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ORIGINAL ARTICLE

Cirrhotic Cardiomyopathy in Bangladeshi Patients: A Pilot Study

Madhusudan Saha, Shasanka Kumar Saha, Khondoker Asaduzzaman, Ranjit Kumar Banik

ABSTRACT

Background: Cirrhotic cardiomyopathy is reported to be a major cause of mortality and morbidity in liver transplant recipient. It might be an emerging issue as liver transplantation has been started in Bangladesh.

Materials and methods: Forty-four cirrhotic patients of varying etiology and 44 healthy volunteers were enrolled as cases and controls, respectively. Hepatic functional status was assessed by clinical examination and biochemical tests. Transthoracic echocardiography was done in both the groups.

Results: Deceleration time of cirrhotic patients was significantly prolonged irrespective of etiology in comparison to controls indicating diastolic dysfunction. Left ventricular systolic diameter was also larger (significant statistically) in cirrhotic patients. Other echocardiographic parameters like E/A ratio, EF, left ventricle (LV) wall thickness, interventricular septal thickness and LV diastolic diameter showed no significant difference. Cardiac dysfunction does not depend on severity of hepatic dysfunction.

Conclusion: Cirrhotic patients irrespective of cause show diastolic dysfunction. Cardiac dysfunction did not correlate the severity of hepatic dysfunction.

Keywords: Liver cirrhosis, Cardiac problem, Myopathy, Bangladesh, Diastolic dysfunction.

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INTRODUCTION

Cirrhosis of liver is associated with several cardiovascular abnormalities. Kowalski et al reported that patients with cirrhosis had abnormal cardiovascular function and a prolonged QT interval.[1] The systemic circulation in patients with decompensated cirrhosis is hyperdynamic and characterized by increased heart rate and cardiac output (CO) and decreased systemic vascular resistance with low normal or decreased arterial blood pressure.[2,3] It is also associated with impaired cardiac contractility and performance in patient with cirrhosis. The term cirrhotic cardiomyopathy implies a condition with defective myocardial contractility under physical and pharmacological strain.[4] It is usually clinically latent or mild. But it may become unmasked and clinically evident by certain treatment interventions that increase the effective blood volume and cardiac preload, including surgical or transjugular intrahepatic portosystemic shunts, peritoneovenous shunt (LeVeen) and orthotropic liver transplantations.[5] It has been reported to be a major cause of morbidity and mortality in liver transplant recipients.[6] It may also contribute to pathogenesis of hepatorenal syndrome. But date regarding cirrhotic cardiomyopathy is scanty reports are available from Asian countries as well as from Bangladesh. So, this study was designed to detect incidence of cardiac dysfunction and its relation with severity of hepatic dysfunction.

MATERIALS AND METHODS

Consecutive patients diagnosed as cirrhosis of liver clinically and supported by laboratory investigations irrespective of age, sex and etiology were included in this study. Patients with history of recent hemorrhage, severe ascites, severe anemia and ischemic heart, bed ridden, diabetes or pregnancy were excluded from the study as these conditions may interfere cardiac function. Patients unwilling to participate in the study were not included in this study. Liver function was assessed by clinical examinations specially assessing encephalopathy and investigations including serum bilirubin, albumin, prothrombin time, ultrasonogram, endoscopy of upper gastrointestinal tract (GIT). In addition serum creatinine, electrocardiogram (ECG) and blood glucose (2 hours breakfast) will also be tested. Then all of the patients underwent cardiac structural and functional assessment noninvasively, using transthoracic echocardiography estimating E/A ratio, deceleration time, ejection fraction, left ventricular relative wall thickness, interventricular septal thickness and left ventricular systolic as well as diastolic chamber dimension.

Same number of healthy nondiabetic age matched volunteers without history of jaundice, clinical evidence of chronic liver disease and ECG evidence of ischemic heart disease were taken as control and cardiac status of them were evaluated by echocardiography similarly as for the patients.

STATISTICAL ANALYSIS

Statistical analysis was done using SPSS 12. Results of demographic and biochemical and echocardiographic parameters were expressed as mean. Hepatic functional status was classified as Child-Pugh grading. Independent t-test was done to compare the cardiac functional change

between cirrhotic and control groups. Kruskal-Wallis test was done to see the correlation of cardiac functional status and severity of hepatic dysfunction. p-value < 0.05 was taken as significant.

RESULTS

Total 44 patients with cirrhosis of liver were included in this study following inclusion and exclusion criteria. Among them 30 had HBV infection, four had HCV infection and remaining 10 were negative for HBV and HCV (further etiological workup was not done). None of the patients were alcoholic. Same number of apparently healthy nondiabetic volunteers without history jaundice and clinical evidence of chronic liver disease and ECG evidence of ischemic heart disease were taken as controls.

Among cirrhosis patients, 40 were male and four were female with age varying from 14 years to 75 years (mean: 39.68 years). Their serum bilirubin level varied from 0.5 to 17.5 mg/dl with mean 1.6 mg/dl. SGPT level of patients varied from 23 to 283 u/l with mean levels of 67.5 u/l. Minimum and maximum level of SGOT of patients were 14 and 75 u/l with mean 39 u/l.

Mean serum albumin was 3.46 gm/dl (maximum: 4.9 gm/dl and minimum: 1.8 gm/dl) of patients. Among them nine patients (20.5%) belonged to Child A class while 28 (64.6%) belonged to Child B and seven (15.9%) belonged to Child C class.

In cirrhotic patients in comparison to controls, left ventricular size was found to be a bit larger in both systole (mean: 29.79 *vs* 28.68 mm) and diastole (mean 45.92 *vs* 45.59 mm) and difference of systolic diameter was statistically significant (p = 0.02) (Table 1).

Mean ejection fraction of cirrhotic patients was 64.188% and it is lesser than that of control (66.2%), but the difference is not statistically significant (Table 1).

Interventricular septal thickness and left ventricular wall thickness of cirrhotic patients were 8.8798 and 8.148 mm respectively. While in controls, interventricular septal thickness and left ventricular wall thickness were 9.068 and 8.20 mm, respectively. Deceleration time, left ventricular diastolic inflow, was prolonged among cirrhotics (mean: 270 ms) in comparison to control (mean: 186 ms). Among cirrhotics, deceleration time was more than 250 ms in 25 case while among control deceleration time was more than 250 ms in only two volunteer and the difference is statistically significant (p = 0.00) (see Table 1).

E/A ratio was found less than 1 in 11 cirrhotic patients. But E/A ratio was also found to be less than 1 in eight controls and the difference in E/A ratio was not statistically significant (p = 0.36).

DISCUSSION

Cirrhotic cardiomyopathy is defined as chronic cardiac dysfunction in patients with cirrhosis characterized by blunted contractile responsiveness to stress and or altered diastolic relaxation with electrophysiological abnormalities in the absence of known cardiac disease (Montreal definition). Its diagnosis is based on the demonstration of cardiac abnormalities in patients with cirrhosis of liver in the absence of other clinically significant cardiopulmonary disease. Diagnosis of cirrhotic cardiomyopathy requires the presence of one or more of the following criteria: (1) Baseline increase of CO but blunted ventricular response to stress, (2) systolic and or diastolic dysfunction, (3) absence of overt left ventricular failure except when stressed and (4) electrophysiological abnormalities including prolonged Q-T interval on an ECG.[7]

The pathophysiological mechanism of cirrhotic cardiomyopathy is poorly understood. Cardiodepressant substances such as nitric oxide, cytokines, endotoxins, endothelins, bile acids and adenosine have all been implicated. Other putative causes include sympathetic dysfunction, impaired beta-adrenergic receptor function and plasma membrane dysfunction.[8]

Table 1: Echocardiographic findings of patients, controls and comparison

Parameter	*Case mean*	*Control mean*	*p-value*
Deceleration time	270 ms SD: 80.02 ms	186 ms SD: 47.296	0.00
Ejection fraction	64.19% SD: 6.48	66.204% SD: 5.605	0.122
E/A ratio	1.33 SD: 0.44	1.2561 SD: 0.3955	0.363
LV wall thickness	8.148 SD: 1.547	8.2045 SD: 1.407	0.859
IV septum thickness	8.879 SD: 1.643	9.068 SD: 1.37	0.561
LV systolic diameter	29.79 SD: 4.68	28.68 SD: 4.60	0.02
LV diastolic diameter	45.92 SD: 4.59	45.59 SD: 5.66	0.549

Most of cirrhotic patients in our study had liver dysfunction of moderate severity-Child class B (28 cases, 63.6% out of 44 cases). Child class A cirrhotic patients are either asymptomatic or have few symptoms and are seeking medical attention less frequently. Therefore, they are under-represented in our study. On the other hand most Child C class cirrhotic patients had been excluded due to exclusion criteria such as severe anemia, gross ascites, and recent history of bleeding. And only ambulant patients were enrolled in this series to eliminate the effect of cardiac deconditioning due to bed rest.

In our study statistically significant prolongation of deceleration time in cirrhotic patients irrespective of etiology in comparison to controls was seen which indicates diastolic dysfunction. But mean E/A ratio in this series was found higher than that of control which contradict the Indian report[6] though the difference is not statistically significant.

Both E/A ratio and deceleration time reflect impedance to ventricular filling. However, E/A ratio is subject to the phenomenon of pseudonormalization whereby the E/A ratio becomes paradoxically normal despite diastolic dysfunction.[9]

There are reports of decrease of E/A ratio in cirrhotic patients with ascites in comparison to cirrhotics without ascites and control[10] and decreased E/A ratio in cirrhotics with nonviral etiologies compared to virus related cirrhosis.[11] But the phenomenon of pseudonormalization of E/A ratio raises doubt about its importance as a marker of diastolic dysfunction.

In our study in cirrhotics ventricular diameter both during systole and diastole are increased than those of control, and the difference at systole was statistically significant ($p = 0.02$). Some published reports showed ventricular diameter both in systole and diastole were increased.[10] While other observations also reported smaller left ventricular volumes in pure virus-related cirrhosis compared to alcoholic cirrhosis and controls.[12]

In our study interventricular septal thickness and left ventricular relative wall thickness were lower than those of controls, but difference was not statistically significant. This is discordant with other published reports.[6]

In this series, left ventricular ejection fraction was found to be a bit lower in cirrhotics than controls but the difference is not statistically significant. Patients with cirrhosis generally tend to have increased ejection fraction. However, some studies have reported that the ejection fraction is slightly but significantly reduced in patients with ascites, but not in preascitic patients.[13] There are reports of higher ejection fraction in virus-related cirrhotics in comparison to alcoholic cirrhosis and controls. In alcoholics it may be that subclinical alcoholic cardiomyopathy may contribute in decreasing EF.[12] But in our series, none of patients was alcoholic. This variability of reports regarding EF may be due to small sample size and lack of uniform diagnostic criteria of cirrhotic cardiomyopathy.

It is important to note that even normal echocardiographic parameters do not rule out presence of cirrhotic cardiomyopathy. Increased production of nitric oxide in cirrhosis causes myocardial contractile dysfunction and also induces systemic vasodilation. The reduction in afterload thus, permits the heart to maintain a normal CO even in the presence of contractile dysfunction and a reduced preload.[14] Echocardiography, thus detects only a small portion of total cases of cardiac dysfunction in cirrhosis.

In this study no correlation between severity of hepatic dysfunction and cardiac functional change was seen which is consistent with one published report from India.[6] But there are reports that cardiac changes parallel the severity of hepatic dysfunction.[15] Due to strict maintenance of selection criteria, patients mostly of mild and moderate hepatic dysfunction are enrolled. In addition sample size is also small. These are the limitation of this series. Further study including larger sample size and patients belonging entire spectrum of severity of hepatic dysfunction may be performed to delineate the extent cardiac functional changes in relation with severity of hepatic dysfunction should be done.

In this series diastolic dimension of left ventricle (LV) was larger in cirrhotics than that of control which is consistent with report from India.[6] But left ventricular systolic dimension was larger in cirrhotics than that of control which is not consistent with other reports.

This study indicates the presence of diastolic dysfunction in cirrhotic patients in Bangladesh. In cirrhotics in absence of risk factors for cardiac disease, this dysfunction can be attributed to cirrhotic cardiomyopathy. No correlation between severity of hepatic dysfunction and cardiac functional change is seen in this series. But further study with large sample size with patients of all spectrum of severity is needed to assess the cardiac functional changes and prognosis of cirrhotic cardiomyopathy.

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ABOUT THE AUTHORS

Madhusudan Saha (Corresponding Author)

Department of Gastroenterology, North East Medical College and Hospital, Sylhet, Bangladesh, Phone: +8801711367847, e-mail: madhunibedita@gmail.com

Shasanka Kumar Saha

Department of Gastroenterology, Sir Salimullah Medical College and Mitford Hospital, Dhaka, Bangladesh

Khondoker Asaduzzaman

Department of Gastroenterology, Sir Salimullah Medical College and Mitford Hospital, Dhaka, Bangladesh

Ranjit Kumar Banik

Department of Gastroenterology, Sir Salimullah Medical College and Mitford Hospital, Dhaka, Bangladesh