



PREVALENCE OF CIRRHOTIC CARDIOMYOPATHY IN PATIENTS WITH CIRRHOSIS OF LIVER : A TERTIARY HOSPITAL EXPERIENCE

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ABSTRACT

Cirrhotic cardiomyopathy is impaired contractile responsiveness to stress, diastolic dysfunction and electrophysiological abnormalities in the absence of known cardiac disease in cirrhotic patients. This Descriptive case series study was conducted in sree balaji medical college and hospitals. This study included 74 consecutive cases of cirrhosis of liver of either sex above 14 years of age. Firstly, resting ECG was done in all the patients. QTc values were calculated from lead II. QTc interval of >0.44 sec were considered as prolonged. Systolic dysfunction was assessed by ejection fraction (value of >55% was considered as increased). Diastolic dysfunction manifested by reduced E/A ratio (<1 was considered as decreased). Thirdly, all patients had determination of proBNP levels. The presence of cirrhotic cardiomyopathy was confirmed by abnormal ECG or echocardiography, along with proBNP abnormalities. Statistical package for social sciences (SPSS) version 16 was used for data processing purpose. Means \pm Standard Deviation of age and pro BNP levels were calculated. Frequency and percentage were computed for cirrhotic cardiomyopathy in cirrhosis patients. A total of 74 patients were selected for this study, out of which 41 (55.41%) were male and 33 (44.59%) were female. The mean age was 46.2 years (\pm 10.8 SD). Out of 74 patients 9 (12.2%) belonged to child Pugh A, 29(39.2%) to child-Pugh B and 36(48.6%) in child-Pugh C. Elevated pro BNP was present in 42(56.8%) cases, E/A ratio < 1 in 15 (20.3%) cases, prolong QT interval (>0.44sec) in 16 (21.6%), Ejection fraction (EF) > 0.55 was present in 25 (33.8%) patients. Cirrhotic cardiomyopathy was present in 33(44.6%) cases. A strong relation was found between cardiomyopathy and severity of cirrhosis of liver ($p=0.001$), pro-Bnp levels ($p=0.003$), QTc > 44 sec (0.004), Ejection fraction > 55% (0.004) and E/A ratio < 1 ($p=0.005$). Cirrhotic cardiomyopathy was present in a sizeable proportion of cirrhotic patients, more so in the later stages of cirrhosis of liver.

KEY WORDS: Cirrhosis, Cardiomyopathy, ECG, Echocardiography, proBNP.



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INTRODUCTION

Cirrhotic cardiomyopathy (CCM)¹ is a clinical syndrome in patients with liver cirrhosis characterized by an abnormal and blunted response in cardiac output and contractility to physiologic, pathologic, or pharmacologic stress but a normal to increased cardiac response at rest. It 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. Diagnostic criteria:

1. Abnormal systolic contractile responses to stress.
2. Diastolic dysfunction at rest.
3. Absence of clinically significant cardiopulmonary disease.

with the frequent use of invasive procedures like surgical portocaval shunts, transjugular intrahepatic port systemic shunt and liver transplantation, the adverse consequences of cardiac dysfunction became evident. Unfortunately there is scanty information on the status of cardiac abnormalities in Indian patients with cirrhosis²

Aim and Objectives

Objectives

- To evaluate the extent of cardiac dysfunction by clinical and echocardiography assessment in cirrhotic patients.
- To assess the prevalence of cirrhotic cardiomyopathy in patients of chronic liver disease

MATERIALS AND METHODS

Source of data

This study was done in the outpatient department as well as patients admitted in the departments of general medicine, cardiology and nephrology, Sree Balaji medical college and hospital, Chromepet, Chennai. The study was approved by the Ethical Board of sree Balaji medical college and hospitals.(approval no: Ref.No.002/SBMC/IHEC/2015/164).

Sample size

90 cases

METHODOLOGY

This Descriptive case series study was conducted in this study included 90 consecutive cases of cirrhosis of liver of either sex above 14 years of age. . Informed consent was obtained from all patients (or next of kin in case patient was unconscious). Patient's bio data regarding age, gender, weight, grade of cirrhosis were entered in a proforma. Blood test for liver functions test, prothrombin time, Protein profile, ultrasound of abdomen was done. Cirrhosis was labeled on the basis of: ³Clinical (reduced liver span <8 cm on clinical exam with ascites and splenomegaly)Biochemical (prolonged prothrombin time >12 seconds and reduced level of serum albumin <3.5 g/dl) Radiological (increased liver echo pattern, shrunken liver <8cm in mid-clavicle line, portal vein diameter >1.3 cm and spleen size >13 cm longitudinally) and confirmed on biopsy (presence of widespread

fibrosis, obliteration of central vein and regenerating nodules).Firstly, resting ECG was done (in Medical Unit by certified ECG technician who has at least 5 year experience of taking ECGs) in all the patients.ECG abnormalities:QTc: QTc values was calculated in all patients by following formula

$$QTc = QT \sqrt{RR}$$

The value of QTc of > 0.44 sec was considered as prolonged⁴

- Heart Rate: was calculated via following formula HR = 1500/rr

Statistical method

All continuous variables were assumed to be normally distributed and are reported as arithmetic mean with their standard deviation. The fisher's exact test was used to compare and analyse the data.

Period of Study

One year (June 2014- June 2015)

Inclusion criteria

Patients with Cirrhosis of liver (alcoholic and non alcoholic)

Exclusion criteria

Patients with valvular heart disease, congenital heart disease, ischemic heart disease, paced rhythm, bundle branch block, hypertrophic cardiomyopathy or evidence of any other gross structural heart disease were excluded from the study.Presence of both prolonged QTc and heart rate >100 was labeled as 'abnormal ECG' and 'positive cardiomyopathy'. Secondly, echocardiographic examination was done (by a consultant cardiologist who had at least 10-year experience of echocardiography and who did not know the primary diagnosis of cirrhosis at Echocardiography room),which included two dimension echo and color flow Doppler study. Systolic dysfunction was assessed ejection fraction (value of >55% was considered as increased).⁵ Diastolic dysfunction manifested by reduced mitral E/ A ratio (<1 was considered as decreased).⁶ Pro B type Natriuretic Peptide (pro BNP): The increased pro-BNP level, determined via Elecsys NT- proBNP assay (Roche diagnostics, Mannheim-Germany), was labeled as 'positive cardiomyopathy'. The cut-off level for males was e"93-pg/ml and the cut-off level for females was e"144-pg/ml.⁷ Cirrhotic cardiomyopathy: cirrhotic cardiomyopathy was diagnosed if evidence of either systolic or diastolic dysfunction, together with supporting criteria such as electrophysiological abnormalities or abnormal serum markers was present.⁸

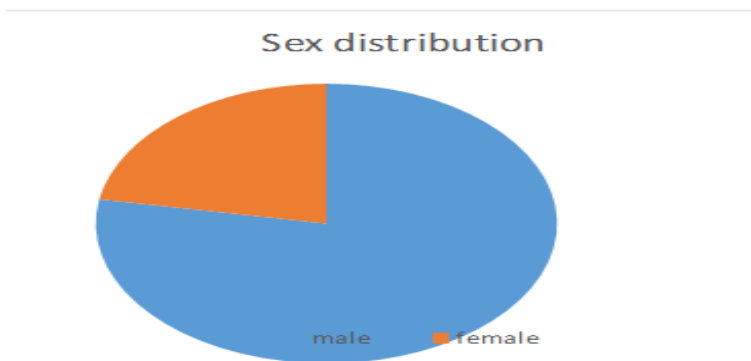
Statistical Analysis

All results are expressed as mean ± standard deviation. Commercial software (SPSS version 20.0) was used for statistical analysis. The coefficients of skewness and kurtosis were used to evaluate normal distribution of data. Multivariate analysis was applied for the estimation of the relationship of clinical features. The x² test or Fisher's exact test, as appropriate, was used to compare categorical variables. Odds ratio (OR) and

95% confidence intervals (95% CI) are reported. P values <0.05 were considered significant.

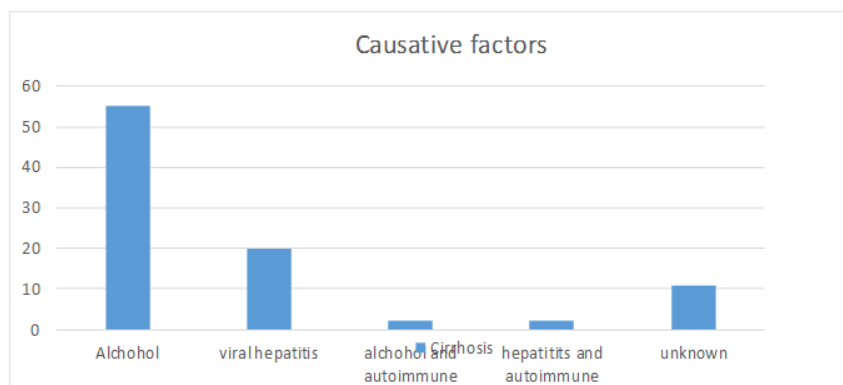
A total of 90 patients were selected for this study, out of which 60 (77.77%) were male and 30 (22.22%) were female. The mean age was 46.2 years (\pm 10.8 SD).

RESULTS



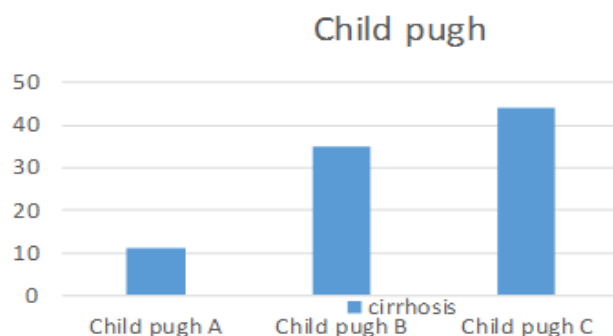
Graph 1
sex distribution

The most common causes of cirrhosis were attributed to alcohol abuse (N =55), followed by viral hepatitis (N = 20). A combination of alcohol and hepatitis virus infection was present in 9 alcohol and autoimmune liver disease in two patient and that of infectious hepatitis and autoimmune liver disease in two. Whereas, cause of cirrhosis was not documented in 11 (12.22%) of the cases



Graph 2
Causative factors

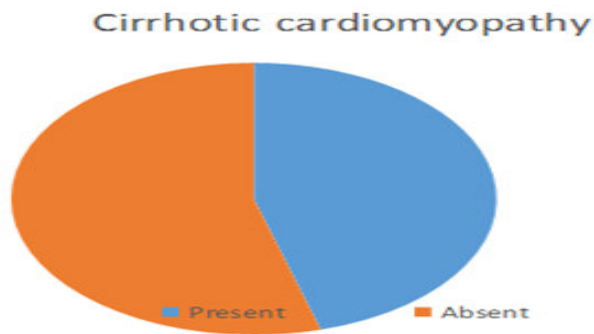
Out of 90 patients 11 (12.22%) belonged to child Pugh A, 35(38.89%) to child-Pugh B and 44(48.89%) in child-Pugh C.



Graph 3
child pugh classification

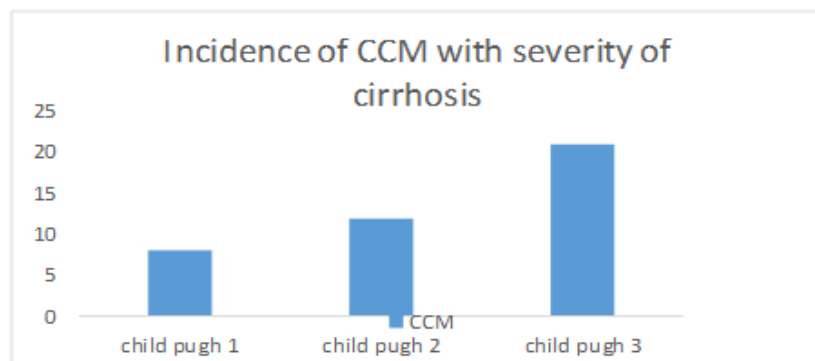
Elevated pro BNP was present in 51(56.67%) cases, E/A ratio < 1 in 18(20%) cases, prolong QT interval (>0.44sec) in 19 (21.11%), Ejection fraction (EF) > 0. 55 was present in 31 (34.44%) patients.

Cirrhotic cardiomyopathy was present in 41(45.55%) cases.



Graph 4
cirrhotic cardiomyopathy

Out of 41, patients with CCM majority are of child Pugh c 21 .(53.65%)



Graph 5
incidence of ccm with severity of cirrhosis

A strong relation was found between cardiomyopathy and severity of cirrhosis of liver ($p=0.001$), $pr0$ -Bnp levels ($p=0.003$), $QTc > 44$ sec (0.004), Ejection fraction $> 55\%$ (0.004) and E/A ratio < 1 ($p=0.005$).

DISCUSSION

Liver cirrhosis is associated with a wide range of cardiovascular abnormalities. These include hyperdynamic circulation producing an increase in cardiac output and a decrease in peripheral vascular resistance. In spite of this increased cardiac output, decreased beta-adrenergic responsiveness (impaired ventricular contractility in response to both physiological and pharmacological stimuli) has been described. Other cardiac abnormalities include electrophysiological changes such as QT prolongation and structural changes like enlargement or hypertrophy of different cardiac chambers. This constellation of cardiac abnormalities is termed CCM⁹.

Diagnostic criteria

1. Abnormal systolic contractile responses to stress.
2. Diastolic dysfunction at rest.
3. Absence of clinically significant cardiopulmonary disease.

Systolic dysfunction (at least one of the following)

1. Blunted increase in cardiac output with exercise, volume challenge or pharmacological stimuli.
2. Resting LVEF $< 55\%$

Diastolic dysfunction (at least one of the following)

1. E/A ratio (age corrected) < 1.0
2. Prolonged deceleration time (> 200 ms)
3. Prolonged isovolumic relaxation time (> 80 ms)

Supportive criteria

1. Electrophysiological abnormalities including the following:
 - Abnormal chronotropic response to stress.
 - Electromechanical uncoupling/dyssynchrony.
 - Prolonged QTc interval.
2. Heart chamber alterations: enlarged LA, increased LVWT.
3. Increased pro-BNP and BNP.
4. Increased troponin I.

CCM is a diagnosis of exclusion b. Cardiac dysfunction due to valvular heart disease, congenital heart disease, ischemic heart disease, Conduction abnormalities, and hypertrophic cardiomyopathy should be excluded. Previous studies on liver transplant candidates have estimated that up to 50% of patients with advanced cirrhosis have features of cardiac dysfunction and 7% - 21% of post-operative deaths were attributed to heart failure¹⁰. Cirrhotic cardiomyopathy has an insidious onset, with a long latency time, and usually it is undiagnosed, or a late diagnosed¹¹⁻¹². Symptoms range

from mild diastolic dysfunction with increasing exercise limitation, to paroxysmal atrial fibrillation and ventricular arrhythmias, to fulminant heart failure with biventricular dilatation, and ventricular hypokinesis which becomes obvious under high circulatory demands. Hepatorenal syndrome might be coexisting¹³. The high cardiac output and circulatory intravascular plasma volume and the hyperdynamic state of cirrhosis induces a volume overload in cardiac muscle which subsequently contributes to the myocardial hypertrophy, left atrial enlargement, isovolumic relaxation time prolongation and a decreased early to late diastolic flow ratio (E/A ratio). However, the decreased left ventricular afterload, due to peripheral vasodilation, conceals the systolic dysfunction, which remains normal at rest and becomes evident only during stress, in the form of an impaired chronotropic and inotropic response¹⁴. CCM is diagnosed based on electrocardiographic and echocardiographic criteria². Electrocardiographic abnormalities in CCM include QT prolongation (corrected QT interval >0.44 s) or bundle branch block and multiple extra systoles due to hyperdynamic state, as well as electromechanical dyssynergy during acute decompensation and hypotension¹⁵. Echocardiographic features of CCM include prolonged isovolumic time (>80 msec), E/A ratio < 1, and decreased pattern of contractility with preserved systolic function (LVEF > 50%) during the hyperdynamic state, as well as decreased wall motion, increased wall thickness and enlarged atrium during acute decompensation and hypotension¹⁶. In our study, 41 had evidence for cardiomyopathy (p = 0.0001). In a previous study it was found that as many as 50% of cirrhotic patients undergoing liver transplantation showed signs of cardiac dysfunction¹⁷. Patients with severe cirrhosis have a higher likelihood of having cardiomyopathy (21 out of 41 CCM patients are of Child Pugh C criteria). Thus the extent of CCM generally correlates to the degree of liver insufficiency¹⁸. Sudden changes of myocardial contractility (introduction of beta blocker therapy), hemodynamic state (vascular filling, surgical or transjugular intrahepatic porto-systemic shunts, and peritoneo-venous shunts), and shortly after liver transplantation, can unmask the presence of CCM, converting latent to overt heart failure. On the other hand, cardiac dysfunction can be reverted by liver transplantation. CCM has a major role in the pathogenesis of hepatorenal syndrome¹³. A large number of cirrhosis patients had no work up for screening for cardiomyopathy. Even those who had tests and fulfilled the criteria for CCM, the diagnosis was not documented. This is due to lack of awareness to the magnitude of the problem. Cirrhosis patients should have screening for cardiac function once diagnosis is made and at least prior to a scheduled major procedure that can unmask the dysfunction and lead to serious morbidity or death¹⁹. Echocardiography identifies a larger proportion of patients with cardiomyopathy than ECG. Current management recommendations of CCM

include nonspecific supportive measures, pharmacological therapy and liver transplantation. Patients may benefit from salt restriction (to prevent water and sodium retention), administration of loop diuretics (to decrease renal reabsorption of sodium and water), spironolactone and angiotensin receptor blockers (to inhibit the renin-angiotensin axis and prevent left ventricular remodeling), beta-blockers and nitrates (beneficial effect on adrenergic receptor density, improve the coronary arteries and have venodilatory effects leading to preload reduction. Most of the humoral and hemodynamic alterations in terminal stage liver disease are restored with time after liver transplantation. However, the exact prognosis remains unclear²⁰.

CONCLUSION

This study demonstrates that cirrhotic cardiomyopathy is a common occurrence. Cirrhotic cardiomyopathy was present in a sizeable proportion of cirrhotic patients, more so in the later stages of cirrhosis of liver. There is a direct relationship of cirrhotic cardiomyopathy with the severity of liver disease. CCM, a diagnosis of exclusion, defined by ECHO and ECG criteria is a common problem among cirrhotic patients attending a gastroenterology practice. CCM was not recognized by our clinicians, and routine screening tests were not performed. Clinical management of cirrhotic patients with early cardiac dysfunction remains uncertain. But there is a scope of future studies to look into the role of newer pharmacological agent such as Endothelins or RAAS antagonist even before this patient develop severe symptomatic cardiac dysfunction. Provider awareness of CCM is needed since implementation of angiotensin receptor blocker and beta-blocker therapy early in the course of cirrhosis may modify the changes in cardiac function. A pertinent issue for forthcoming studies is whether cirrhotic cardiomyopathy affects mortality. At present no specific treatment can be recommended and evident ventricular failure in patients with cirrhotic cardiomyopathy should be treated as non-cirrhotic causes with sodium restriction, diuretics, and afterload reduction. Cardiac glycosides may not be expected to be of significant value in cirrhotic cardiomyopathy as these failed to improve cardiac contractility after angiotensin infusion. Special caution should be taken during and after stressful procedures such as surgery, shunt implantation, and liver transplantation. Effects of beta blockers on cardiac function, QT interval prolongation, and mortality are subjects for future research. Newer treatments with anticytokines may also prove to be of interest in patients with cirrhotic cardiomyopathy.

CONFLICT OF INTEREST

Conflict of interest declared none.

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