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Original Research Article

Cirrhosis of liver is a risk factor for gallstone disease

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ABSTRACT

Background: Gallstones are common clinical finding in general population. Mean prevalence rate in Indian population is 4-5%. The prevalence of gallstones is found to be high in cirrhotic patients compared to the general population in some western studies. Cause of this increased prevalence however is not known. Aim of the study was to evaluate prevalence of the gall stones in the cirrhotic patients, assess risk factors in cirrhotic patients and clinical presentation.
Methods: This is the cross sectional observational study, included cirrhotic patients (compensated or decompensated). Risk factors for gallstone formation (age, gender and diabetes mellitus), characteristics of liver cirrhosis (etiology, Child Turcotte Pugh class, hypersplenism and varices) and clinical presentation were assessed in all cirrhotic patients with gallstones.
Results: 336 patients with liver cirrhosis are included in this study; 201 (59.80%) male and 135 (40.2%) female. Mean age of the patients is 44.95±13.1 years. Overall prevalence of gall stones was 12.8% (43/336). Out of 43 patients, 23 (53.5%) are male and 20 (46.5%) are female. As child status progresses from A to B to C, prevalence of gall stone increases, with 60.46% (26/43) of gall stones occurring in the patients with CTP class C. Only 8 (18.6%) patients had gallstone related symptoms while rests were asymptomatic. 5 (11.6%) had concurrent CBD stones. Cholecystectomy was possible in only 2 patients with symptomatic gallstones.
Conclusions: The prevalence of gall stones in cirrhotic is higher than general population which increases with the severity of liver cirrhosis. Most cirrhotic patients are asymptomatic for gallstones.

Keywords: Cirrhosis, Cholelithiasis, Gallstone disease

INTRODUCTION

Gallstones are a common clinical finding in the general population. Various ultrasound survey studies have shown prevalence rate of 10-15% in adult European, and of 3–5% in African and Asian populations.[1] Study by Unisa S et al in northern India showed gall stones prevalence of 4.15% in healthy adults >30years of age (5.59% in female and 1.99% in males).[2] More than 80% of gallstone carriers are asymptomatic, but about 1–2% per year will develop complications and needs surgery.[3-5] The prevalence of gallstones is found to be high in cirrhotic patients as compared with the general population in various studies mostly in western countries.[6]

Cause of this high prevalence of gallstones in cirrhotic patients is not known. Whether cirrhosis per se or presence of portal hypertension influences this increased frequency is unknown.

Gallstones occur in up to one third of the patients having liver cirrhosis.[6] Pigment gallstones are the most common type stones in these patients, while cholesterol stones represent only about 15% of all stones in cirrhotic patients.[7] Increased secretion of unconjugated bilirubin, increased hydrolysis of conjugated bilirubin, reduced concentration of various bile acids and phospholipids in bile increases lithogenic potential of bile in cirrhotic patients. Gallbladder hypo-motility, autonomic dysfunction also proposed as contributor for lithogenesis in these patients.[8,9]

The risk of cholelithiasis in cirrhotic male patients is much higher than in the healthy male population. Fornari et al proposed cirrhosis of liver as a risk factor for gall stones in males and suggested that high levels of estrogen due to decreased clearance by cirrhotic liver could play a role by an impairment of gallbladder emptying; as observed also in pregnant women.[5] Age, Gender and BMI are relevant risk factors for gall stones formation in general population, but these factors are less important in cirrhotic patients with gallstones. Main risk factor considered in these patients are severity of underlying liver disease, HCV related cirrhosis, presence of autonomic dysfunction. Gallstones in cirrhotic patients are often asymptomatic, and discovered incidentally on ultrasound imaging. However natural history of gallstone disease in cirrhotic patients is not clear. If asymptomatic, expectant management is recommended, as for asymptomatic gallstones in the general population. However, a closer follow-up of these cirrhotic patients is recommended in order to prevent complications. For symptomatic stones, laparoscopic cholecystectomy has become the therapy of choice. Child-Pugh class and MELD score are the best predictors of surgical outcome after cholecystectomy.

This study was formulated to assess prevalence of gallstones in Indian cirrhotic patients, assess risk factors for gallstone formation (age, gender and diabetes mellitus), characteristics of liver cirrhosis (etiology, Child Turcotte Pugh class, hypersplenism and varices) and clinical presentation in cirrhotic patients with gallstones.

METHODS

This is a cross sectional observational study, conducted in Department of Gastroenterology, Government Medical College and Super-Specialty Hospital, Nagpur. We included the cirrhotic patients visiting Gastroenterology OPD and patients admitted in the Ward with cirrhosis of liver, presented during July 2015 to June 2016. We excluded the patients with history of biliary surgery, hemolytic disorder and secondary biliary cirrhosis. The risk factors for gallstone formation (age, gender, diabetes mellitus) and the characteristics of liver cirrhosis (etiology, CTP class, presence of hypersplenism, varices), were assessed in all patients. Detailed history and physical examination of the patients were done. All patients underwent necessary investigations to determine the etiology of the cirrhosis and portal hypertension and received treatment as necessary. The detection of gall stone was done using ultrasonography by an experienced radiologist. All patients, after an overnight fast, underwent ultrasound abdominal scanning, performed with a 3.5-or 5-MHz transducer. The number and size of gallstones, presence of cirrhosis, ascites and Doppler scan of portal, splenic vein and presence of collaterals were assessed.

Institutional ethics committee permission was obtained before starting the study. Written informed consent of each patient was obtained. Statistical analysis was performed using SPSS 20 statistical software. Measure of central tendency and dispersion were estimated. Proportions were compared with Chi-square test. P value <0.05 considered for statistical significance.

RESULTS

A total of 336 patients with liver cirrhosis are included in this study. Of these 336 patients 201 (59.8%) were male and 135 (40.2%) were females. Mean age of the patients is 44.9±13.1 years. Most common cause of cirrhosis in study population was alcohol (162) followed by Viral [hepatitis B related cirrhosis (44), hepatitis C related cirrhosis (16)], Cryptogenic cirrhosis (58), NASH related CLD (28), Autoimmune liver disease (21) and Wilson's disease (9). Baseline characteristics of the patients are mentioned in Table 1.

Table 1: Baseline characteristics.

Characteristics	Number
Total patients	336
Male/ Female	201/135
Etiology of cirrhosis	
Alcohol	162
Hepatitis B	44
Hepatitis C	16
Autoimmune liver disease	21
Cryptogenic	58
NASH related cirrhosis	28
Wilson's disease	9
Gall stones	
Total	43/336 (12.8%)
Alcohol	16
Hepatitis B	4
Hepatitis C	2
Autoimmune liver disease	3
Cryptogenic	11
NASH related cirrhosis	5
Wilson's disease	2
Distribution according to CTP class in cirrhotic patients with gallstones	
Child A	10 (23.25 %)
Child B	7 (16.2 %)
Child C	26 (60.46%)

Overall prevalence of gall stones in cirrhotic patients in this study was 12.8% (43 out of 336 patients). Out of these 43 patients, 20 (46.5%) are female and 23 (53.5%) are male. Prevalence of gallstones in male cirrhotic patients is 11.44% (23/201) and in female cirrhotic patients is 14.8% (20/135). But there is no significant difference between gender and presence of gallstones in cirrhotic patients (p=0.364). Among all the patients with gall stone, alcoholic cirrhosis is the most common etiology (16/43), followed by cryptogenic cirrhosis (Table 2). There is no statistically significant association observed between etiology of cirrhosis and presence of gallstones in this study (p=0.385).

Table 2: Distribution of gall stones according to etiology of liver cirrhosis.

Etiology	No. of patients with gall stone	
Alcohol	17/126	13.49%
Hepatitis B	4/44	11.11%
Hepatitis C	5/25	20%
Autoimmune liver disease	3/10	30%
Cryptogenic	7/40	17.5%

Out of these 43 patients 26 (60.5%) patients are in CTP class C (Table 2). There is statistically significant association between CTP class and gallstones (p=0.003). This suggests that advanced liver disease is associated with increased prevalence of gallstones. We did not observe any association between hypersplenism, presence of varices and presence of gallstones in cirrhotic patients. Out of 43 patients having gall stones 10 patients had multiple stones; rest had a solitary stone in gall bladder on ultrasound scan. Among 43 patients with gall stones, only 8 (18.6%) were symptomatic while rest were asymptomatic and detected on routine ultrasonography. 5 (11.6%) patients also had concurrent common bile duct stones. ERCP and stone removal was successful in 4 patients. Out of the 8 symptomatic patients 2 underwent laparoscopic cholecystectomy while other 6 patients did not consent or considered unfit for surgery in view advance cirrhosis and high risk of perioperative complications.

DISCUSSION

All the published series confirm that cirrhosis represents a relevant risk factor for gallstones.[10,11] Results from our study also suggest same, with higher prevalence (12.8%) of gall stones in cirrhotic population compared to general population. Exact reason for this is not known but various factors have been postulated like un-physiological biliary supersaturation from hypersecretion of cholesterol, gallbladder hypomotility and the accumulation of mucin gel. In this study, prevalence of gallstones in male cirrhotic patients is 11.44% (23/201) and in female cirrhotic patients is 14.8% (20/135); this difference is not statistically significant. So role of gender as risk factor for gallstone formation is not significant in patients with cirrhosis, which is in contrast with general population where gender is strong risk factor for gallstone formation. In this study, alcoholic cirrhosis and cryptogenic cirrhosis were common etiology of liver disease in cirrhotic patients with gall stones. But there was no significant association between etiology of cirrhosis and presence of gallstones. We also observed increasing prevalence of gallstones with increasing severity of underlying cirrhosis from CTP class A to class C. This suggest that pathogenesis of gallstone formation in these patients may be related to liver dysfunction and duration of cirrhosis. Similar observations were noted in study by Conte D et al (no association between etiology of cirrhosis and gallstones and higher prevalence of gallstones in CTP B and C class).[11]

Some studies, such as that conducted by Grassi et al found that the incidence of complications such as Gastrointestinal bleeding, hepatic encephalopathy and hepato-renal syndrome was similar in cirrhotics with and without Gallstones.[12] They conclude that biliary lithiasis does not aggravate the course of liver cirrhosis. Acalovschi et al in a necroptic study on the prevalence of cholelithiasis in liver cirrhosis suggested that the average age of death was lower, but without statistical significance, in cirrhotic patients without gallstones than in those with.[13] As present study was a cross sectional observational study, we did not measure the effect of gall stone on complication related to cirrhosis and mortality. In this study, patients with gallstones are more frequently asymptomatic and surgery is rarely required but, when surgery is mandatory, these patients carry a higher risk of morbidity than the general population undergoing cholecystectomy.

CONCLUSION

The prevalence of gall stones in cirrhotic is higher than general population which increases with the severity of disease i.e. more common in CTP class C. However, there is no association between etiology of cirrhosis, hypersplenism, presence of varices and gallstone prevalence in these patients. Gender is not strong risk factor for gallstone disease in cirrhotic patients. So, cirrhosis of liver can be considered as a significant risk factor for development of Gallstones.

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