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Incidence & types of gall bladder cancer in chronic calculus cholecystitis in Al-Nasseryia city

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Abstract:

Chronic cholecystitis is a persistent inflammatory disorder of the gallbladder, commonly arising from recurrent mild or subclinical episodes of acute cholecystitis. It is marked by mucosal atrophy, fibrotic thickening, and distortion of the gallbladder wall. The condition is strongly associated with gallstones, whose continuous mechanical irritation and intermittent obstruction lead to progressive fibrosis, structural alterations, and chronic inflammation Laparoscopic or open cholecystectomy operations are the typical operations done in AL nassiriya city due to acute or chronic calculus cholecystitis. Chronic calculus cholecystitis may be associated with malignant changes due to chronic irritation, which is usually preceded by metaplasia, dysplasia, carcinoma in situ, and then invasive carcinoma. Three hundred sixty patients undergoing successful laparoscopic or open cholecystectomy for chronic calculus cholecystitis, all gall bladders are sent for histopathological examination to detect any malignant changes. Several cases of chronic calculus cholecystitis have developed malignant changes. Tubular adenocarcinoma, most frequently observed in women with gallstones, exhibits a downward invasive growth pattern and carries a poor prognosis. Chronic cholecystitis and epithelial metaplasia are commonly present, while undifferentiated carcinomas, which are also prevalent among females with gallstones, demonstrate the most adverse clinical outcomes.
Patients with chronic calculus cholecystitis should be treated by laparoscopic or open cholecystoctomy as soon as possible to prevent hazards of malignant changes that may be associated with chronic irritation of the stones to the gall bladder mucosa and because of histopathological types of ca. bladder that associated with gall stones are either tubular adenocarcinoma or undifferentiated carcinoma which have bad prognosis thus, after operation should send the gall bladder for histopathological examination to detect any malignant changes and deal with it as early as possible.

Keywords: chronic calculus cholecystitis, malignancy

1-Introduction:

Gallbladder carcinoma represents a relatively uncommon malignancy within the United Kingdom, with an estimated annual incidence of approximately 660 cases. It exhibits a marked gender predilection, occurring more frequently in females, who constitute nearly 70% of all reported cases [1].

Epithelial dysplasia unrelated to gall bladder malignancy occurs in about 1% of cholecystectomies for symptomatic cholelithiasis and is graded as mild, moderate, or severe. In carcinoma cases, adjacent mucosa often shows metaplasia, dysplasia, and carcinoma in situ in 66%, 81.3%, and 69% of cases, respectively. The mean ages for non-cancerous dysplasia (51.9 years), early carcinoma (56.8 years), and advanced carcinoma (62.9 years) suggest a progressive sequence of lesion development. Metaplasia may be gastric, intestinal, or mixed in type [2].

Gallstones and chronic inflammation of the gallbladder (cholecystitis) constitute the principal risk factors for gallbladder carcinoma. Gallstones are solid concretions, primarily composed of cholesterol combined with other biliary constituents. Approximately 80% of individuals diagnosed with gallbladder cancer present with either gallstones or coexisting cholecystitis at the time of diagnosis [3].

Certain studies have demonstrated that a familial history of cholelithiasis is associated with a two-fold increase in the risk of developing gallbladder carcinoma. Moreover, individuals who not only possess a family history of gallstones but also have gallstones themselves exhibit an approximately 60-fold elevation in gallbladder cancer risk compared with the general population [4].

Types of gall bladder cancer:

There exists a multitude of classifications for gallbladder cancer due to the diverse array of cellular types present in the gallbladder. Each of these cellular varieties possesses the potential to undergo malignant transformation. The specific cellular origin from which the malignancy arises within the gallbladder dictates the precise classification of the cancer. For instance, if the neoplasm originates within glandular cells, it is classified as an adenocarcinoma. Conversely, if the malignancy arises from the squamous-like epithelial cells that line the gallbladder, it is termed squamous cell carcinoma, among other classifications [5].

Over 85% of gallbladder malignancies are categorised as adenocarcinomas. The remaining infrequent variants collectively account for approximately 15 out of every 100 cases (15%), indicating that these cancers originated from the glandular cells in the gallbladder's mucosal layer. Glandular cells are typically responsible for producing mucus (a viscous fluid). There are three recognised subtypes of gallbladder adenocarcinomas [3].

These subtypes include papillary adenocarcinoma, tubular adenocarcinoma, and undifferentiated carcinoma, which have been analysed in both clinical and pathological contexts. The findings are as follows: papillary adenocarcinoma shows minimal gender bias and shows little correlation with gallstone presence. Chronic cholecystitis or epithelial metaplasia as underlying conditions are seldom encountered; this subtype typically arises from polyps or adenomas (either villous or tubular), as in other regions of the gastrointestinal tract (GIT). A majority of cases are diagnosed at an early stage and are associated with a favourable prognosis. Only approximately 6 out of every 100 diagnosed gallbladder adenocarcinomas (6%) are papillary adenocarcinomas. These neoplasms develop within the connective tissues that anchor the gallbladder. This variant of gallbladder cancer exhibits a reduced propensity to metastasize to the liver and adjacent lymph nodes. It generally has a more favourable prognosis than most other adenocarcinoma types [7].

In contrast, tubular adenocarcinoma, which predominantly affects females with gallstones, demonstrates a downward invasive growth pattern and is associated with an unfavorable prognosis. Chronic cholecystitis and epithelial metaplasia are prevalent in these cases. Undifferentiated carcinomas are frequently observed in females with gallstones and are characterized by the poorest prognostic outcomes among the three subtypes. It can be concluded that papillary adenocarcinoma exhibits distinct biological behavior compared to both tubular adenocarcinoma and undifferentiated carcinoma. The former appears to primarily originate from the native gallbladder epithelium, while the latter two types more commonly arise from metaplastic epithelium [6]. More than 75 out of every 100 gallbladder cancers (75%) are non-papillary adenocarcinomas. Other scarce types of gall bladder cancers are mucinous adenocarcinomas, the cancer cells are often in pools of mucus, which is how the cancer gets its name. Only about 1 or 2 out of every 100 gallbladder cancers (1 or 2%) are mucinous adenocarcinomas [7].

Squamous cell carcinomas arise from the squamous-like cells that comprise the gallbladder lining, along with the glandular cells. Medical practitioners manage these malignancies in a manner analogous to that of adenocarcinomas. Adenosquamous carcinomas contain both squamous and glandular cancer cells, which may be referred to as having mixed histology. These tumors are also treated similarly to adenocarcinomas [8]. Small cell carcinomas, alternatively designated oat cell carcinomas, derive their name from the distinctive morphology of the cancer cells.

The gallbladder cancer represents the most prevalent cancer of the biliary tract, with notably high incidence rates reported in Chile, Japan, and northern India. The pathogenesis of this neoplasm is multifactorial, yet a strong correlation with cholelithiasis has been consistently observed. Due to its typically nonspecific clinical presentation, gallbladder carcinoma is often diagnosed at an advanced stage. However, in patients with preexisting gallstones, a sudden alteration in symptomatology should prompt consideration of a malignant etiology. When gallbladder carcinoma is identified through histopathological examination, comprehensive staging and evaluation are warranted, with radical surgical resection indicated for tumors classified as T1b or higher. In cases where laparoscopic cholecystectomy has already been performed, additional port-site excision is recommended. Conversely, patients with an intact gallbladder who are suspected of harboring carcinoma should avoid laparoscopic cholecystectomy. For individuals with advanced, unresectable disease, palliative management remains the standard of care, though the efficacy of chemotherapy and radiotherapy in this context requires further investigation [10].

Gallstone disease is a metabolic disorder of the hepato-biliary system, resulting from dysregulation of cholesterol and/or bilirubin and characterised by the formation of calculi in the gallbladder or biliary tract [11]. Gallstones are categorized as cholesterol, mixed, black pigment, or brown pigment stones [12]. Cholesterol stones predominate, with mixed stones containing >50% cholesterol, both arising from persistent biliary sludge composed of cholesterol monohydrate crystals, calcium bilirubinate granules, and polymerized mucin [13–14]. The transformation from sludge to cholesterol stone follows a defined sequence—from diffuse sludge to stones with acoustic shadowing—over 3–36 months, with conversion rates of 5–50% [15–16].

Black pigment stones consist of calcium bilirubinate or polymerized complexes with calcium, copper, and mucin, whereas brown pigment stones comprise calcium salts of unconjugated bilirubin, often associated with infection [17].

Clinically, most gallstones remain asymptomatic (“silent”), with biliary pain developing in ~2% annually over five years, and prophylactic cholecystectomy is generally unwarranted [18]. Among symptomatic patients, recurrence occurs in 38–50% per year, whereas 30% experience no further episodes. The annual risk of biliary complications remains low, at 1–2%, and appears stable over time [19].

Gallstone disease is a disorder of the hepato-biliary system arising from metabolic disturbances in cholesterol and/or bilirubin. Chronic calculous cholecystitis is typically diagnosed in patients presenting with recurrent biliary pain, often localized to the right upper quadrant or epigastrium and frequently radiating to the right scapular region. The pain varies in intensity and duration, is commonly precipitated by fatty foods, and may be accompanied by a bitter taste, nausea or vomiting, abdominal bloating with borborygmus, and altered bowel habits such as constipation or diarrhea. Impaired gallbladder emptying is frequently observed, and ultrasonography typically reveals gallbladder wall thickening (3–4 mm) along with the presence of intraluminal gallstones. Cholecystectomy is generally reserved for patients who develop clinically significant symptoms [1,20].

2- Patients and methods

This study was conducted at Al Hussein Teaching Hospital, a private hospital, and a private lab. Through 4 years from February 2020 till January 2024 on 360 patients . after we diagnose the cases by history, clinical examination and specific investigation, take inform concept from the patients we did for them successful laparoscopic and open cholecystectomy due to chronic gall stones cholecystitis, we send the gall bladders to the histopathological examination either to AL hussien teaching hospital lab. or to the private lab. To detect any malignant changes to the gall bladder. We classified patients with any malignant changes according to malignancy type, age, duration of gallstones, gallstone type, and number and size of stones.

3- Results

From 360 patients 22 patients (6.1%) have malignant changes by histopathological study, 20 patient (90.9%) have adenocarcinoma while 2 patients (9.1%) have sequamous carcinoma, about types of adenocarcinoma 16 patients (80%) are tubular types while four patients (20%) are undefrentiated type, 13 patients (59%) of those 22 patients have duration of gall stone more than 15 years, seven patients (31.8%) duration between 10—15 years, two ptients (9%) have 5—10 years duration. Sixteen patients (72.7%) are females, and 6 patients (27.3%) are males. According to stone type, 18 patients (81.8%) had malignant changes associated with mixed stone types, while only 1 patient (4.5%) had cholesterol stones, and three patients (13.6%) had pigment stones. Eight patients (36.3%) with malignant changes have multiple small stones, while 14 patients (63.3%) have single or double stones.

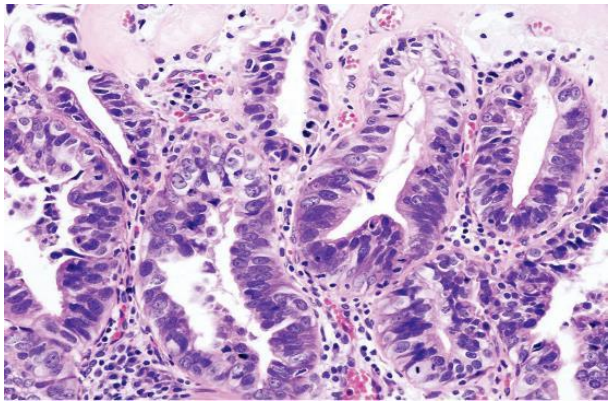

Figure 1: Shows moderate differentiation of gall bladder malignancy. 40 X power field.

Figure 2: Gall bladder section shows papillary type adenocarcinoma of the mucosa.

Figure 3: Shows innumerable gallstones and diffuse neoplastic mural thickening (white arrows).

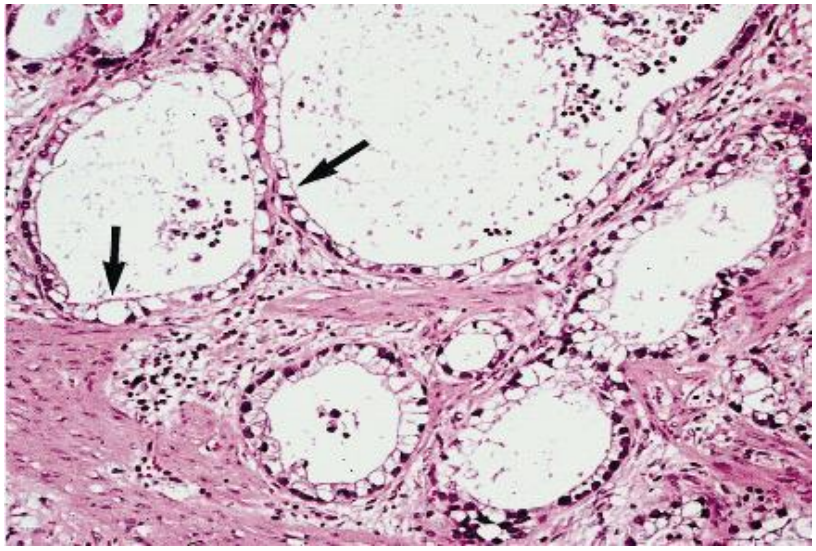

Figure 4: shows gallbladder adenocarcinoma with intestinal metaplasia glands and showing goblet cells (black arrows). 40X power field.

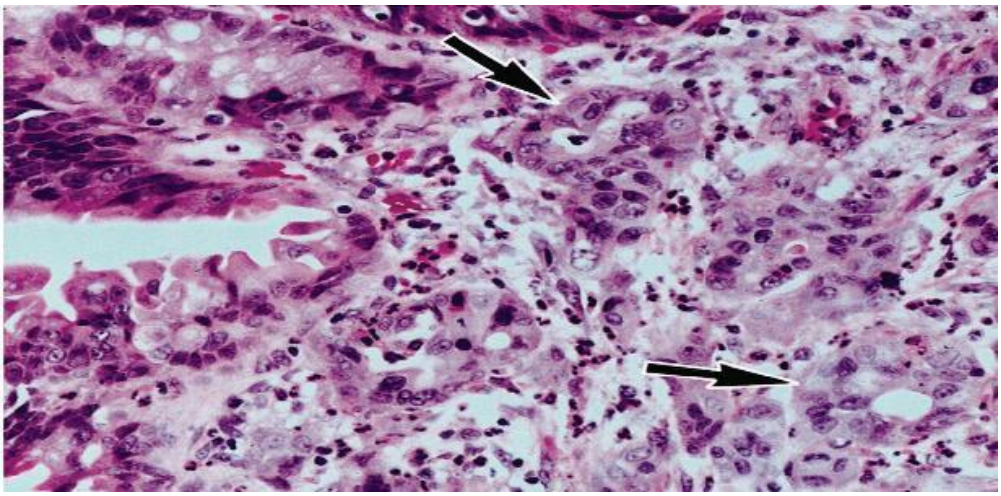

Figure 5: Moderate and well-differentiated adenocarcinoma. Shows mucosa lined by highly a typical epithelium consistent with high-grade dysplasia. Below the surface are malignant glands (arrows) and small clusters of tumor cells infiltrating the lamina propria. The stroma is scant, and there is a mild infiltrate of acute and chronic inflammatory cells.

Figure 6: Gross section in poorly differentiated adenocarcinoma of the gallbladder with pancreatic and liver metastasis

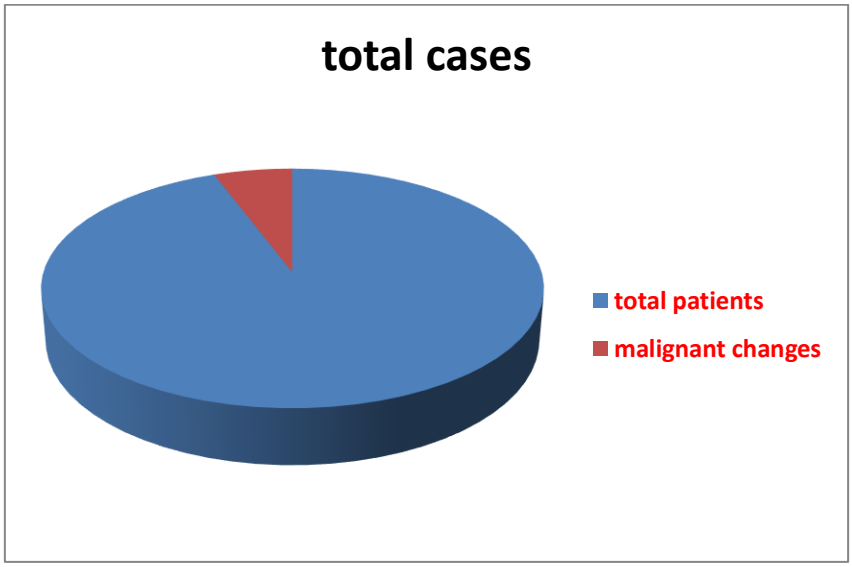

Figure 7: Percentage of malignant changes

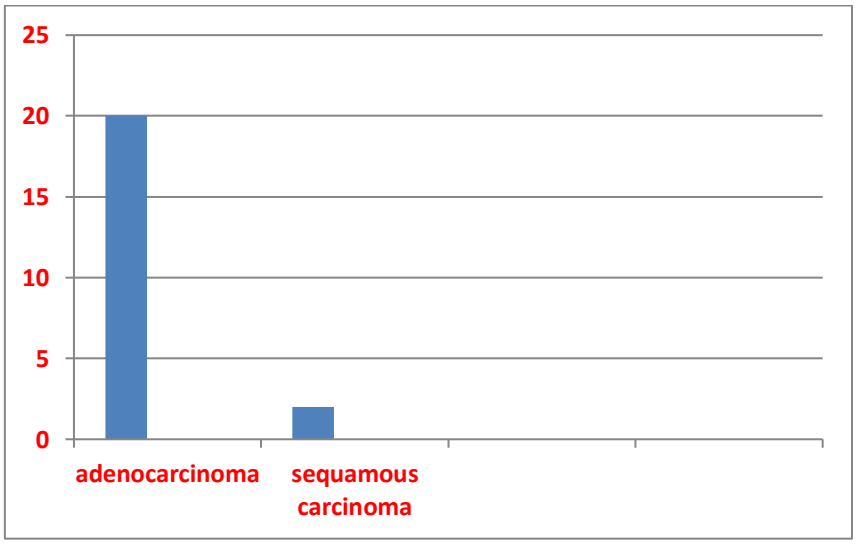

Figure 8: According to the types of malignancy;

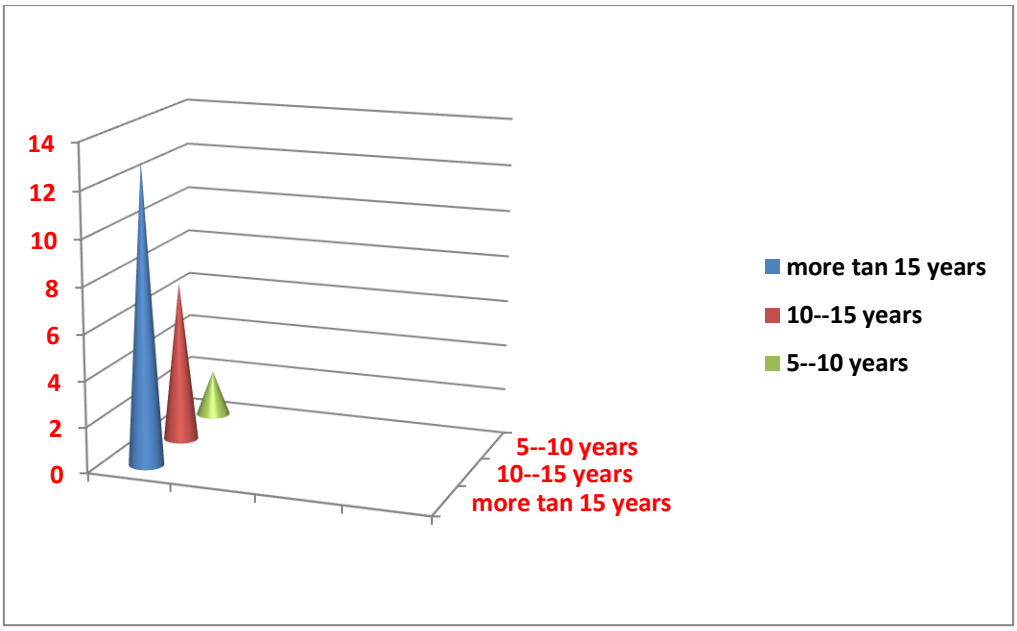

Figure 9: Malignant changes. According to the duration of gallstones

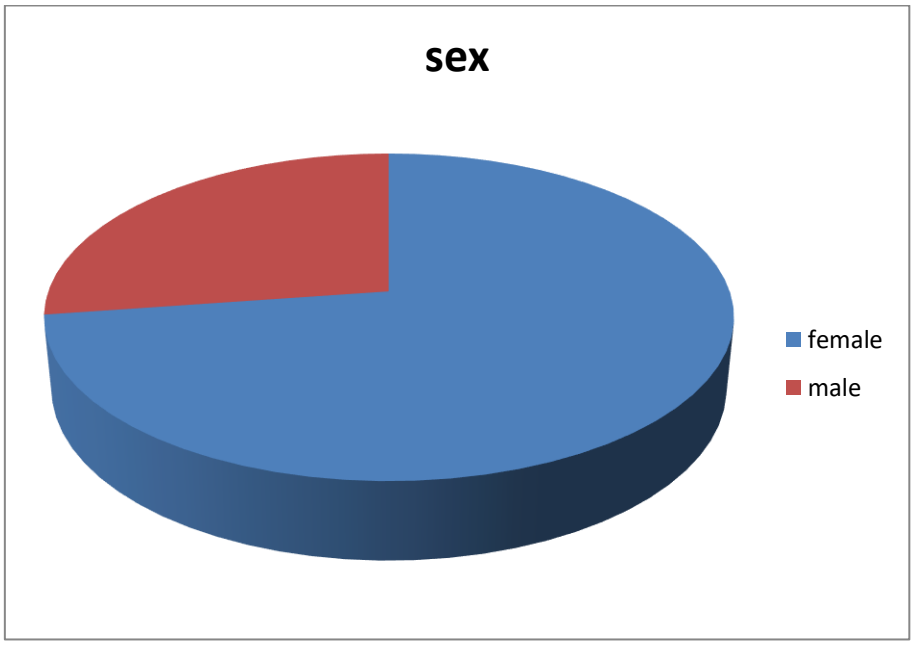

Figure 10: Malignant changes according to the sex

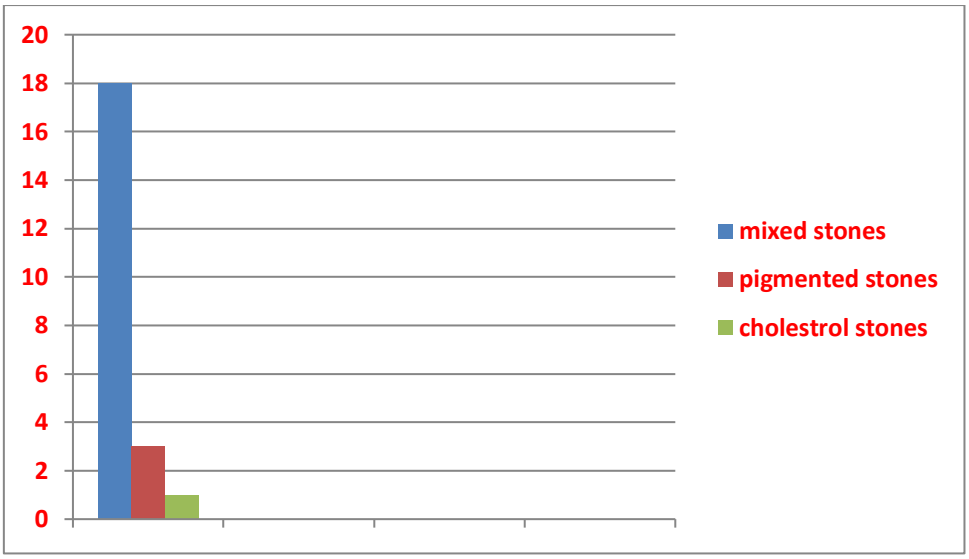

Figure 11: Incidence of malignant changes according to the types of stones

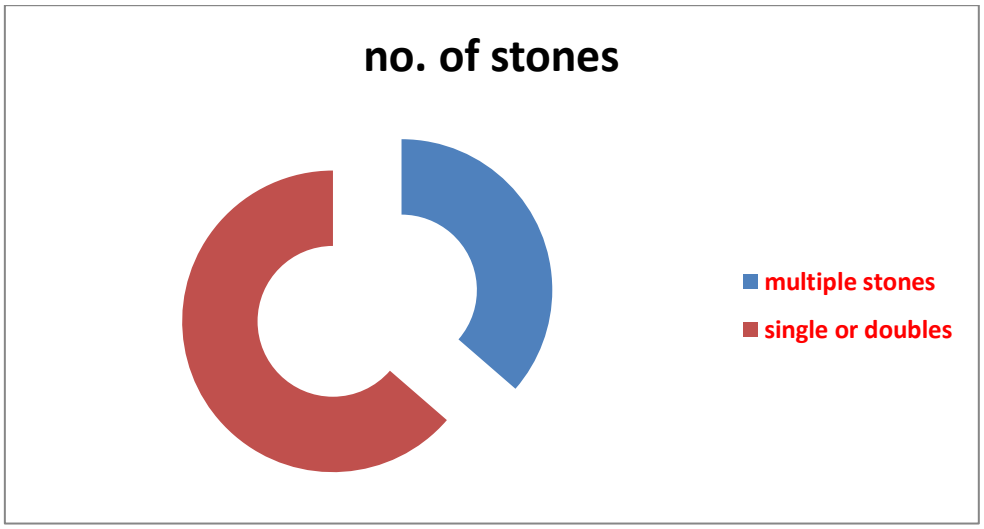

Figure 12: Malignant changes according to the number of gallstones

4- Discussions

Gallbladder cancer represents the most common type of tumour in the biliary tract. The etiology of this tumour is complex, but there is a strong association with gallstones from chronic irritation cause metaplasia pyloric or intestinal or both then dysplasia and then carcinoma in situ , from our study we found malignant changes in gall bladder more common in female ,adenocarcinoma which arise from the glandular lining epithelial cells in the gall bladder is the predominant pathological types while sequamous carcinoma which arise from the skin like cells in lining epithelium of mucosa of gall bladder is a rare in relation to the causative agents that we dell with it which is the gall stones tubular type of adenocarcinoma is the commons' type of adenocarcinoma then undefrentiated type which carry poor prognosis ,the malignant changes highly related to the duration of gall stones 59% associated with duration more

than 15 years, mixed type of stone are related more with malignant changes 81.8%, while malignant changes more related with single or double large stones 63.7%.

5- Conclusion

From our study, we detect that there are some percentages of malignant changes associated with chronic calculus cholecystitis mainly adenocarcinoma especially tubular and undefrentiated types of adenocarcinoma which are carry poor prognosis so we advised for early laparoscopic or open cholecystectomy when patient discover to have a gall stones even if he or she asymptomatic to prevent malignant changes and early detection of gall stones patients by an regular ultrasongraphy to the people who are more susceptible to gall stones people who carry 5F (female, fifty, fertile, fatty. ect) and patients who complaining from GIT upset after fatty meal.

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