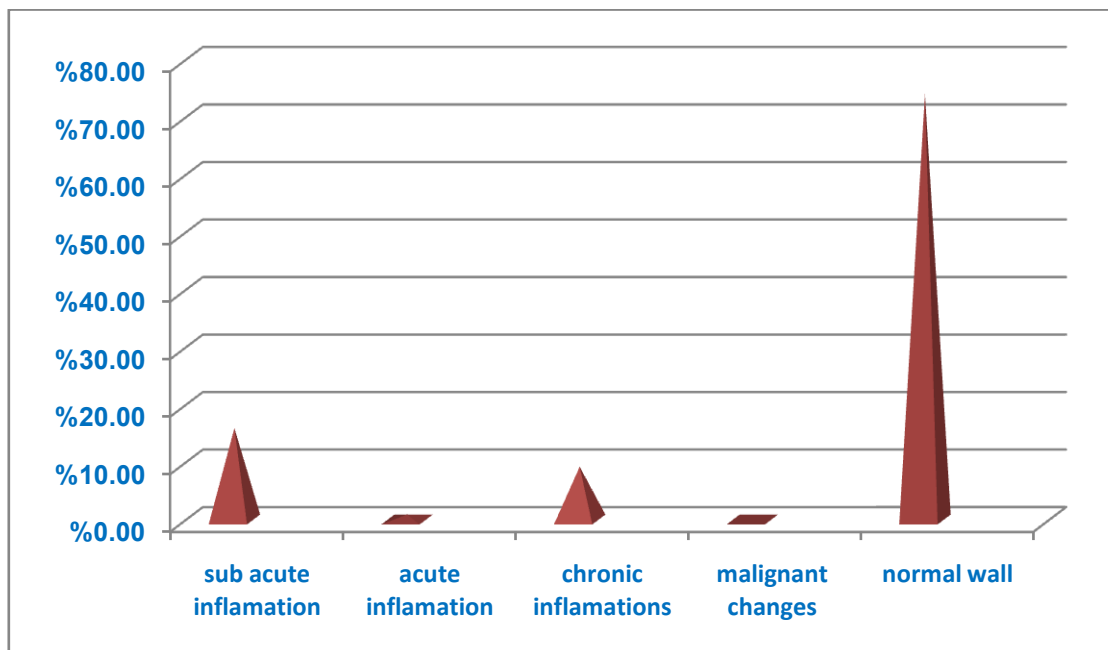


Durations of gall stones

**Figure 2**



**Age distribution of gall stones**  
**Figure 3**



**Figure 4**  
**Histopathological results of gall bladder wall**

#### **IV. DISCUSSION;**

This study was done through 3 years on 458 cases of normal looking gall bladder wall with gall stones, our results were gall stones more common in females (65.3%) than males (34.7) this is corresponding to the other results as a research done by Douglas M Heuman, Apr 01, 2019) durations of gall stones most common in patients with 1--2 years 43% while least occur those who have gall stones 8--10 (6.3%) years this due to most of people did sonography due to any abdominal pain which lead to early discover silent gall stones who are later did elective laparoscopic cholecystectomy.. Most common ages that occur gall stone as in figure 3 in age between 40--49 years while least common at age less than 20 years 1.52% this corresponding to many study as ( study done by Douglas M Heuman, Apr 01, 2019 ) who said 8%-15% of patients younger than 60 years have common bile duct stones, compared with 15%-60% of patients older than 60 years. due to

five predisposing factor followed in ages between 50–59 (29.25%). About the histopathological results as in figure 4 there were no any case detected with malignant cells in the normal looking wall of gall bladder with gall stones even with long duration of gall stones up to 8–10 years this results not corresponding with other study as (Laparoscopic cholecystectomy and unsuspected gallbladder cancer. *Eur J Surg Oncol.* 2001;27:225–228. Which said A gallbladder carcinoma is found in 0.2–3% of all cholecystectomies and 0.09–2% of all laparoscopic cholecystectomies and Completion radical surgery after cholecystectomy for accidentally undiagnosed gallbladder carcinoma. *World J Surg.* 2003;27:266–271. And Surgical management of gallbladder carcinoma: a review. *J Gastrointest Surg.* 2007;11:1188–1193. Which said A gallbladder carcinoma is suspected preoperatively in only 30% of all patients ) in which there were some cases get with percentage of malignant changes in the wall of gall bladder with gall stones . About 15,9% of cases the results were sub acute inflammations , only 0.87 % of cases were acute inflammations this because we excluded the acute inflamed gall bladder in our research ,about 9.17% of cases with chronic inflammations, and 74.01% with normal wall gall bladder

## V. CONCLUSIONS;

Due to negative results of any malignant cells for those a large number of normal looking gall bladder wall with ultrasound with gall stones with different duration even long duration 8–10 years so we don't need to send a histopathological study for a normal looking gall bladder after laparoscopic or open cholecystectomy whatever the durations .by this we prevent more cost on the patients for this examinations and decrease the load on the lap.

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