**Echocardiographic study of left ventricular structure and functions in patients with chronic liver disease and its correlation to disease severity**

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**ABSTRACT**

Background: The concept of cirrhotic cardiomyopathy includes impaired cardiac contractility, decreased beta-adrenergic receptor function, abnormal beta-adrenergic post-receptor function, defective excitation-contraction coupling, and cardiac conduction abnormalities. The aim of our study is to assess the cardiac dysfunctions in patients of cirrhosis of liver, irrespective of etiology, and establish correlation between severity of disease and incidence of cardiomyopathy.

Methods: This was a cross-sectional, observational study of patients with CLD without any known cardiac disease attending the medical outpatient and inpatient department of the tertiary care center. Selected patients after informed consent were investigated further along with M-mode and Doppler echocardiographic studies to determine the cardiac structure and systolic and diastolic cardiac functions.

Results: A total of 60 subjects were enrolled for the study. Maximum cases of this study, that is, 70% patients were in the age group of 40–60 years with the mean age of 51.82 ± 6.48 years and male: female ratio of 3.1:1. Prolongation of QTc is observed in 35% of the study group. Diastolic dysfunction (E/A <1.0) was found in 43.33% of cases, varying from 60% in model for end-stage liver disease Group III to 41.6% in Group I and 39.5% in Group II, showing a positive correlation between severity of cirrhosis and E/A ratio. The left ventricular mass index in subject showed its proportional increase in relation to degree of severity of cirrhosis.

Conclusion: We demonstrated an increase in cardiac dysfunction, especially diastolic in the subjects and its significant associations with the severity of disease.

Key words: Cardiomyopathy, chronic liver disease, cirrhotic cardiomyopathy, CLD, diastolic dysfunctions

**INTRODUCTION**

Chronic liver disease is a common disease in India as well as in western country mostly caused by alcoholism, viral hepatitis, and malnutrition. The clinical picture of patients with cirrhosis is dominated by the classical complications such as ascites, bleeding from esophageal varices, portal hypertension, and encephalopathy.[1] Liver cirrhosis is a systemic disease with widespread functional consequences affecting almost any other organ including the cardiovascular system. Cardiovascular abnormalities also have been reported by several investigators. Cirrhotic cardiomyopathy is the term used to describe a collection of characters expressive of abnormal heart structure and function in patients with cirrhosis.[2] Many studies indicated that some level of diastolic dysfunction exists in most patients with cirrhosis.

Cirrhotic patients have hyperdynamic circulation with decreased peripheral vascular resistance, increased cardiac output and stroke volume, and low systemic arterial pressure. The level of circulating vasoactive substances which are not inactivated by the liver is increased such as vasoactive intestinal peptide, glucagon, and tumor necrosis factor-α, prostacyclin, nitric oxide, endothelin-1, and endothelin-3. These circulatory changes in cirrhosis are responsible for diastolic dysfunctions.[3] Most studies on the impact of CLD on cardiac structure and function have emanated from developed countries.

The aim of our study is to assess cardiac dysfunctions in patients of cirrhosis of liver, irrespective of etiology, and establish correlation between severity of disease and incidence of cardiomyopathy.

**MATERIALS AND METHODS**

It is a cross-sectional and observational study done on 60 patients admitted to two tertiary care centers, Rajendra Institute of Medical Sciences, Ranchi and Indira Gandhi Institute of Medical Sciences, Patna. Patients were selected from outpatient department and inpatient department of medicine of the hospital as per inclusion and exclusion criteria after informed consent.
Inclusion Criteria
The following criteria are included in the study:
1. Age group > 18 years and
2. Patients with clinical features, laboratory tests, and imaging suggestive liver cirrhosis.

Exclusion Criteria
The following criteria are excluded from the study:
1. Patients suspected of liver malignancy.
2. Patients of ischemic heart disease, valvular heart disease, conduction defects, cardiac arrhythmias, and congenital heart disease.
3. Known cases of diabetes and hypertension.
4. Patient with hepatic encephalopathy.
5. Patients having congenital corrected QT (QTc) interval prolongation.

After inclusion in the study, patients were subjected to following minimum investigations:
1. Complete blood count.
2. Serum bilirubin/ALT/aspartate transaminase.
3. Prothrombin time (PT) with international normalized ratio (INR).
4. Blood urea nitrogen/serum creatinine/serum electrolytes.
5. Ultrasonography.
6. 12-lead electrocardiogram was done to calculate QT interval manually and QTc using Bazett’s formula as QTc = QT INTERVAL/TI INTERVAL. Prolonged QT interval was defined as value > 440 ms (0.44 s).
7. 2D Echo was done by Philips HD (7× E) with adult probe and was used to assess cardiac anomaly with special reference to the left atrial diameters, left ventricle end diastolic volume, I.V. septal thickness, and left ventricular posterior wall thickness and to assess E/A ratio where E stands for early maximum left ventricular filling velocity and A for late diastolic left ventricle filling velocity; the left ventricle systolic function was calculated using ejection fraction (EF%) and diastolic function was assessed by E/A and if ratio was < 1, it was taken as diastolic dysfunction.

Biochemical Profile
Mean serum bilirubin in MELD Group I was 1.41 ± 0.13 mg/dl, 2.62 ± 0.40 mg/dL in MELD Group II, and 6.86 ± 1.87 mg/dl in MELD Group III.

Statistical Analysis
All data generated were entered into a standard pro forma. Continuous variables were summarized as mean and standard deviation while nominal/categorical variables as proportions (%). ANOVA was used for analysis of continuous variables, whereas Chi-square test was used for nominal/categorical variables. P < 0.05 was taken as statistically significant. Microsoft Word and Excel were used to generate graphs, tables, and derivation.

The study was approved by institutional scientific and ethics committee.

RESULTS AND OBSERVATIONS
In our study, most of the patients, that is, 70% (42/60) were in the age group of 40–60 years, followed by 16.6% (10/60) in 60–80 years and 13.33% (8/60) were in 18–40 years of age with the mean age of 51.82 ± 6.48 years. 38 of 60 were males (63.33%) and 12 (36.67%) were females [Figure 1].

Categorization of the patient according to the MELD classification shown in Figure 2 where around 64% (38/60) of cases belong to MELD Group II followed by 20% in Group I and 16% in Group III.

Patients grading for cirrhosis was done by model for end-stage liver disease (MELD) criteria as follows:

MELD = 3.78 [Ln Serum bilirubin (mg/dL)] + 11.2 [Ln INR] + 9.57 [Ln serum creatinine (mg/dL)] + 6.43

MELD Scoring:
Stage I - MELD Score < 9.
Stage II - MELD Score 10–19.
Stage III - MELD Score > 20.

Figure 1: Composite distribution of age and sex in study group

Figure 2: Distribution of patient among model for end-stage liver disease groups
6.86±1.87

In a study performed by Fu-Rong Sun et al., demonstrated QTc prolongation in 32% in study population.

Similarly, Kosar et al. demonstrated QTc prolongation in 32% in study population. All these studies showed the frequency of prolonged QTc similar to our study. Sidmal et al. and Patil et al. also showed similar age group and sex distribution in their study done on patient with cirrhosis.

In this study, prolongation of QTc is observed in 35% of study group. QTc prolongation was seen in 38.33% patients of cirrhosis studied by Patil et al. Similarly, Kosar et al. demonstrated QTc prolongation in 32% in study population. All these studies showed the frequency of prolonged QTc similar to our study. Furthermore, Li et al. demonstrated QTc prolongation in a similar study in 46.93% of patients which is slightly higher than our study.

Diastolic dysfunction (E/A <1.0) were noted in 48.33% of patients by Patil et al., varying from 70% in MELD Group III and 50% (10/20) in MELD Group I which is comparable to our study. Similar study conducted by Achecar and Gonzalez-Tallon, in 2011, showed that 50% of cirrhotic patients had left ventricular diastolic dysfunction. The prevalence of diastolic dysfunction was 51% in a study conducted by Salari, in 2013.

The left ventricular mass index as calculated by the left ventricular mass/body surface area (m²), and it was 81.320±14.48 g/m² in MELD Group I and 118.40 ± 14.78 g/m² in MELD Group III, therefore, showing a proportional increase in the left ventricular mass index in relation to degree of severity of cirrhosis. Patil et al. showed significant correlation between the left ventricular mass index and disease severity in their study and their results are comparable to results in our study. Similar results were also demonstrated in the study by Silvestre et al.

In a study performed by Fu-Rong Sun et al., in 2011, of 82 patients, MELD score was positively correlated with enlarged left atrial diameter, increased interventricular septum thickness (IVST). This association between enlarged left atrial diameter and IVST with disease severity (MELD score) was also significant in our study.
CONCLUSION

Cardiac dysfunction is a common complication of advanced cirrhosis that can make a variety of disturbances including diastolic dysfunction. Duration of disease, increased age, and severity of cirrhosis can increase the severity of diastolic dysfunction. Due to high prevalence of diastolic dysfunction in cirrhotic patients and risk of decompensation following invasive procedures, it could be suggested that all patients would be screened routinely by echocardiography before invasive procedures.\[13\]

Early detection of systolic/diastolic myocardial dysfunction by 2D Echo and appropriate early treatment of this cirrhosis will delay the onset of cardiac dysfunction associated with the disease. A high alerting social awareness programed to promote alcoholic withdrawal and nutritional supplementary drive to overcome hepatic assault will minimize cirrhosis and thereby decreasing the incidence of cardiomyopathy and national burden on economy of nation.

In our study, diastolic and other cardiac dysfunctions are significantly associated with severity of disease.

However, there are currently no specific guidelines for the diagnosis and treatment of cardiovascular disease in this patient population. Thus, new prospective studies are needed to identify more specific criteria and standardized procedure for cardiovascular assessment and treatment of cardiac dysfunction in patients with liver cirrhosis.

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Table 3: Diastolic dysfunction among study group

| MELD group | Total number of cases | Cases with E/A<1.0 |
|------------|-----------------------|-------------------|
| I          | 32                    | 5                 |
| II         | 38                    | 15                |
| III        | 10                    | 6                 |
| Total      | 60                    | 26                |

MELD: Model for end-stage liver disease