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Original Article

Internal Medicine Section

Incidence of Cirrhotic Cardiomyopathy among Hundred Patients of Tamil Nadu, India- A Cross-sectional Study

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ABSTRACT

Introduction: Cardiac dysfunction in cirrhosis may affect quality of life, prognosis and also may aggravate the course in patients undergoing invasive procedures such as surgery, insertion of a Transjugular Intrahepatic Portosystemic Shunts (TIPS), and liver transplantation.

Aim: To evaluate the association of cardiomyopathy in cirrhotic patients of Tamil Nadu region in India.

Materials and Methods: This cross-sectional study included 100 diagnosed cirrhotic patients. The patient's cardiac status was obtained from Electrocardiography (ECG) and echocardiography. Liver profile was obtained from biochemical assays and ultrasonography of abdomen. The patients were classified as per cirrhosis grading system, Child Toucotte Pugh (CTP) scoring. The association was analysed using frequency analysis, percentage analysis and Chi-square test.

Results: Prolonged QTc (>0.44 sec) was seen in 35% of the study population (p-value-0.014). A 10% of patients had systolic dysfunction and 25% showed diastolic dysfunction. Also, these patients showed positive troponin T and elevated Brain Natriuretic Peptide (BNP). The incidence of cardiomyopathy in cirrhotic patients was 28% in this study.

Conclusion: This study established 28% incidence of cardiomyopathy in cirrhotic patients. This association may further be evaluated in larger study samples to provide a better prognosis and quality of life in cirrhotic patients treated with liver transplantation or other surgical procedures.

Keywords: Cardiac dysfunction, Cirrhosis, Child toucotte pugh scoring, QTc interval, Troponin T

INTRODUCTION

Cirrhosis causes cardiac and vascular dysfunction mostly due to peripheral vasodilatation and activation of potent vasoconstrictor system [1,2]. This aggravates hyper dynamic circulation and cardiac strain. Cardiac abnormalities in cirrhosis were initially attributed to the toxic effect of alcohol on the heart. However, experimental studies in animals [3,4] and clinical studies have shown that cirrhosis per se cause impaired myocardial contractility and electrophysiological abnormalities. Thus, it is been recognised as a distinct clinical entity and termed as "Cirrhotic Cardiomyopathy" (CCM) [5,6]. About 50 years ago, cirrhosis was not shown to have been associated with any cardiac disorder, conversely circulatory abnormality has been found [7]. Later, circulatory changes were attributed to the alcohol effects. During the latter part of 1980's, few descriptive case reports of mortality due to cardiac failure and related to cirrhosis were published [8,9]. Although Lee SS coined the term "CCM" almost two decades ago, the landmark study by Carameloc and colleagues changed the perception on CCM [3,10]. After few years, clinical studies of non-alcoholic cirrhosis showed comparable consequences.

Cirrhotic Cardiomyopathy (CCM) is defined as "a form of chronic cardiac dysfunction in patients with cirrhosis, characterised by blunted contractile responsiveness to stress and altered diastolic relaxation with electrophysiological abnormalities, such as prolongation of the QT interval, all occurring in the absence of any other cardiac disease" [11]. Cardiac insufficiency affects patient's quality of life due to fatigue. The CCM may influence the prognosis or worsen the course during invasive procedures [12,13]. Overt cardiac failure was seen in 7-15% of liver transplantation cases and cardiac complications were reported risk factors for worsening prognosis of cirrhosis. Ruíz-del-Árbol L et al., revealed cardiac dysfunction as sensitive marker of advanced cirrhosis. Premkumar M et al., revealed a positive association between the severity of cardiac dysfunction and mortality in cirrhotics. Also, stated that presence of class II/III symptoms of heart failure is predictor of mortality in two years [14-17]. Thus, management of cardiac complication may provide better prognosis and quality of life in patients with CCM. Further, the incidence of CCM in South Indian population, though studied in small population by previous researchers and the effects of severity of liver dysfunction on cardiac complications is lacunae in this area.

This present study aimed to analyse the frequency of CCM and its correlation with severity of liver dysfunction.

MATERIALS AND METHODS

This was a cross-sectional study including 100 patients of cirrhosis admitted in Department of Medical Gastroenterology, Sri Ramachandra Medical College, a tertiary care centre in Chennai, Tamil Nadu, India, during the period from February 2016 to February 2018. The study was initiated after obtaining the departmental ethical approval (MGE03/2017) and patient consent.

Inclusion criteria: All cirrhotic patients confirmed with hepatocellular dysfunction by clinical, biochemical, and radiological evidences (abridged liver span <8 cm with ascites, splenomegaly, lengthened prothrombin time >12 seconds and decreased serum albumin levels <3.5 g/dL, amplified hepatic echo pattern and/or portal vein diameter >1.3 mm, respectively) were included in the study.

Exclusion criteria: Patients with recent bleeding, gross ascites, severe anemia that could alter cardiovascular status; previous history of heart valve disease, myocardial infarction, heart block, cardiac failure, diabetes mellitus, hypertension, electrolyte disturbances; history of medication with anti-arrhythmics, calcium channel blockers and digoxin; liver diseases associated with pregnancy; patients with malignancy; mental illness or conditions which make it difficult for the potential participant to participate in the study were excluded.

The study enrolled only 100 patients. The eligible patient's basic demographic details were noted. Biochemical tests for liver function and prothrombin time; abdominal ultrasonography was performed along with clinical assessment for degree of ascites and hepatic encephalopathy. CTP scoring was done for each patient [17].

Resting ECG was performed in all the patients. The QTc >0.44 sec was defined as prolonged. Then, cardiac structural and functional assessment was performed non-invasively using transthoracic echocardiography. Diagnostic criteria for systolic dysfunction was resting Ejection Fraction (EF) <55% and for diastolic dysfunction was early diastole/late diastole (E/A) ratio <1.0. CCM was diagnosed as per World Congress of Gastroenterology 2005 definition (systolic dysfunction, blunted increase in cardiac output on exercise, volume challenge or pharmacological stimuli, resting Left Ventricular Ejection Fraction (LVEF) <55%, diastolic dysfunction, E/A ratio < 1 (age-corrected), prolonged deceleration time (>200 ms), prolonged isovolumetric relaxation time (>80 ms), supportive criteria, electrophysiological abnormalities, abnormal chronotropic response, electromechanical uncoupling, prolonged QTc interval, enlarged left atrium, increased myocardial mass, increased BNP and pro-BNP, increased troponin T [11].

STATISTICAL ANALYSIS

The study data was analysed with IBM Statistical Package for the Social Sciences (SPSS) 23.0 software. The descriptive statistics were used for categorical variables and mean±Standard Deviation (SD) was used for continuous variables. The significance was obtained with Chi-square test and the Fisher's-exact. The p-value <0.05 was taken as significant.

RESULTS

This descriptive study included 100 cirrhotic patients. Among 100 cirrhotic patients' majority (53%) were in 41 to 50 years age group [Table/Fig-1]. The mean age of the patients was 47.53±6.933. Majority of cirrhotic patients were males (92%) and females being 8%. Among 92 male cirrhotic patients, 26 of them had CCM and among 8 female patients 2 had CCM [Table/Fig-1].

The aetiology of cirrhosis was due to alcohol in 76% and remaining 24% were related to Hepatitis B Virus (HBV), Hepatitis C Virus (HCV), Non-alcoholic Steatohepatitis (NASH) and cryptogenic causes [Table/Fig-1]. CCM was present in both Alcoholics (42.9%) and Non-Alcoholics (57.1%). The CCM frequency in alcoholics was significantly different from non-alcoholics. Out of 100 patients, majority (72%) belonged to Child-Pugh C. Frequency of occurrence was more in advanced cirrhosis (CTP C > B >A) [Table/Fig-1].

Resting ECG was done in all patients which showed prolonged QTc (>0.44 sec) in 35 patients. Total 25% patients had diastolic dysfunction in the form of E/A ratio being <1. Systolic dysfunction was noted in 10% of patients in the form of EF being <55%. The BNP was done only in 40 cirrhotic patients (>100 was considered elevated), among them 13 cirrhotics had elevated BNP, whereas 11 patients had CCM. This shows BNP is significantly high in CCM patients. Troponin T was done in 40 cirrhotic patients among them 13 patients have CCM. Of these13 patients, 9 (23%) patients had positive troponin T [Table/Fig-1]. The overall frequency of cirrhotic liver associated cardiomyopathy in the study was 28%.

Factors				Total	p-value
Age groups (years) (N)	31-40	11		100	0.0001
	41-50	53			
	51-60	36			
		CCM			
		Absent	Present		
Gender (N%)	Female	6 (8.3)	2 (7.1)	8	1.000
	Male	66 (91.7)	26 (92.9)	92	
	Total	72 (100.0)	28 (100.0)	100	
Aetiology (N%)	Non-alcoholic	8 (11.1)	16 (57.1)	24	0.0001
	Alcoholic	64 (88.9)	12 (42.9)	76	
	Total	72 (100.0)	28 (100.0)	100	
Child turcotte pugh scoring categories (N%)	A	7 (9.7)	3 (10.7)	10	0.002*
	B	7 (9.7)	11 (39.3)	18	
	C	58 (80.6)	14 (50.0)	72	
	Total	72 (100.0)	28 (100.0)	100	
Brain natriuretic peptide (pg/mL) (N%)	>100	25 (92.6)	2 (15.4)	27 (67.5)	0.0005
	<100	2 (7.4)	11 (84.6)	13 (32.5)	
	Total	27 (100.0)	13 (100.0)	40 (100.0)	
Troponin T (N%)	Negative	27 (100.0)	4 (30.8)	31 (77.5)	0.0005
	Positive	0 (0.0)	9 (69.2)	9 (22.5)	
	Total	27 (100)	13 (100)	40 (100)	
QTc interval (sec) (N)	<0.44	65		100	0.014
	>0.44	35			
E/A ratio (N)	<1	25		100	0.0001
	>1	75			
EF (%) (N)	<55	10		100	0.0001
	>55	90			

[Table/Fig-1]: Factors associated with CCM and their analysis.
CCM-Cirrhotic cardiomyopathy; p-value obtained with Fisher's Exact test; *p-value obtained with Chi-Square test; CTP-Child turcotte pugh scoring, E/A ratio-early diastole/late diastole ratio; EF-Ejection fraction, BNP-Brain natriuretic peptide, CCM-Cirrhotic cardiomyopathy; p-value <0.05 considered as statistically significant

DISCUSSION

The aim of the present cross-sectional study was to evaluate the CCM frequency in cirrhotic patients and its association with severity of hepatic disease. The incidence was 28% and increased with severity of liver disease.

Bernardi M et al., Kwon HM and Hwang GS, Huette P et al., showed prolonged myocardial contractility index independent of alcoholism and ascites in cirrhotic patients, respectively [12,18,19]. Contractile abnormality was seen more severe in ascitic cirrhosis, recommending association between cardiac dysfunction and hepatic disease severity. Kwon HM and Hwang GS found significantly decreased E/A ratio in ascitic patients, showing a greater decrease in venous return compared to pre-ascitic cirrhotic patients [18].

Alexander J et al., study further highlighted that diastolic dysfunction was seen in more cirrhotic patients [20]. The prolonged QT interval is frequently seen in patients of cirrhosis, irrespective of the disease aetiology. Its prevalence is 45% and is relative to the cirrhosis severity [12].

In the present study, the QT interval prolongation was observed in 35% and increasing association correlated directly with hepatic disease severity as per Child-Pugh classification, class A with 10% to 18% in class B and 72% in class C. Elevated serum BNP in cirrhotic patients reveals increased cardiac ventricular production of these peptides and thus shows the presence of cardiac dysfunction, more than circulatory changes seen in such patients.

In this study, BNP was significantly high in CCM patients. Troponin was prominent in CCM, possibly revealing the causal myocardial damage. Cardiac troponin was observed in 23% of cirrhotic patients. Elevated BNP and Troponin levels recommended the possible role of these indicators for evaluating cirrhotic patients for the incidence of CCM, and thereby recognising cirrhotic patients for further examination. The overall frequency of CCM in this study was 28% while it was 33% in an Asian study by Shaikh S et al., [21]. Alcoholic and non-alcoholic group patients showed significant difference in CCM incidence, this shows cirrhosis per se was the cause for cardiomyopathy. Previous studies conducted in southern India revealed prevalence of CCM to be 33%-36% (approximately) [22,23].

Limitation(s)

The study limitations include a small sample size and the fact that few biochemical parameters like troponin I and BNP were not done in all the patients.

CONCLUSION(S)

CCM is one of the most common complications of advanced liver disease per se and is related to alcohol. The frequency correlates directly with severity of hepatic disease. Impact of this clinical entity on prognosis and liver transplantation needs future studies. Clinical trials related to CCM are eagerly awaited. Treatment of cirrhosis with liver transplantation may also cure the associated cardiomyopathy. Also, poor cardiac response may decide the risk, prognosis and quality of life in patients of liver transplantation and other related invasive procedures. Understanding CCM is essential to prevent complications in the future with respect to cirrhosis. Furthermore, studies are required to evaluate the prevalence and association through larger population and multicentric studies all over India. CCM may be present in most of the patients with cirrhosis and it can complicate several procedures performed in treating cirrhosis.

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