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A Gallstones diseased man have a higher risk of its Complication

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ABSTRUCT

The aim of this study was to determine the effect of male gender on the clinical presentation of symptomatic gallstones disease and its sequel complications like acute Cholecystitis, common bile duct stone, obstructive jaundice, acutecholangitis, acute pancreatitis and rate of conversion from laparoscopic to open Cholecystectomy. Laparoscopic cholecystectomy (LC) has been accepted as standard procedure for the management of symptomatic cholelithiasis even when the gallbladder is acutely inflamed. With the accumulated experience in the management of acute cholecystitis, some factors including male gender were recognized to influence the clinical presentation of symptomatic cholelithiasis and increase the conversion rate during LC. So this retrospective study tried to clarify the correlation between male gender and the clinical presentation of symptomatic cholelithiasis and rate of convertions.

Methods: The medical records of all patients presenting with symptomatic cholelithiasis from March 2019 to August 2019 were evaluated. These cases were divided into four groups as follows: (1) elective laparoscopic Cholecystectomy group: patients with a history of biliary colic or acute attack of cholecystitis but whose LC was performed electively without any inflammatory change in the gallbladder during operation; (2) acute gallstones complication group: patients presenting with acute cholecystitis, and treated conservatively ,common bile duct stone and cholangitis and acute pancreatitis due to slipped stone to common bile duct(CBD). (3) acute conversion group: patients who underwent LC during the course of acute cholecystitis but the procedure were disturbed by severe inflammatory change so they were converted to open surgery; (4) outpatient group: patients presented with right upper quadrant pain and diagnosed as they got gallstone disease. The correlation of gender, gallstones disease complications, and admission as inpatient in surgical word, rate of elective operation and rate of conversions were assessed among these four groups.

Result: We found that: (1) the male odd ratio for post-operative complication was 1.9 and relative risk of 1.87 (men have higher risk for post-operative complication than women, although there was no significant difference statistically). (2) in the operative LC group: male patients had significantly more open conversions than females (p=0.05, t-test); (3) there was significant difference between the men and women regarding the pre-operative complication of gallstones (p= 0.01, t-test). the male odd ratio was 2.6 and relative risk was 2.5. in the acute Cholecystitis groups.

Conclusion: men have higher risk for gallstones disease complication , so the early management and operation is important to prevent and decrease the risk.

Keywords: gallstones disease, Cholecystitis, male gender Cholecystitis ,Laparoscopic Cholecystectomy, Male Gender Acute Cholecystitis, Open Cholecystectomy

1-INTRODUCTION

Gallstone disease is common in the adult western population (10–15%), particularly amongst females and the older population.[13-14-15] Between one and four percent of patients with gallstones become symptomatic each year[3] and may need to be considered for operative intervention. Untreated gallstones can cause life-threatening illnesses such as acute cholecystitis, cholangitis, obstructive jaundice and acute pancreatitis.LC has become the operation of choice for symptomatic gallstone disease[16-17-18-19-20] and is considered to be the most common laparoscopic intervention in general surgery[21]Due to its reduced post-operative pain, shorter hospital stay, operative morbidity and mortality, Laparoscopic cholecystectomy is performed selectively in acute cholecystitis.. Although LC has generally a low incidence of complications, the conversion rate to open surgery and occurrence of morbidity and mortality are particularly affected by the presence and severity of inflammation[19-22] advancing patient's age, male gender[23-24-25-26-27] greater body weight[16-19-23] and previous abdominal surgery.[7] Gallbladder stones have high prevalence among gastrointestinal disorders.developing gallstones are dependent on several factors including age, sex, and race. Obesity, pregnancy, nutrition habits, sickle cell disease and thalasemia also have been identified to increase risk of gallstones formations.

Women are three times more likely than men to develop gallstones, and its prevalence in the first-degree relatives of complicated patient is two times more [1].

In most people gallstones develop without symptoms; however some of them also experience symptoms such as severe pain due to bile duct obstruction. Diagnostic procedures of gallstones include:, ultra-sonography, computed tomography (CT) scan and typical symptoms in case of symptomatic Cholecystitis.

More than 80% of gallstone carriers are unaware of their gallbladder disease [33-34], but about 1–2% per year of patients develop complications and need surgery [35]

Aim of this study was to evaluate the following:

1. Is male gender have correlation with pre-operative complications of gallstones disease.
2. Is male gender have correlation with post-operative Cholecystectomy complication.
3. Is male gender have correlation with open conversions of laparoscopic Cholecystectomy.

Risk factors: Female gender, fecundity, and a family history for gallstone disease are strongly associated with the formation of cholesterol gallstones [36] Obesity [37-38-39] as well also other factors contributing to the metabolic syndrome [28] such as dyslipidemia (in particular hyperlipoproteinemia type IV [29-30] with hypertriglyceridemia and low HDL cholesterol), hyperinsulinemia-insulinresistence [31, 32] or overt type 2 diabetes are risk factors for the development of gallstones, itself supposed to be a complication of the metabolic syndrome [Among specific dietary factors, short-time high cholesterol [39] as well as high-carbohydrate diets were associated with increased risk for gallstones [40, 41], and independent of weight reduction. On the other hand, rapid active weight loss [42, 43] and weight cycling [44, 45] strongly increase the risk for the development of gallstones.

Complications: Complications of gallstone disease are inflammations of the gallbladder (Cholecystitis), the biliary tract (cholangitis), and the pancreas (biliary pancreatitis). Persistent pain, fever, and jaundice indicating acute cholangitis are known as Charcot's Triad. Cholecystits/cholangitis are treated with biliary secreted antibiotics; however, early laparoscopic cholecystectomy in acute cholecystitis shortens hospital stay without increasing complication rates [46]. Bile duct stones are removed endoscopically (ERCP with endoscopic papillotomy, EPT) [47]. Gallbladder cancer is rare but closely related to gallbladder stones[48], nevertheless for cancer prevention, prophylactic cholecystectomy is not recommended[49]. However, empiric laparoscopic cholecystectomy seems to be a reasonable option for idiopathic pancreatitis [51] for which occult gallstone disease or biliary sludge [50] seem to be a frequent cause.

2-METHODS

In a retrospective and epidemiological study, a total of 787 patients who were consult the surgical outpatient clinic ,were selected from March 2019 to August 2019 in Al-numan teaching hospital, Iraq/Baghdad city. Inclusion criteria were women or men with gallstones disease and acute or chronic cholecystitis from 25 to 70 years of age who seek managements of their condition. Exclusion criteria were pregnancy with gallstones, elderly with sever co-morbidity who manage with cholecystostomy alone, emergency cases as acute abdomen with perforated gallbladder, as well as diabetic patients and cardiovascular disease patients. Information about patient's age, gender, time diagnosis of being gallstones carrier, pre-operative inpatient admissions due to gallstones complication and type of complications, post-operative complications, and switch from laparoscopic to open Cholecystectomy were recorded. Data analysis was done with the Statistical Package for Social Science (SPSS), IBM (Armonk, New York), version 21. A Kolmogorov–Smirnov test was significant for all the variables investigated [1] Therefore a normal distribution was not probable. Thus the study population was statistically described using absolute number of cases, percentages, medians, ranges, odd ratio and relative risk. Significances were calculated using the Mann-Whitney *U* Test with levels of significance at $P < 0.05$ [2] Furthermore, a multivariate analysis was used to examine if the male gender was an independent risk.(odd ratio and relative risk) Primary endpoints included the numbers of outpatient clinic patients ,number of pre-operative complication, the rate of operations and rate of conversion. Secondary endpoints included post-operative complication and its type.

3-RESULT

Among 787 patients were assessed in our study, 358 (45.4%) were men and 429 (54.5 %) were women. Table 1 shows characteristics information of study's subjects. Evaluating of patients according to sex and age revealed that the men average age were 42.2 years (stander deviation $\pm$ 8.76)and women average age were 43.4 years (stander deviation $\pm$ 8.6) of gallbladder stones, the outpatients cases were 634 cases 286 men and 348 women , the total operations were 105 of

which 32 cases of male labroscopicaly done with 7 cases were open converted , 62 cases of laproscopicaly done in female add 4 cases switch to open Cholecystectomy, the laparoscopic Cholecystectomy and open conversion were different statistically and were higher in men than women(p = < 0.05). But Odd ratio of conversion was less than one which is mean (male gender has no effect of conversion)(table 5). The total number of per-operative complications and post- operative complications were also mentioned and outlinedin Table 1.

Table 1: Characteristics information of 787 patients with gallstones disease (data of the study).

Variable	Number	Mean (average)	Stander deviation
Men	358	42.2 years	8.76
Women	429	43.4 years	8.6
Outpatient **Male:** **Female:**	634 286 348	317	43.8
Total operations **Male:** **Female:**	105 39 66	52.5	21.2
Laparoscopic operation **Male:** **Female:**	94 32 62	47	21.2
Open conversion **Male:** **Female:**	11 7 4	5.5	21.2
Pre-operations complication **Male:** **Female:**	30 22 8	15	9.8
Post operations complicatios **Male:** **Female:**	18 11 7	9	2.8
Total cases male and female:	787		

Table 2 shows in addition to means and stander deviation ,the percent of operations for male and female were it was 13.6% of male consult the outpatient and 18.9 % of the female consult the outpatient clinic in the same period .- Table 3 described the overall risk of per-operative complications of gallstones diseases in male and female ..while the number and type of complication of pre-operative complications of gallstones in both male and female was outlined in Table 4-,the overall post operative complications of the Cholecystectomy in male and female were showed in Table 6 followed by Table 7 in which the type of post Cholecystectomy complications were outlined .

In Figure 1 the subject of study was outlined and compared which were statistically significant, followed by Figure 2 were the correlations of laparoscopic Cholecystectomy and open conversions were compared.

Table 2: Total outpatient gallstone disease and the total operations (male and female):

Variables	outpatients	operations	Mean	St. deviation	Percent	Total
Male	286	39	159	179.6	0.136 (13.6%)	325
Female	348	66	205	202.2	0.189 (18.9%)	414
Total	634	105				739

Table 3: the overall risk of pre-operative complication gallstones.

varaible	complications	Outpatient	Total	Mean	SD±
Male	33	286	319	159.5	178.8
Female	15	348	363	181.5	235.4
Total	48	634	682		

Odd ratio of men= 2.67
Relative risk of men = 2.5
***P value = < 0.01**

Table 4: types of pre-operative complications of gallstones:

complications	Male	Female	Total	Mean	SD±	Odd ratios
acute Cholecystitis	16	6	22	11	5.6	**2.8**
CBD and obstructivejaundice	7	4	11	5.5	0.7	1.52
cholangitis	4	2	6	3	1.4	2.4
pancreatitis	6	3	9	4.5	2.1	**2.43**
Total	33	15	48			

***P value for acute Cholecystitis in men is less than 0.01**

Table 5: lab and conversions

varaible	Lap	Open conversions	Total	Mean	SD±
Male	32	7	39	19.5	21.2
Female	62	4	66	33	21.2
Total	94	11	105		

Odd ratio =0.29 (< 1)
***p value = < 0.05.**

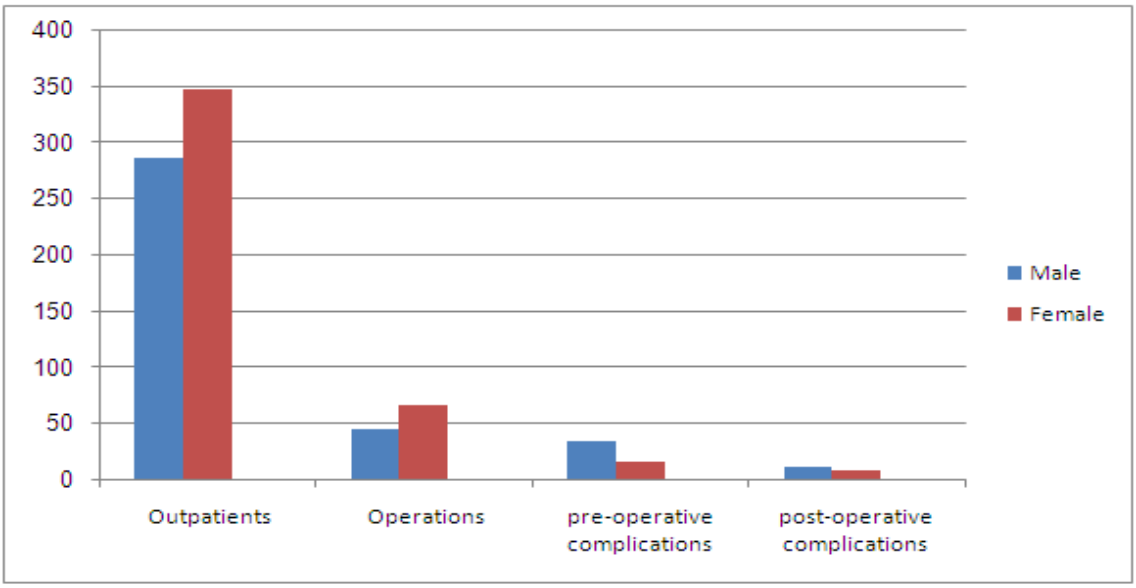
Table 6: overall post- operative complications:

varaible	complications	Outpatient (gallstone)	Total	Mean	St ±
Male	11	286	297	148.5	194.4
Female	7	348	355	177.5	241.1
Total	18	634	652		

Odd ratio:1.9
RR: 1.87
P value: > 0.1 (no statistical significant)

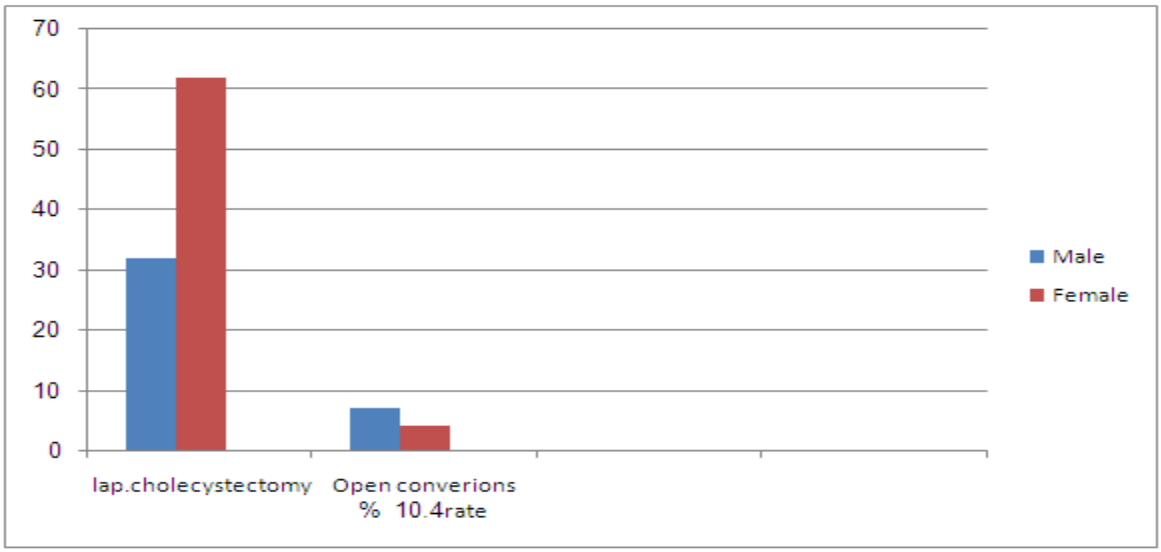
Table 7: types of post- operative complications of Cholecystectomy:

complications	Male	Female	Total	Mean	St.Deviation	Odd ratio
Bile leak	9	5	14	7.5	2.8	2.1
CBD and obstractive jaunduce	2	1	3	1.5	0.7	2.4
cholengitis	0	0				
pancraetitis	0	0				
Other	0	1	1			
Total	11	7	18			



Rate of operation 18.9% for male and 13.6% for female ..p value=>0.1

Fig 1: Demographic distributions of the result of the data in the study.



Odd ratio =0.29 (< 1) ….***p value = < 0.05 .**

Fig 2: laparoscopic cholecystectomy and conversions rate in male and female

Rate of conversion 10.4% (6.6 % for male group and 3.8% for the female group

Rate of conversion: Eleven cases (10.4%) were converted from laparoscopic operation to open Cholecystectomy. The rates of conversion were 6.6% (7/105) and 3.8% (4/105) in the male and female group, respectively. This difference was statistically significant .thatis mean, the rate of conversion was significantly higher in male patients compared to female patients of the same age group ($P = < 0.05$). nevertheless the odd ratio for male was less than one(0.29) that is mean there was no effect of gender on the operations however the Conversion usually was performed due to the inability to clearly identify the structures within the triangle of calot [11-22]. All cases that has been converted to open Cholecystectomy was have more hospital admission probably due to post operative complications. as well as the durations of surgery was more long in male age group nevertheless it s not included in the study

Complications: Postoperative complications included 18 cases . were 11 cases in male nine of these were bile leak post-operatively and 2 cases were slipped stone to CBD (common bile duct) yielded to obstructive jaundice .seven complicated cases were in female group , three of these was bile leaks and one was slipped stone to CBD to produces obstructive jaundice and one was only wound infection. All of these complicated cases were management conservatively or with ERCP and sphenterotomy . There was no significant difference amongst both groups with respect to postoperative complications (Table 6). There was no mortality in this series

.

4-DISCUSSION

Although the gallstones Cholecystitis are more common in female population [14] the duration of lap Cholecystectomy operation is longest and more complex in male age group [5].This study was conducted on 787 patients. In our study association of gallbladder gallstones disease and its associated complication pre- and post operation were compared between male and female gender (Fig.1 and Table 3), the result was statistically significant the odd ratio was **2.6** , relative risk of men was **2.5** and the **p** value was less than **0.01** . In similar study done by Al-Jaberi and et al. (2003) had been indicated that gallbladder gallstones disease complications was more prevalent in men [51]. Our results about prevalence of gallbladder gallstones diseases complications in sex type showed high prevalence in men relative risk **2.5** and It is in accordance with study of Stefanidis and et al. (2006) [54].

If we have a look to Table 6, the rate of conversion were studied were it was evident in male age group and it was statistically significant ($p = < 0.05$).and if we have a look to the Fig 2 we find the overall rate of conversions was 10.4 % it was higher in men 6.6 % than women 3.8% , although the odd ratio for men operative conversion was less than one (Odd ratio = **0.29**) which mean the men gender is not an indicator for conversion per see however, the result was statistically significant ($p < 0.05$, df =1) in other mean the conversion was mostly due to long operation and the difficulty of operation in male group than female , this also found in the study done by polychorinis and et al., a total of 1804 patients who were enderwent Cholecystectomy, from 1992 to 2004, They found that factors such as men, age of more than 60-year-old, surgery of upper abdominal, diabetes, severity of inflammation were associated with switch to open surgery[54].[55]. Our results showed high prevalence of pre-operative acute Cholecystitis in men than women Table 4 with odd ratio **2.8 and p value < 0.01**…Merriam LT and et al, (1999) studied on 154 patients in USA.

They found that risk of gallbladder gangrene and then switch to open surgery is higher in men[54].In a study by Gharaibeh and et al. (2001)995 patients from 1994 to 1999 who underwent laparoscopic cholecystectomy were evaluated. They showed that 791 patients were with acute cholecystitis and 204 patients with chronic cholecystitis. From those with acute cholecystitis, 27.8 % were needed to open surgery. From 27.8 %, 4% were women and 23.8 were men[51].. Based on their results, .In our study the rate of operation for both male and female were evaluated in table 2 the rate of laporoscopic operation were higher in female aged group 18.9 % while in men were 13.6 % nevertheless it was statistically not significant because the p value was more than 0.1 . Laparoscopic Cholecystectomy is the standard procedure for benign gallbladder disorders.

With increasing experience, LC has been increasingly employed to manage acute Cholecystitis. Over the last decades many authors have sort to characterize predictive factors for a challenging or complicated laparoscopic Cholecystectomy [3-8] Donkervoort *et al,* [4] and Lee *et al,* [9] have described the male gender as a risk factor for complication in patients undergoing LC. According to Van der Steeg *et al* [10]the male gender, age (>65 years), acute Cholecystitis and recent obstructive jaundice represent independent predictive factors for conversion in patients undergoing LC. Al-Mulhim [7]on the other hand, did not find any difference between both genders after reviewing 391 cases of LC. Therefore, it is still not clear whether or not the male gender is an independent risk factor for complicated LC.Surgery lasted significantly longer in the male group compared to the female group. A multivariate analysis confirmed the male gender as an independent risk factor for prolonged surgery.

The rate of conversion in this study was 10.4%. This is higher than the rates reported in other series [5-6-13] The rate of conversion was higher in the male cohort (6.8% versus 3.6%). This difference, however, was statistically significant p = < 0.05 t-test. A similar trend was reported by Peng and colleagues [12]

The post- operative complications were included in our study Table 6 and Table 7 , were the result of statistical analysis of chi-square and p value were not significant (p > 0.1) nevertheless the odd ratio and relative risk of male in post-operative complication were 1.9, 1.89 respectively and its mean the male gender might be risk of post – operative complications .regarding the kind of post-operative complication Table 7 we find the bile leak were more prevalent in both sex but slightly more in male with odd ratio 2.1 the second complication was slipped stones and post-operative rising bilirubin and obstructive jaundice, odd ratio for male was 2.4 .

As mentioned above the gallstone disease is more prevalent in female [14], however in our study we find the pre- operative complications is more prevalent in male Table 3 and Table 4, the total cases were 48 in total , male group were 33 and the rest 15 cases were female . again in statistical point of view it were significant as the chi-square test was used and yielded **p value less than 0.01** , the odd ratio of male for the overall pre-operative complication of gallstones was **2.67**with relative risk RR was **2.5** ...acute Cholecystitis was more prevalent complications in both gender 16 out of 33 male and 6 out of 15 female this bring about odd ratio for men **2.8.and p value less than 0.01** which mean statistical significant another complication (CBD slipped stones with or without jaundice, cholangitis, and acute pancreatitis)were more prevalent in male group with odd ratio **1.5/2.4/2.43** respectively .

From the above we defined factors such as acute Cholecystitis, CBD stones , obstructive jaundice, cholangitis, acute pancreatitis and switch to open surgery, and gender were evaluated. All these factors were higher in men than women. Therefore, man factor was key element in increasing risks of cholecystitis's complications. Nevertheless , gallstones disease was higher in women than men. Also Our results suggest that the male gender is an independent risk factor for a challenging or complicated laparoscopic Cholecystectomy (LC) in patients with gallstones disease.

CONCLUSION

- As our findings demonstrated, we suggest that men with gallstones disease need rapid surgical intervention to prevent and reduce complications of disease.
- Men have a higher risk for pre-operative complications of gallstones disease.
- Men have higher post-operative complication of Cholecystectomy although not significant statistically
- Men have higher rate of open conversions type of operations which is statistically significant. Male gender is an independent risk factor for complication in patients undergoing laparoscopic Cholecystectomy for acute Cholecystitis.

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