wjpmr, 2023,9(5), 41-44

SJIF Impact Factor: 5.922

WORLD JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.wjpmr.com

Research Article

ISSN 2455-3301

WJPMR

BILIARY LITHIASIS IN CIRRHOTIC PATIENTS: PREVALENCE AND RISK FACTORS

I. Ouchicha*, H. Cherkaoui, A. Lamine, M. Lahlali, N. Lahmidani, A. El Mekkaoui, M. Elyousfi, DA. Benajah, A. Ibrahimi, M. Elabkari and H. Abid

Hepato-gastroenterology department of the university hospital hassan II fez - Faculty of Medicine and Pharmacy - Sidi Mohammed Ben Abdellah University, Fez.

***Corresponding Author: I. Ouchicha**
Hepato-gastroenterology department of the university hospital hassan II fez - Faculty of Medicine and Pharmacy - Sidi Mohammed Ben Abdellah University, Fez.

Article Received on 08/03/2023 **Article Revised on 28/03/2023** **Article Accepted on 18/04/2023**

ABSTRACT

Gallstones occur in about one-third of patients with cirrhosis, the pathophysiology is complex and multifactorial and could be due to decreased secretion of bile acids and phospholipids into the bile and hypomotility of the gallbladder. Our work aims to study the prevalence of biliary lithiasis in cirrhotic patients and to identify risk factors for cholelithiasis in cirrhotics. In our retrospective and analytical study, gallstones were found more frequently in cirrhotic patients (45.45%, P=1.046.10^(-8), RR=2.17) than in non-cirrhotic patients (10%). The prevalence of gallstones in decompensated cirrhotic patients was higher (P=1.272.10^(-5)) than in compensated cirrhotic patients.

KEYWORDS: Liver cirrhosis; Gallstones; Cholelithiasis; Risk factors; Asymptomatic.

INTRODUCTION

Gallstones are twice as common in patients with liver cirrhosis.[1] The incidence of gallstones in cirrhotic patients is 9.5-29.4% compared to 5.2-12.8% in non-cirrhotic patients[1,2], This predisposition has been attributed to several factors such as hypomotility of the gallbladder in the transformed fibrous liver, Reduced bile acidity due to mucin hypersecretion, increased excretion of unconjugated bilirubin due to conjugation defect or intravascular hemolysis due to hypersplenism.[3,4]

OBJECTIVE

The present study aimed to assess the prevalence of biliary lithiasis in cirrhotic patients and to identify risk factors for cholelithiasis in cirrhotics.

MATERIALS AND METHODS

This is a retrospective analytical study conducted over a period of 11 years (2011-2022) having included 220 patients presenting to the department of functional exploration of the UH HASSAN II of Fez for an abdominal ultrasound during the follow-up of their chronic liver disease, these patients were divided into 2 groups: group A (cirrhotic patients: 110 patients) and group B (patients with chronic non-cirrhotic liver disease: 110 patients). Quantitative data were expressed as the mean and the median and statistical analysis was performed with SPSS software. Univariate and multivariate analyses were performed to investigate cirrhosis as a risk factor for the development of gallstone disease.

RESULTS

The mean age of our patients was 55.44 years (20 - 93) with a sex ratio F/M of 1.11.

In group A: 19.09% of patients were hypertensive, 15.45% were diabetic and 70% were overweight, the predominant etiology of cirrhosis was viral hepatitis B in 32.73% of cases, followed by viral hepatitis C in 25. 45%, primary biliary cirrhosis in 4.55% of cases, nonalcoholic steatohepatitis was found in 2.73% of cases, autoimmune hepatitis was found in 1.82%, post-alcoholic cirrhosis in 0.91% of cases, and in 26.36% of cases the etiology of the cirrhosis was undetermined. Cirrhosis was compensated in 48.18% of cases, hemorrhagic decompensation was observed in 30% of cases, ascitic decompensation in 33.64% of cases and neurological decompensation was observed in 3.64% of cases. Child A was observed in 65.46% of cases, Child B in 28.18% of cases, and Child C in 6.36% of cases.

In group B: 10% of the patients were hypertensive, 7.27% were diabetic and 68.18% were overweight, the predominant etiology of chronic liver disease was viral hepatitis B in 60.36% of the cases, followed by the fatty liver in 2% of the cases, viral hepatitis C was found in 5.41%, primary biliary cholangitis in 3.6% of the cases, hepatic steatosis was found in 2.73% of the cases, and autoimmune hepatitis was found in 2.7% of the cases.

		Group A	Group B
Medical history	Arterial Hypertension	19.09%	10%
	Diabetes	15.45%	7,27%
	Overweight	70%	68.18%
Etiologies	Hepatitis B	32.73%	60.36%
	Hepatitis C	25.45%	5.41%
	hepatic steatosis	2.73%	23.42%
	Alcoholic related disease	0.91%	0%
	Primary biliary cirrhosis	4.55%	3,6%
	Autoimmune hepatitis	1.82%	2.7%
	Unknown etiology	26.36%	0.9%
Prognosis	Child C	6.36%	
	Child B	28.18%	
	Child A	65.46%	

Gallstones were found more often in cirrhotic patients (45.45%, P=1.046.10^(-8), R R=2.17) than in non-cirrhotic patients (10%). The gallbladder was the predominant site of calculus (100% of cases) and associated with common bile duct lithiasis in 4.92%, it was asymptomatic in 72.13% of patients, hepatic colic was present in 24.59% of cases and jaundice was present in 3.28%.

In univariate analysis: hypertension (p=0.016; RR=2.3), diabetes (p=0.008; RR=2.82), and overweight (p= 0.007978) were significantly associated with the presence of gallstones, and the etiology of cirrhosis, namely viral hepatitis B (p=0.0002729), hepatic steatosis (p=0.008097), and post alcoholic cirrhosis (p=0. 0003298) were significantly associated with the presence of gallstones in patients with cirrhosis. In our series, no association was found between lithogenesis and other etiologies like HVC (p=0.6549), PBC (p=0.1728), autoimmune hepatitis (p=0.4839).

The prevalence of gallstones in decompensated cirrhotic patients was higher (P=1.272.10^(-5)) than in compensated cirrhotic patients. cholecystectomy was performed in 32% of the cases in group A and 40% of the cases in group B, and sphincterotomy with extraction of gallstones was performed in 4.92% of the patients in the 2 groups combined. Intraoperative complications were marked by bleeding from the vesicular bed in 3 cirrhotic patients (18. 75%). No intraoperative complications were observed in non-cirrhotic patients.

In multivariate analysis: cirrhosis (p= 2.08.10^(-5).), high blood pressure (p=0.007481), obesity (p=0.0146), etiology of cirrhosis including hepatitis B (p=0.00393) and fatty liver (p=0. 0021087), decompensated cirrhosis (p=0.004360) were significantly associated with the presence of gallstones in patients with liver cirrhosis.

DISCUSSION

The first data indicating a higher prevalence of gallstones in cirrhotics were derived from necropsy studies.[1-5] Prospective ultrasound studies subsequently confirmed the higher prevalence[6-7] and incidence[8,9-10] of gallstones in cirrhotic patients. The overall cumulative incidence of gallstones was evaluated for the first time in 72 patients followed for a mean of 2 years: 12 patients (16.6%) developed gallstones. The cumulative incidence was 5.5 cases/100 cirrhotics/year, and it was higher in advanced (decompensated) cirrhosis, regardless of etiology.[11] In the study of Conte et al[10], 618 cirrhotic patients were followed for nearly 4 years, and 141 (22.8%) developed gallstones during this period, in our study gallstones were found more often in cirrhotic patients (45.45%, P=1.046.10^(-8), RR=2.17) than in non-cirrhotic patients (10%). In multivariate analysis, cirrhosis (p= 2.08.10^(-5)) was significantly associated with the presence of gallstones. In most cirrhotic patients, gallstones are asymptomatic, the prevalence of symptomatic gallstones in cirrhotic patients is not known. In our study gallstones were asymptomatic in 72.13%, hepatic colic was present in 24.59% and jaundice was present in 3.28%. Friedman et al[11] did not find an association between chronic alcoholism and lithogenesis. Trotman and Soloway[12] observed that a history of alcoholism in cholecystectomies patients did not influence the type of gallstones. Some clinical studies found a protective effect of alcohol in moderate consumers (39 g/d), suggesting a reduced lithogenicity of the bile responsible for this effect.[13] Other studies noted an association between pigment stones and chronic alcoholism without cirrhosis[14], which could be explained by the effect of chronic alcohol consumption on the liver, bile, and red blood cells resulting in decreased solubilization of unconjugated bilirubin in bile. In summary, studies were conflicting regarding the protective vs. promoting effect of alcohol on gallstone formation in non-cirrhotic patients, But all studies agree that alcohol-related liver cirrhosis is associated with an increased prevalence of gallstones.[15] This is consistent with the results of our study (p= 0.0003298). The association between viral liver infections and gallstone formation has been evaluated in several studies. The increased prevalence of gallstones was associated with the duration and severity of HBV-related liver disease.[8] This means that the risk of gallstones increases with time in HBV patients, in our study the predominant etiology of cirrhosis was hepatitis B in 32.72% (p = 0.0002729).

Prospective[16] and retrospective[15,17] studies have shown a higher risk of gallstones in patients with chronic HCV infection at the cirrhosis stage. A study in the United States (NHANES Ⅲ) found that HCV-positive patients had a higher prevalence of gallstones than HCV-negative patients, and the prevalence of gallstones was higher in those with severe disease.[18] Stroffolini et al[19] noted a significantly higher prevalence of gallstones in post-viral C cirrhosis versus post-viral B or alcohol-related cirrhosis. These results diverge from those of our study where hepatitis C was not significantly associated with the presence of gallstones (p=0.6549).

In previous studies, the prevalence of cholestatic gallstones was found to be higher in patients with NAFLD than in healthy subjects because they share the same risk factors: obesity, type 2 diabetes, dyslipidemia, and insulin resistance.[20-21] The association between biliary lithiasis and hepatic steatosis has also been found in some recent articles.[22-23] Fracanzani et al[24] demonstrated that the prevalence of gallstones increases progressively with the severity of fibrosis and necrotic-inflammatory activity from a prevalence of 15% of gallstones in fibrosis stages 0-2 to 29% in stage 3 and 56% in stage 4 (cirrhosis).

In a large series of 482 Slovak patients with metabolic risk factors, Koller et al.[25] demonstrated that NAFLD was an independent risk factor for predicting gallstones. In our study, hepatic steatosis was significantly associated with the presence of gallstones (p = 0.008097).

The main determinant of gallstone formation in cirrhotic patients seems to be the severity of liver disease; advanced liver cirrhosis indicates a long duration of the disease. Most authors have shown that the prevalence of gallstones is higher in advanced stages of the disease: decompensated versus compensated cirrhosis, or in Child C versus Child A patients, respectively.[26,8,27,28,9,11]

This has been confirmed in NAFLD patients, in whom the prevalence of gallstones is significantly correlated with the severity of liver fibrosis.[24] This is consistent with the results of our study where the prevalence of gallstones in decompensated cirrhotic patients was higher (P=1.272.10^(-5)) than in compensated cirrhotic patients, which was statistically significant also with multivariate analysis.

Table 1: The prevalence of biliary lithiasis in cirrhotic patients.

Study	Year	Study type	Prevalence of biliary lithiasis
Bouchier et Al	1969	Autopsy	29.4%
Goebell et Al	1981	Autopsy	21.5%
Segala et Al	1991	Ultrasound	29.4%
Fornari et Al	1994	Ultrasound	31.9%
Acalovschi et Al	2009	Ultrasound	19%
Our series	2022	Ultrasound	45.45%

CONCLUSION

In uni and multivariate analysis, our study confirms that cirrhosis is a risk factor for the occurrence of biliary lithiasis even more so if it is decompensated or if its etiology is post-B viral or a nonalcoholic steatohepatitis.

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