Prevalence of Gall Stones in Egyptian Patients with Chronic Liver Disease

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Abstract: Liver cirrhosis and chronic hepatitis are risk factors for inflammation of gall bladder. *Aim of the work:* The primary aim of this study was to determine the prevalence of gallstone disease (GSD) in Egyptian patients with chronic liver disease. The secondary aim was to study the risk factors and the association of GSD with the severity and underlying aetiology of liver disease. The prevalence of gallstones in Egypt with high rate of hepatic infection especially HCV was studied. *Methods:* 1260 patients included in this study with liver cirrhosis and chronic hepatitis based on histological diagnosis or compatible clinical, laboratory and ultrasonographic findings. All patients underwent ultrasound abdominal scanning. The presence of gallstones, its number and size were noted. *Results:* There was highly significant difference regarding the presence of gallstones in chornic HCV group (5%), in chronic HBV group (1%), in HCV-induced cirrhosis group (33.7%) and in HBV-induced cirrhosis group (15.7%). *Conclusion:* Our study suggests that chronic HCV infection is an important risk factor for the development of GSD in Egyptian patients with chronic liver disease.

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1. Introduction

Gallstones are major cause of morbidity and mortality throughout the world (**Zhang *et al.*, 2006**). The prevalence of gallstones in patients with chronic liver disease (CLD) is significantly higher when compared with the general population (**Stroffolini *et al.*, 2007**). Moreover, its prevalence is related to the degree of liver dysfunction (**Bini *et al.*, 2005; Stroffolini *et al.*, 2007**). The pathogenesis of this phenomenon is unclear but may be related to altered pigment secretion, increased oestrogen levels and/or abnormal gallbladder motility in cirrhosis (**Shaffer *et al.*, 2006**). Despite the high prevalence of chronic HCV infection in Egypt, little is known about its relation to gall stone disease (GSD) and there are no population-based studies of GSD among persons with HCV infection.

Aim of the study:

The primary aim of this study is to determine the prevalence of gallstone disease (GSD) in Egyptian patients with CLD and their association with the underlying aetiology and severity of liver disease.

2. Patients and methods:

The study included 1260 patients with CLD who were selected randomly from the outpatient and inpatient departments of the National Liver Institute, Menoufiya University. NLI is a research and referral centre for liver diseases especially from the Delta region which is an endemic area of liver disease in Egypt. The study was approved by the local institutional review board. Informed consent was provided by all participants. For each subject, demographic, clinical and aetiological data were recorded by using a precoded questionnaire. A number of laboratory tests, such as fasting plasma glucose, total cholesterol, triglyceride, aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), hepatitis B surface antigen (HBsAg), hepatitis B core IgG antibody (HBc IgG), and antibody to hepatitis C virus (HCV-Ab) and HCV-RNA by PCR method were analyzed.

All patients, underwent ultrasound abdominal scanning, performed with a 3.5-or 5-MHz transducer. The number and size of gallstones, the gallbladder wall thickness and the inside diameter of the portal vein were noted.

Cirrhosis of the liver was diagnosed based on typical clinical features and sonographic findings according to the following criteria: surface nodularity of the liver; coarsening and nodularity of the liver parenchyma with ascites, splenomegaly, or evident collateral circulation shown in US. The severity of cirrhosis was categorized according to the Child–Pugh classification.

Patients with infection, gastrointestinal bleeding, diabetes mellitus, or uremia were excluded.

Statistical analysis:

Statistical analysis was done using the Statistical Package for Social Science software (SPSS, Chicago, IL, USA). A *P* -value less than 0.05 was considered statistically significant.

3. Results

The current work studied 1260 patients with CLD were: Their mean age was 47.7±11.7 years with a range from 17-86 years. There were 931 (74%) males and 329 (26%) females. Chronic HCV infection was found in 1009 (80%) patients and 251 (20%) had chronic HBV infection. The high prevalence of HCV (80%) in the studied patients was due to the fact that all of them were chosen from the in and outpatient clinic of the National Liver Institute. Table 1 summarises the demographic and clinical characteristics of patients included in the study

The prevalence of GSD in the examined patients was 21.8% (275 of 1260 patients). Patients with GSD tend to be older (p value <0.05), but they did not differ significantly according to sex. Patients with GSD tend to have thickened gallbladder wall (≥4 mm) when compared to patients without GSD (33.8% *Vs* 66.2%; p value <0.05).

In patients with GSD, the mean serum albumin level was significantly lower than in patients without GSD (2.2 g/dL *vs* 3.1 g/dL, p value <0.05). Other factors, including AST, ALT, GGT, cholesterol and TG and BMI, were not significantly associated with GSD.

When the data analysed according to the severity of liver disease, patients with liver cirrhosis had the highest GSD prevalence in each aetiological category when compared to patients with chronic hepatitis without cirrhosis (30.4% *Vs* 4.1%; p value <0.05) as shown in table (2). The risk of GSD in patients with liver cirrhosis was 7.3 times the risk in patients with chronic hepatitis (odds ratio 10). In addition, the prevalence of GSD increased with severity of the disease according to Child-Pough classification. In Child-Pugh A, it was 9.2%. In Child-Pugh B it was 18%, and in Child-Pugh C it was 36.8%. This difference was statistically significant (p value < 0.05) as shown in table (3).

GSD was more encountered in patients with chronic HCV infection than HBV infection (24.7% *Vs* 10.4%; p value <0.05). The risk of GSD in patients with chronic HCV infection was 2.4 times the risk in patients with chronic HBV infection (odds ratio 2.8, CI 95%) as shown in table 4. Sex is an additional risk factor in patients with CLD as the risk was higher in females than in males (OR 3.7 vs 2.5)

Multiple logistic regression analysis of possible risk factors for gallstones in patients with CLD showed that severity of liver disease and HCV infection were independent risk factors for the development of gallstone in those patients.

Table 1: Baseline characteristics of enrolled subjects stratified according to presence or absence of gallstone disease (GSD)

	All patients	Patients with GSD	Patients without GSD	p value
Number	1260	275 (21.8%)	985 (78.2%)	
Age (mean±SD)	47.7± 11.7	52±9.9	46.5±11.9	<0.05
Sex(No of patients,%) Male Female	 931 (74%) 329 (26%)	 193 (15.3%) 82 (6.5%)	 738 (58.6%) 247 (19.6%)	0.1
Albumin (mean±SD)	2.95±1.49	2.24±0.78	3.15±1.5	<0.05
ALP (mean±SD)	106.84±51.94	100±50	108±52	0.06
GGT (mean±SD)	60.05±65.32	59±58	60±67	0.75
Stage of liver disease Chronic hepatitis Liver cirrhosis	 410 (32.5%) 850 (67.5%)	 17 (4%) 258 (30.5%)	 393 (96%) 592 (69.5%)	<0.05
Aetiology of liver disease (No of patients,%) Chronic HCV Chronic HBV	 1009 251	 249 (24.7%) 26 (10.4%)	 760 (75.3%) 225 (89.6%)	<0.05
Increased GB wall thickness (No of patients,%)	740	250 (33.8%)	490 (66.2%)	<0.05

Table 2: Comparison of patients with chronic hepatitis and liver cirrhosis

	Patients with chronic hepatitis	Patients with liver cirrhosis	p value
Number	410 (32.5%)	850 (67.5%)	
Aetiology of liver disease (No of patients,%) Chronic HCV infection Chronic HBV infection	 249 (24.7%) 26 (10.4%)	 760 (75.3%) 225 (89.6%)	<0.05
Gall stones	17 (4.1%)	258 (30.4%)	<0.05
Increased GB wall thickness (No of patients,%)	0 (0%)	740 (87%)	<0.05

Table 3: Child--Pough class of patients with liver cirrhosis with and without gallstone disease

Child--Pough class	All patients	Patients with GSD	Patients without GSD	p value
C-P A C-P B C-P C	76 182 592	7 (9.2%) 33 (18%) 218 (36.8%)	69 (11.6%) 149(25.2%) 374(63.2%)	<0.05

Table 4: Prevalence of gallstone disease among patients with chronic liver disease of different aetiologies by sex and stage of liver disease, liver function tests and gallbladder pathology.

	Chronic HCV infection	Chronic HBV infection	p value
Number	249	26	
Age	52.32±9.95	48.15±9.38	0.11
Sex Male Female	 175 74	 18 8	0.9
AST	87.04±96.29	128.54±167.01	0.06
ALT	53.29±56.71	73.23±86.2	0.10
ALP	99.68±49.19	107.73±58.59	0.43
GGT	58.09±59.56	68.31±45.01	0.39
Albumin	2.23±0.8	2.33±0.60	0.54
Stage of liver disease Chronic hepatitis Liver cirrhosis	 16 (6.4%) 233 (93.6%)	 1 (3.8%) 25 (96.2%)	0.53
Child--Pough class C-P A C-P B C-P C	 7 30 196	 0 3 22	0.78
GB mud	79	6	0.36
GB wall thickness	225	25	0.33

4. Discussion

GSD is one of the major health problems in the world. Liver cirrhosis is an important risk factor for the development of gall stones. The risk increases with the severity of liver dysfunction. However, the prevalence of GSD among patients with CLD varies among different studies. This study was conducted on 1260 patients with CLD. They were selected randomly from the inpatient and outpatient departments of the National Liver Institute, Egypt..

In this study, we found that the prevalence of GSD in patients with CLD was 21.8 %. In addition, the prevalence of gallstones increased significantly with the progression of liver disease. Many studies confirmed the relation between liver cirrhosis and GSD (**Acalovschi *et al.*, 2004; Hsing *et al.*, 2007; Stroffolini *et al.*, 2007; Yong *et al.*, 2006**). The prevalence varied in these studies from 23 - 40%.

Bile secretion is diminished in patients with liver cirrhosis which may be due to diminished liver reserve and damaged bile ductules. This may lead to precipitation of cholesterol and the formation of gallstones (**Avaro *et al.*, 1990; Li *et al.*, 2000**). In addition, increased gall bladder wall thickness caused

by hyperemia and edema and decreased contractility and impaired gallbladder emptying contribute to gallstone formation (**Acalovschi 2004; Hsing *et al.*, 2007; Li *et al.*, 2000**).

The risk of GSD varies according to the aetiology of liver cirrhosis. Many studies have shown that the risk of GSD increases significantly with chronic HCV infection rather than other causes of liver cirrhosis. In a Taiwanese study, the prevalence of GSD among patients with chronic HCV infection was 11.7 % and it was 6 % among patients with chronic HBV infection (**Chen *et al.*, 2006**). Also, a population based study from USA has been shown that men with chronic HCV infection had an increased risk for the development of GSD (**Bini and McGready, 2005**). Furthermore, an Italian study has shown that patients with chronic HCV infection have a high prevalence rate of GSD than patients with chronic HBV infection (23% *Vs* 12.4%) (**Stroffolini *et al.*, 2007**). This was consistent with our findings as we found that chronic HCV infection is an independent risk factor for the development of gall stones. The prevalence of GSD in patients with chronic HCV infection was 24.7% *vs* 10.4% in patients with chronic hepatitis B infection.

Many factors have been stated to explain the high prevalence of gall stones in patients with chronic HCV infection. HCV may bind to apolipoprotein A1 and contribute to hepatic steatosis and increased cholesterol lithogenesis (**Hwang *et al.*, 2001**). HCV RNA was detected in the biliary epithelium and it may potentially impair gall bladder function and contribute to gall stone formation (**Lai *et al.*, 2002**).

These findings have important implications, as cholecystectomy for symptomatic gall stones in patients with advanced liver disease is associated with a high risk of morbidity and mortality (**Clark *et al.*, 2001; Puggioni *et al.*, 2003**).

5. Conclusion:

In conclusion, our study suggests that chronic HCV infection is an important risk factor for the development of GSD in Egyptian patients with CLD. The risk is increased with the severity of CLD. This is an important parameter to be considered in a country with high prevalence of HCV as Egypt.

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