

## FREQUENCY OF GALLSTONES IN PATIENTS OF LIVER CIRRHOSIS - a study in Lahore

Naheed T<sup>1</sup>, Akbar N<sup>2</sup> & Akbar N<sup>3</sup>

### ABSTRACT:

**Objective:** To determine the frequency of gall stones amongst patients suffering from liver cirrhosis in a general medical ward of a teaching hospital, Lahore, Pakistan.

**Design:** Cross-sectional, clinical study.

**Setting:** Hospital based study on patients who were admitted in a medical ward at Mayo Hospital, Lahore, Pakistan

**Subjects:** One hundred adult cirrhotics of any age and either sex who presented with symptoms of chronic liver disease.

**Main outcome Measures:** Gall stones.

**Results:** Out of 100 patients, 50 were male and 50 female in the age range of 30-70 years with the mean of 45.0 ±10.95 years. Among them 31% had gall stones. Out of these 17/50 (34%) were females and 14/50 (28%) were males. There was also associated oedema of gall-bladder wall. Thirty out of the hundred patients were HbsAg reactive, 70/100 were Anti HCV reactive and 10 were positive for both HbsAg and Anti HCV. 70% of patients were in Pugh's modification of Child criteria B and 30 % in class C and none in class A.

**Conclusion:** Gall-stones are more frequent in patients suffering from chronic liver disease. They do not affect the survival, and most of the patients come to know about it incidentally when they are subjected to investigations. Ultrasonography is a good non-invasive tool for this purpose.

**KEY WORDS:** Chronic liver disease (CLD), cirrhosis, ascites, gall-stones, HbsAg, Anti HCV, Ultrasonography.

Pak J Med Sci July-September 2004 Vol. 20 No. 3 215-218

1. Dr. Talat Naheed MD  
Associate Prof. Medicine,
2. Nabeel Akbar  
Research Medical Student
3. Naueen Akbar  
Research Medical Student

1-3. King Edward Medical College,  
Lahore, Pakistan

### Correspondence:

Dr. Talat Naheed  
E-mail: talat\_naheed@hotmail.com

\* Received for publication: November 11, 2003

Accepted: April 15, 2004

## INTRODUCTION

Cirrhosis is a cause of morbidity and mortality amongst Pakistani population, most common cause being viral hepatitis as compared to West where alcohol is more common. HCV is now more common as compared to HBV in our country<sup>1,2</sup>, whereas both can be a cause in the same patient. Since the invention of ultrasound it has been noted that gall-stones are common in patients suffering from cirrhosis. Patients suffering from chronic liver have been associated with gall stones. Their frequency is 4-5 times higher than general population and gallstones do not affect survival<sup>3</sup>.

Gall stones are the most common biliary pathology. They are of different types, cholesterol, mixed and pigment stones. Cholesterol stones are usually solitary whereas mixed and pigment stones are usually multiple but can also be single. There are many reasons for the occurrence of these stones. For cholesterol and mixed stones metabolic defect is thought to be responsible. Cholesterol is insoluble in water so held in solution form by the detergent actions of bile acids and phospholipids. Bile becomes lithogenic if cholesterol is in excess with relation to bile salts and phospholipids. Concentration of bile salts is reduced in bile by increased level of oestrogens and factors which interrupt enterohepatic circulation of bile salts. The question is that in cirrhosis is it the liver or gall bladder which is responsible? Perhaps both, because liver architecture is disturbed with increased oestrogen levels, gall bladder contractility is reduced, there is a reduced bile acid pool<sup>4</sup>, enhanced conversion of cholic acid into deoxycholic acid so cholic acid is replaced by increased amount of deoxycholic acid and may lead to defective vesicle formation, cholesterol is rich in these vesicles and aggregates into larger multilamellar vesicles<sup>5</sup>.

Most of CLD patients are not aware of gallstones. In view of these facts, an attempt was made to determine the frequency of gall stones in patients suffering from cirrhosis in a teaching hospital of Lahore.

## PATIENTS AND METHODS

One hundred consecutive patients, among which fifty were males and fifty females with ascites or history of chronic liver disease were presented in outpatient department or admitted through emergency in one of the general medical wards of Mayo Hospital, Lahore, during the period of January 2001 to December 2001 were included.

All these patients were thoroughly examined and confirmed as suffering from liver cirrhosis. Complete blood examination, urine examination, liver function tests, gastroscopy and abdominal ultrasonography were performed.

All those patients who were not confirmed to be cirrhotics on these investigations, were excluded. Liver biopsy was not performed on these patients. Later the main stress was laid on ultrasonography, as the purpose was to determine the frequency of gall-stones in these patients. There were three ultrasonographic findings for the diagnosis of stones in gall bladder (i) One or more echogenic, distally shadowing possible moveable structures within the gall-bladder. (ii) One or more echogenic, moveable, but not shadowing structures within the gall-bladder. (iii) Echogenic structures with constant shadowing in the region of gall-bladder fossa, with little or no visualization of the gall-bladder.

## RESULTS

The age of these one hundred patients ranged between 30-70 years with the mean age of  $45.0 \pm 10.95$  years, 64% of patients were between the age of 40-60 years and 31% of the patients had gallstones. It is pertinent to note that this was a highly selective group of patients who had presented in a tertiary care hospital of Southern Punjab. Seventeen, out of fifty (34%) females had gall stones whereas 14/50 (28%) males had gall stones. There is no significant difference. ( $P < 0.5$ ).

Out of these seventeen females, 13 had a single stone and four had more than one stones. Similarly 12/14 males had single stone

TABLE-I  
Demographic Data  
(n = 100)

Total patients	= 100
M:F	= 1:1
Age range	= 30-70 years $45.0 \pm 10.95$ years
Positive for gall stones	= 31/100 (31%)
Males	= 14/50
Females	= 17/50
Anti HCV positive	= 70
HBsAg	= 30
Both (B+C) positive	= 10

and only 2/14 had more than one stone. All these patients had oedema of gall bladder wall, which was more marked in patients with severe intractable ascites.

Thirty of these patients were HbsAg reactive and 70 were Anti HCV reactive whereas 10 were both HbsAg and Anti HCV reactive. Thirty percent (30%) of these patients were classified in Pugh's modification of Child criteria C, whereas 70% were in class B and none in class A.

## DISCUSSION

Cirrhosis is a major health problem and causes significant morbidity and mortality in our country. In this group of patients under study, age ranged between 30-70 years with the mean of  $45.0 \pm 10.95$  years and this is very close to a study carried out in the same city<sup>1</sup>. These are the most productive years of life and patients suffering from cirrhosis start out on complications. In this study 31% patients had gall stones, which were not a bother to the patients and were silent. Although this is a high figure, but we have to keep in mind that this consist of highly selective population but still is comparable with Conte De et al<sup>6</sup> and Elzouki et al<sup>7</sup> who reported that 29.5% and 30% of cirrhotic patients had gall stones. Maggi A et al<sup>8</sup> and Chung Pi Si et al<sup>9</sup> had shown still a higher frequency of 38% and 41% cirrhotics having gall stones. Sheen et al<sup>10</sup> reported that amongst cirrhotics they detected 18.5% males and 31.2% females who had gall stones, which in case of males is not in accordance with the present study. Razi et al<sup>11</sup> in Karachi thought that prevalence of gall stones if calculated amongst Pakistani population should be 15%, which is much less as compared with cirrhotics. Many factors have been proposed to explain the increased incidence of gall stones in cirrhosis. These include alcoholism<sup>12</sup>, lithogenic role of haemolysis<sup>13</sup>, decreased secretion of cholesterol and diminished bile acid pool<sup>14</sup>, still the exact mechanism has not been established. Impaired<sup>15</sup> gall bladder emptying has been suggested as a possible risk factor for gall stone formation. High oestrogen levels may impair

gall bladder motility during pregnancy so Fornari et al<sup>16</sup> suggests that increased levels of oestrogen and progesterone cause gall bladder stasis amongst these patients similar to pregnant women. Autonomic neuropathy<sup>17</sup> is common in patients with chronic liver disease irrespective of etiology of liver disease. Chawla A et al<sup>18</sup> also suggests that autonomic neuropathy may contribute to formation of gall stones in patients with advanced cirrhosis, perhaps by impairing gall bladder emptying and sphincter of oddi dysmotility. Acalovschi M et al<sup>19</sup> and Kao CH et al<sup>20</sup> also support that gall bladder contractility and emptying is markedly diminished in liver cirrhosis whereas Chung Pin Li et al<sup>8</sup> and Pompili et al<sup>21</sup> do not agree with this. Elzouki et al<sup>7</sup> in his study reported gall stones in patients of cirrhosis due to viral hepatitis whereas Fornari et al<sup>16</sup> observed that it was more common in cirrhotics who were alcoholics. Although it was said that gall stones are more prevalent in fatty females in their fertile years but in the present study it was found to be equally high amongst male patients so it goes with the findings of Elzouki et al<sup>7</sup>. Majority of the patients, (23/31) had a single stone whereas only 8/31 had more than one stone. Severity of liver disease<sup>22,23</sup>, is also a risk factor for gall stones in patients with cirrhosis and is thought to be another contributory factor which supports this study as multiple gall stones were more common in patients who were in child C of Pugh's classification and is also in accordance with studies of Conte D et al<sup>6</sup> and Elzouki et al<sup>7</sup>, that biliary lithogenesis increases with degree of liver dysfunction and could be a contributory factor for formation of gall stones amongst cirrhotics.

It was also noted that 70% of these patients were anti HCV reactive, 30% were HBsAg reactive whereas 10% of these had both viral markers. Various studies have shown anti HCV reactive in the range varying from 18%<sup>24</sup> 37.5%<sup>25</sup>, 62.2%<sup>26</sup> and 65.5%<sup>1</sup> amongst cirrhotics and both were positive in 24.4%<sup>1</sup>. Whereas in the present study it was only 10% which shows a change of pattern of viral markers.

## CONCLUSION

Gall-stones are more frequent in patients suffering from chronic liver disease. They do not affect the survival, and most of the patients come to know about it incidentally when they are subjected to investigations. Ultrasonography is a good non-invasive tool for this purpose.

## REFERENCE

1. Naheed T. Antigenemia in Chronic liver disease *SPECIALIST (Pak J Med Sci)* 1998; 14(4): 303-8.
2. Hussain I, Nasrullah M, Shah AA. Prevalence of hepatitis B and C viral infections in liver cirrhosis in Pakistan. *Pak J Gastroenterol* 1998; 12(1-2): 7-11.
3. Finnucci G, Tirelli M, Bellon S, et al. Clinical significance of cholelithiasis in patients with decompensated cirrhosis. *J Clin Gastroenterol* 1990; 12:538.
4. Beckingham JJ. "Gall stone disease": ABC of diseases of liver, pancreas, and biliary system. *BMJ* 2001;322:91-4.
5. Alvaro D, Angelico M, Gandin C et al. Physioco-chemical factors predisposing to gall stones formation in liver cirrhosis. *J Hepatol* 1990; 10:228.
6. Conte D, Fraquelli M, Fornari F, Lodi L, Bondini P, Buscarini L. Close relation between cirrhosis and gallstones: cross-sectional and longitudinal survey. *Arch Intern Med* 1999; 159(1): 49-52.
7. Elzouki AN, Nilsson S, Nilsson P, Hans Verbann, Mecislovas Simanaitis, Stefan Lindgren. The prevalence of gallstones in chronic liver disease is related to degree of liver dysfunction. *Hepato-gastroenterology* 1999; 46: 2946-50.
8. Maggi A, Solenghi D, Panzeri A, Borroni G, Cazzaniga M, Sangiovanni A et al. Prevalence and incidence of cholelithiasis in patients with liver cirrhosis. *Ital J Gastroenterol Hepatol* 1997; 29(4): 330-5.
9. Li CP, Hwang SJ, Lee Fy, Chang FY, Lin HC, Lu RH et al. Evaluation of gall bladder motility in patients with liver cirrhosis relationship to gallstone formation. *Dig Dis Sci* 2000; 45(6): 1109-14.
10. Sheen IS, Liaw YF. The prevalence and incidence of cholecystolithiasis with chronic liver diseases: a prospective study. *Hepatology* 1989; 9: 538.
11. Razi M, Nadia I, Qamar A, Omar I. Pattern of gall bladder diseases in Pakistan. *SPECIALIST (Pak J Med Sci)* 1999; 15(2): 109-12.
12. Sherlock S. Hepatic cirrhosis. Diseases of the liver and biliary tract, 11<sup>th</sup> ed. Blackwell Scientific Publication. London 2002; 1: 371-84.
13. Barbara L, Sama C, Morselli-Labate AM, Taroni F, Rusticali AG. A population study on the prevalence of gallstone disease: the Sirmione study. *Hepatology* 1987; 7: 913-17.
14. Vlahcevic ZR, Bell CC Jr, Buhac I. Diminished bile acid pool size in patients with gall stones. *Gastroenterology* 1970; 59: 165.
15. Donovan JM & Carey MC. Physical-chemical basis of gallstones formation. *Gastroenterology Clin North Am* 1991; 20: 47-66.
16. Fornari F, Imberti D, Squillante MM, Squassante L, Civerdi G, Buscarini E: Incidence of gallstones in a population of patients with cirrhosis. *J Hepatol* 1994; 20: 797-801.
17. Del Olmo JA, Garcia F, Serra MA, Maldonado L, Rodrigo JM. Prevalence and incidence of gall stone in liver cirrhosis. *Scan J Gastroenterol* 1997;32(10): 1061-5.
18. Chawla A, Puthumana L, Thuluvath PJ. Autonomic dysfunction and cholelithiasis in patients with cirrhosis. *Dig Dis Sci* 2001 Masc, 46(3): 495-8.
19. Acalovschi M, dumitrascu DL, Csakany I. Gastric and gall bladder emptying of a mixed meal are not coordinated in liver cirrhosis: a simultaneous sonographic study. *Gut* 1997; 40: 412-17.
20. Kao Ch, Hsieh JF, Tsai SC, Ho YJ, Che SD. Evidence of impaired gallbladder function in patients with liver cirrhosis by quantitative radionuclide cholescintigraphy. *Am J Gastroenterol* 2000; 95(5): 1301-4.
21. Pompili M, Rapaccini GL, Caturelli E, Curro D, Montuschi P, D'Amato M. Gallbladder emptying, plasma levels of estradiol and progesterone, and cholecystokinin secretion in liver cirrhosis. *Dig Dis Sci* 1995; 40:428-34.
22. Leone N, Garino M, De Paolis P, Pellicano R, Fronza GR, Rizzetto M. Laparoscopic cholecystectomy in cirrhotic patients. *Dig Surg* 2001; 18(6): 449-52.
23. Morino M, Cavuoti G, Miglietta C, Giraudo G, Simone P. Laparoscopic cholecystectomy in cirrhosis: contraindication or privileged indication. *Surg Laparosc Endosc Percutan Tech* 2000; 10(6): 360-3.
24. Malik IA, Tariq WU. "Editorial" The prevalence and pattern of viral hepatitis in Pakistan. *J Coll Physicians Surg Pak* 1995; 5(1): 16-8.
25. Hussain T, Bhatti S, et al. "Hepatitis C" clinical profile and treatment. *J Coll Physicians Surg Pak* 1995;5(1):21-5.
26. Shafi T, Iqbal J, Ahmed S. Prevalence of anti HCV in hemodialysis patients *Pak J Med Res* 1992; 31:42-5.