

Cardiac Dysfunction In Patients Of Cirrhosis Of Liver And Its Correlation With Child-Pugh Score, A Cross-Sectional Study At A Tertiary Care Centre In Northern India

Dr. Suman Roy¹, Dr Anubha Garg², Dr Kashish Mittal³

(Junior Resident, Internal Medicine, Pt BD Sharma PGIMS Rohtak, India)

(Professor, Internal Medicine, Pt BD Sharma PGIMS Rohtak, India)

(Junior Resident, Internal Medicine, Pt BD Sharma PGIMS Rohtak, India)

Abstract:

Background: Chronic liver disease is a process of destruction and regeneration process of the liver parenchyma leading to an extensive spectrum of changes in the liver. Liver cirrhosis is associated with a wide range of cardiovascular abnormalities including hyperdynamic circulation, cirrhotic cardiomyopathy, pulmonary vascular abnormalities, and QT interval prolongation. Peripheral and splanchnic vasodilatation are the main causes of hyperdynamic circulation. Cirrhotic cardiomyopathy was first defined in 2005 at the Montreal World Congress of Gastroenterology. Cirrhotic cardiomyopathy is considered a condition of latent heart failure that manifests only under stress, resulting in a blunted increase in cardiac index and cardiac output during exercise or pharmacological stimuli. The main objective of this study is to determine whether or not there is any correlation between the severity of cirrhosis and the incidence of cardiac abnormalities in cirrhotic patients, regardless of the etiology of the cause of cirrhosis.

Materials and methods

A total of 100 cases as per the diagnostic criteria of liver cirrhosis were enrolled in the patient and outpatient department of General Medicine of PGIMS, Rohtak. Assessment of cardiac function was done in all the patients. 2D ECHO was done to find evidence of cardiomyopathy, and ECG was done to find QT interval prolongation. CTP score was calculated for severity. The cardiac dysfunction was compared to the seriousness of the CTP score.

Results: In our study population, 57% of patients had shown diastolic dysfunction. Systolic dysfunction was not seen in any case. Also, 56% of the cases had prolonged QTc interval in ECG. Our study also shows that there is a definitive association between QTc prolongation and disease severity. Our study also found that the sensitivity and specificity of QTc prolongation for the detection of diastolic dysfunction are 75.4% and 69.7% respectively.

Conclusion: Cirrhotic cardiomyopathy is considered an important predictor of morbidity and mortality as per various studies done in the past. It is a condition of latent heart failure, characterized by diastolic dysfunction and left ventricular hypertrophy. The left ventricular ejection fraction at rest is normal in cirrhotic cardiomyopathy, but there is a blunted increase in cardiac index and cardiac output during exercise. This is difficult to identify because these symptoms are similar to fatigue and exercise intolerance commonly seen in cirrhotic patients. Our study found a significant prevalence of cardiac dysfunction in cirrhotic patients and a correlation between cardiac dysfunction and the severity of liver disease.

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I. Introduction

Liver cirrhosis is a hyperdynamic condition characterized by increased cardiac output and decreased peripheral vascular resistance. Advanced cirrhosis redistributes blood to the splanchnic bed, reducing central blood volume and activating compensatory systems. Because of these hemodynamic profiles, several cardiac abnormalities can develop, leading to cirrhotic cardiomyopathy which includes abnormal contractile response to stress or altered diastolic relaxation with electrophysiological abnormality. Cirrhotic cardiomyopathy (CCM) is characterized by blunted inotropic and chronotropic stress responses, diastolic dysfunction, and QT interval prolongation. These abnormalities occur independently of liver etiology and affect 40% to 50% of cirrhotic patients¹. CCM is a significant risk factor for perioperative and postoperative heart failure following liver transplantation, with 3%-14% developing heart failure. It is a condition of latent heart failure that manifests only under stress, resulting in a blunted increase in cardiac index and cardiac output during exercise or

pharmacological stimuli². However, these are barely identified at rest because it is confused with other symptoms of liver cirrhosis, such as exercise intolerance, fatigue, and dyspnea. Advanced cirrhosis leads to arterial underfilling, triggering the renin-angiotensin system, sympathetic activation, and antidiuretic hormone release, resulting in salt and water retention, ascites, and disease progression. Vasodilators like nitric oxide (NO), adrenomedullin, natriuretic peptides, and cytokines mediate systemic vasodilatation³. The diagnostic criteria for cirrhotic cardiomyopathy (CCM) proposed by the Cirrhotic Cardiomyopathy Consortium (2019)⁴.The criteria are categorized into three sections: Systolic dysfunction, Advanced diastolic dysfunction, and Areas for future research requiring further validation

Diastolic dysfunction is the hallmark of CCM, affecting over 50% of cirrhotic patients and correlating with disease severity. It results from myocardial hypertrophy, fibrosis, and subendothelial edema, leading to reduced ventricular compliance and abnormal filling. The E/A ratio, E/e', and other echocardiographic parameters assess diastolic function. Studies link diastolic dysfunction to reduced survival, though function improves within 6-12 months post-liver transplantation.

Cirrhosis-associated electrophysiological abnormalities include QT interval prolongation, electromechanical dyssynchrony, and chronotropic incompetence. Up to 50% of cirrhotic patients exhibit prolonged QTc (≥ 440 ms), attributed to potassium channel dysfunction and adrenergic hyperreactivity. ECG abnormalities, including low voltage, correlate with higher mortality.

II. Materials And Methods

This cross-sectional study was conducted at the Department of Internal Medicine, Pt BDS PGIMS Rohtak, Haryana, India from September 2022 to July 2024 for a total duration of 2 years. A total of 100 patients from the inpatient and outpatient departments of the medicine department were enrolled after obtaining consent from the patient and after receiving approval from the ethical committee.

Inclusion criteria: All patients above 18 years of age who fulfill the diagnostic criteria for liver cirrhosis. Liver cirrhosis is diagnosed based on the USG feature of altered echotexture in the liver and liver stiffness measurement by fibroscan.

Exclusion criteria: Any patient with known overt cardiac disease, chronic kidney disease, history of intake of hepatotoxic drugs, diabetes Mellitus and hypertension were excluded from the study.

Procedure: 100 patients from inpatient and outpatient department after fulfilling the mentioned criteria were enrolled in the study. A detailed history was recorded, including the patient's demographic profile and any previous comorbidities. A complete general physical and systemic examination was done. Blood samples were taken for a Complete hemogram (CH), Liver function test (LFT), Renal function test (RFT), PT INR, Viral marker, and Blood gas analysis. All underwent USG to evaluate liver cirrhosis based on liver echotexture. Those without ascites underwent Fibroscan for LSM value. Each patient underwent ECG and 2D ECHO for cardiac evaluation. The collected data were evaluated to calculate Child Turcotte Pugh score⁵ for severity and the cardiac findings were compared with the severity of liver cirrhosis using Child Pugh scoring.

Statistical analysis: Data analysis was carried out using SPSS (IBM version 28.0). Clinical, Laboratory, Radiological and 2D echo findings were expressed in numbers and percentages.

III. Result

This study included a total of 100 patients of chronic liver disease mostly males(94%). A majority of patients belonged to the age group of 31 to 50 years(72%). Patient were classified as per Child Turcotte Pugh(CTP) score to Class A, B and C.The highest number belonged to Class B(47%), followed by Class A(29%) and lowest in Class C(24%). Alcohol was found the most common etiology of cirrhosis in this study (85%), followed by Chronic viral hepatitis(7%), NASH (4%), autoimmune hepatitis (3%) and NCPF(1%).

In this study, 56% of patients were found to have QTc prolongation in ECG (Table 1). QTc prolongation was most commonly seen in Class C group(75%), followed by Class B (52.17%) and and Class A (44.82%) (Table 2)

Table 1: QTc interval prolongation

QTc interval	No of patients
Prolonged	56
Normal	44

Table 2: Comparison Of QTc prolongation with CTP Class

CTP class	Total Patients	No of patients having prolonged QTc
Class A	29	13 (44.82%)
Class B	46	24 (52.17%)
Class C	24	18 (75%)

On ECHO all patients had normal systolic function. However, out of total patients, 57% patients had diastolic dysfunction (Table 3). Out of these, 41% of the patients had grade 1 Diastolic dysfunction, 14% had grade 2 and 2% had grade 3 DDF (Table 4).

Table 3: Patients having cardiac dysfunction on Echocardiography

Cardiac dysfunction in ECHO	No of patients
Systolic dysfunction	0%
Diastolic dysfunction	57%

Table 4: Distribution of study population according to diastolic dysfunction. (N = 100)

Diastolic dysfunction	Number of cases
Grade 1	41 (41%)
Grade 2	14 (14%)
Grade 3	2 (2%)
No DDF	43 (43%)

This study found that a higher CTP score was associated with a higher degree of diastolic dysfunction. Highest Grade 3 diastolic dysfunction was found in only CTP Class C group (8.33% of the patients) in this study. Grade 2 and Grade 1 DDF was also found more in CTP Class C than in CTP Classes B and CTP Class A.

Table 5: Distribution of cases according to CTP class with grade of diastolic dysfunction. (N = 100)

CTP Class	Grade 0	Grade 1	Grade 2	Grade 3	Total	p-value
Class A	18 (62.06%)	10 (34.48%)	1 (3.44%)	0 (0%)	29	<0.001
Class B	23 (48.93%)	19 (40.42%)	5 (10.63%)	0 (0%)	47	
Class C	2 (8.33%)	12 (50%)	8 (33.33%)	2 (8.33%)	24	

This study also found that the presence of diastolic dysfunction on ECHO correlated with the presence of QTc prolongation in ECG. Out of the patients who had diastolic dysfunction 75.43% had QTc prolongation (Table 6). In grade 3 DDF, 100% of the patients had QTc prolongation, followed by 85.7%, 70.7%, and 30.23% in patients having Grade 2, Grade 1 and No diastolic dysfunction. So more the severity of diastolic dysfunction, more the number of patients having QTc prolongation (Table 7).

Table 6: Comparison between Diastolic dysfunction with QTc prolongation

	QTc prolonged(n=56)	QTc normal(n=44)
DDF (+) (n=57)	43	14
DDF (-) (n=43)	13	30

Table 7: QTc abnormality compared with Diastolic dysfunction

Grade of diastolic dysfunction	No of patients with diastolic dysfunction(57)	No of patients having QT prolongation (n=56)
Grade 3	2	2 (100%)
Grade 2	14	12 (85.7%)
Grade 1	41	29 (70.7%)
No DDF	43	13(30.23%)

Diastolic dysfunction also correlated with the liver stiffness measurement (LSM) value. Patients with grade 1 DDF had mean LSM value of 36.6, followed by 49.79 and 54.2 for grade 2 and grade 3 patients (Table 8).

However, this study did not find any significant correlation between QTc interval abnormality with LSM value.

Table 8: Comparison of Fibroscan according to grade of diastolic dysfunction. (N = 91)

Grade of diastolic dysfunction	Mean LSM value (SD)	p-value
No DDF	39.06 (15.79)	0.034
Grade 1	36.61 (13.17)	
Grade 2	49.79 (13.78)	
Grade 3	54.2 (3.11)	

IV. Discussion

Cirrhotic patients can have multiple organs involved including hematologic, renal, pulmonary, cardiovascular and endocrine systems etc. Cirrhotic patients can have various cardiovascular abnormalities. Cirrhotic cardiomyopathy is considered an important predictor of morbidity and mortality regardless of the etiologies. It is a condition of latent heart failure, characterized by diastolic dysfunction and left ventricular hypertrophy. The left ventricular ejection fraction at rest is normal in cirrhotic cardiomyopathy, but there is a blunted increase in cardiac index and cardiac output only during exercise. This is difficult to identify because these symptoms are similar to fatigue and exercise intolerance is commonly seen in cirrhotic patients. The criteria for diastolic dysfunction in ECHO include the septal e' velocity <7 cm/s, E/e' ratio >15, left atrial volume index >34 mL/m² and tricuspid regurgitation velocity > 2.8 m/s. Apart from ECHO findings, there are some other supporting criteria like prolonged QTc interval, enlarged left atrium, increased myocardial mass, increased level of BNP or pro-BNP and increased troponin I which also favors the diagnosis of cirrhotic cardiomyopathy.

In this study, QTc interval was found prolonged in 56% of the total patients and was found most frequently associated with CTP Class C (in 75%) followed by class B and A. In a study done by M Bernardi et al The prevalence of QTc prolongation was found to be more than 60% in advanced disease and they had lower survival rates as compared to those having normal QTc⁶. In this study also QTc interval was correlating to the severity of cirrhosis. On 2D ECHO all the patients had normal systolic function. Which is similar to the studies done in the past. In a study done by Maurizio Cesari et al⁷ they found that none of the patients had LVEF <50%. However, 57% of patients were found to have diastolic dysfunction. Among them, the majority had grade 1 DDF. In a study done by A. Salari et al 51% of patients had diastolic dysfunction⁸

In this study diastolic dysfunction was compared with QTc prolongation and it was found that out of 57% patients who had diastolic dysfunction, 75.43% had QTc prolongation as well and the rest 14 had normal QTc. Out of 43% of patients who had no diastolic dysfunction on ECHO, 30% had prolonged QTc interval. As per previous studies, QTc prolongation is associated with diastolic dysfunction. In a study done by Jane E Wilcox et al, a QTc interval of >435 ms had a sensitivity of 73% and specificity of 74% for the detection of diastolic dysfunction. Patients with moderate or greater diastolic dysfunction had more prolonged QTc compared to patients with no or mild diastolic dysfunction⁹. In our study, 100% of the patients in Grade 3 DDF had QTc prolongation. As per this study, the sensitivity and specificity of QTc prolongation for the detection of diastolic dysfunction are 75.4% and 69.7% respectively. Also, there can be some confounding factors as well causing QTc prolongation e.g. Age, female gender, hypokalemia, hypocalcemia, hypomagnesemia etc. This study also discovered that higher CTP class were associated with a higher degree of diastolic dysfunction. This finding was comparable to a study done by A. Salari et al where they found that with the increase in severity of cirrhosis from Child A to Child C, the grade of diastolic dysfunction was also increasing¹⁰.

In this study, it was also found that diastolic dysfunction was also correlating with the fibroscan value. As in our study, patients having Grade 1 DDF had a mean LSM value of 36.6, followed by 49.79 and 54.2 for grade 2 and grade 3 patients. Which was statistically significant (p-value 0.034). although we could not find any previous studies comparing fibroscan value with the presence of diastolic dysfunction. This study did not find any significant correlation between QTc interval abnormality and fibroscan value.

V. Limitation

A small sample size in our study and the number of patients enrolled in CTP classes A, B, and C were not equal, so the result may not be generalized.

VI. Conclusion

Cirrhotic cardiomyopathy is a latent cardiac dysfunction exacerbated under stress, often overlooked in advanced liver disease. Accurate diagnosis and updated criteria, combined with echocardiographic and biomarker analysis, are critical for early detection and management, particularly in transplant candidates. Further research is needed to refine prognostic models and improve outcomes in this population.

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