

# Study of cardiovascular dysfunction in chronic liver disease in a tertiary care hospital in eastern India



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## ABSTRACT

**Background:** Chronic liver disease (CLD) exhibits characteristic hemodynamic changes along with pathological changes in the myocardium. Compensated by the decreased systemic vascular resistance, overt heart failure is usually not seen, and thus cardiac pathology is frequently overlooked. **Aims and Objectives:** The objectives of the study were to study the presence, types, and severity of cardiovascular (CV) dysfunction in patients of CLD. **Materials and Methods:** An observational cross-sectional study on 50 patients of CLD at Calcutta National Medical College and Hospital, with all relevant investigations. **Results:** Out of a sample of 50 patients, of which 14.3% were mild, 34.3% moderate and 51.4% severe CLD (by Child-Pugh Class), 28.6% had a high normal heart rate (90 to 100/min), 45.7% had increased stroke volume index, and 42.9% increased cardiac index, reflecting hyperdynamic circulation. In 42% cases, left ventricular ejection fraction was increased more than 65%, reflecting hyperdynamic circulation, but decreased < 55% in 23% cases, which may be an indicator of cirrhotic cardiomyopathy. Ejection fraction is significantly ( $P=0.016$ ) increased after paracentesis in 33.3% patients, reflecting the mechanical effect of ascites on cardiac function. Diastolic dysfunction was present in 60% ( $P=0.012$ ) and left ventricular mass index was increased in 45.7% cases. All the parameters correlated with increasing Child-Pugh Class severity of CLD. **Conclusion:** A high level of awareness is needed to take into account the presence of CV dysfunction and cirrhotic cardiomyopathy in patients of CLD and predict the risk of adverse cardiac events. Specific treatment modalities need further study to improve prognosis in these patients.

**Key words:** Cardiomyopathy; Chronic liver disease; Cirrhosis; Heart failure

## INTRODUCTION

Cardiovascular (CV) dysfunction is an overlooked complication of chronic liver disease (CLD), especially with increasing severity of the disease, and it is an important factor for reduced exercise tolerance, and suboptimal response to various stresses such as infections, ultimately contributing to increased mortality in these patients.

Cardiac disease itself can cause hepatic dysfunction, for example, long standing Right Ventricular dysfunction or chronic congestive cardiac failure causing passive hepatic venous congestion and cardiac cirrhosis, or poor cardiac output with malperfusion causing liver and multisystem dysfunction.

However, there are also secondary effects of liver disease on the CV system. Progressive CLD is associated with decreased systemic venous resistance, which is mainly due to splanchnic arteriolar vasodilation resulting in a hyperdynamic circulation.<sup>1</sup> Circulating vasoactive substances, mainly of endothelial origin, escape hepatic degradation due to portosystemic shunting and hepatocellular damage, and induce vasodilatation. This leads to reduced vascular resistance and thereby reduction in effective arterial blood volume and blood pressure.<sup>2</sup> This, in turn, leads to counter-regulatory activation of the sympathetic nervous system, renin-angiotensin-aldosterone-system, and increased antidiuretic hormone.

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The consequences are an increase in fluid and salt retention, cardiac output, and heart rate.

Manifestations of CV dysfunction are not very evident clinically, that is, it is essentially latent. The most striking hemodynamic feature is increased cardiac output. Left ventricular ejection fraction (LVEF) is found to be increased in many patients.

CV dysfunction and cirrhotic cardiomyopathy<sup>3</sup> are significant but under-recognized factors involved in morbidity and mortality of patients of CLD, especially those exposed to different stressors such as exercise, infections, or surgical procedures such as transjugular intrahepatic portosystemic shunt (TIPS) or liver transplantation. In such situations, the latent heart failure may be unmasked. Our study was conducted to analyze the occurrence of CV dysfunction in CLD and correlate its severity with the severity of the liver disease.

#### Aims and objectives

To study the presence, types and severity of CV dysfunction in patients of CLD.

#### MATERIALS AND METHODS

This was an observational cross-sectional study conducted on 50 patients of CLD admitted in the inpatient Department of General Medicine of Calcutta National Medical College and Hospital from May 1, 2009, to April 30, 2010. The study was pre-approved by the Institutional Ethics Committee (IEC) for the final permission. After obtaining the permission of IEC the study was conducted. CLD was diagnosed by history, clinical examination, and investigations, showing features of hepatocellular dysfunction and portal hypertension. The investigations included liver function test, Prothrombin Time/International Normalized Ratio, abdominal ultrasound, upper gastrointestinal endoscopy, ascitic fluid study including cytology and serum ascites albumin gradient, HBsAg, anti-HCV, serum ceruloplasmin, and antinuclear antibody.

Child-Pugh Score was calculated to classify the severity of CLD.

#### Inclusion criteria

Patients of CLD diagnosed by history, clinical examination, and investigations were included in the study.

#### Exclusion criteria

The following criteria were excluded from the study:

- Known IHD
- Valvular heart disease
- Pre-existing cardiomyopathy or other heart disease

- Uncontrolled hypertension
- Diabetes mellitus
- Chronic renal failure
- Long standing anemia with Hb <7 g/dl

Among the included subjects, the following parameters were studied to assess CV dysfunction –

- Pulse, BP, and Orthostatic hypotension
- Chest X-ray, and ECG
- 2D, M-mode and Doppler Echocardiography –

Measures of Systolic function: LVIDs, LVIDd, EF, Stroke Volume Index (SVI), and Cardiac Index (CI).

$$SVI = \frac{LVEDV - LVESV}{BSA}$$

That is, the difference between LV end diastolic volume and LV end systolic volume, divided by the body surface area (BSA).

CI = SVI × Heart Rate

Measures of diastolic function:

E/A Ratio

Deceleration time of E-wave (DT). Prolongation >150 ms indicates DD<sup>4</sup>

Prolonged Isovolumetric Relaxation Time (IVRT) >90 ms<sup>4</sup>

LVMI: Left Ventricular Mass calculated by modified D<sup>3</sup> formula, using the Penn convention. Increased LVMI, that is, LVM divided by BSA if >149 g/m<sup>2</sup> in males, or 122 g/m<sup>2</sup> in females.

#### Statistical analysis

Results were expressed as rates for categorical data; Mean and Standard Deviation for numerical data. Chi-square test is a test for association between two categorical variables and a method of testing the significance of difference between them. Chi-square test has been used with P<0.05 considered statistically significant. Similarly Fisher's Exact Test has been used where applicable with P<0.05 considered statistically significant.

Microsoft Excel was used for tabulating and comparing data. SPSS version 16 and NCSS 2007 software was used for analysis of data.

## RESULTS

In our study, we investigated 50 patients of CLD. The mean age was 48.2 years, with a male: female ratio of 2.5:1. Causes were found to be alcoholic liver disease in 25.7%, Hepatitis B in 37.1%, Hepatitis C in 28.6%, both Hepatitis B and C in 2.8%, and Cryptogenic in 5.7%.

The patients were further scored and classified according to Child-Pugh criteria (Table 1). About 14.3% were Class A (score 5–6), 34.3% Class B (score 7–9), and 51.4% Class C (score 10–15).

Chi-square test for SVI, EF with Child-Pugh's Class is statistically significant ( $P=0.032$  and  $0.047$ , respectively) and for CI it is statistically not significant ( $0.48$ ). Fisher's exact test for diastolic dysfunction (DD) improvement after paracentesis is statistically significant ( $0.016$ ).

SVI and CI were increased in 16 (45.7%) and 15 (42.9%) patients, respectively. The increase in SVI and CI were more with increasing severity of liver disease (Child Class C), ( $P=0.032$ ). Similarly LVEF > 65% was found in 15 patients. However, a low EF, that is, <55% was found in eight patients. The following parameters were measured by Echocardiography to assess diastolic function: of the three variables E/A, DT, and IVRT, presence of at least two indicates DD. In our study, DD was seen in 60% of cases. LVMI was also found to be increased in 16 patients and increased left atrium (LA) size was found in 18 patients. All these values showed association with increasing child class of severity, and in case of DD it was statistically significant ( $P=0.012$ ).

**Table 1: SVI, CI, EF, DD, LVMI, LA, Changes of EF and DD after paracentesis according to Child-Pugh's Classes A, B, and C**

Child Class	A	B	C	Total	P-value
↑ SVI	1	5	10	16	<b>0.032</b>
↓ SVI	4	3	4	11	-
↑ CI	1	4	10	15	0.48
↓ CI	1	4	3	8	-
↑ EF (>65%)	0	6	9	15	<b>0.047</b>
↓ EF (<65%)	1	1	6	8	-
DD	0	8	13	21	<b>0.012</b>
LVMI	1	4	11	16	0.15
LA	1	5	12	18	0.128
↑ EF after para				5/15	-
Impr. DD after para				6/15	<b>0.016</b>

SVI: Stroke volume index, CI: Cardiac index, EF: Ejection fraction, DD: Diastolic dysfunction, LVMI: Left ventricular mass index, LA: Left atrium  
Bold values are statistically significant.

## DISCUSSION

CLD of various etiologies has been observed to cause hyperdynamic circulation and cardiac dysfunction. Cardiac dysfunction is usually not clinically apparent, but it may be unmasked by exercise, pharmacological stress, for example, Dobutamine, or by surgery such as TIPS or liver transplantation.<sup>5</sup> Increased SV and CO at rest reflect the state of vasodilatation and hyperdynamic circulation, whereas inability to increase EF, SI, and CI on stress demonstrate systolic dysfunction. A low EF at rest may

also reflect the underlying cirrhotic cardiomyopathy, or may be due to the mechanical effect of ascites. DD and electromechanical abnormalities have also been found to be present in these patients. It is important to screen patients of CLD to evaluate for CV dysfunction as this may be a cause of increased morbidity and mortality. However, there are few studies in our country on this subject.

Features of hyperdynamic circulation were found in the form of increased SVI, CI in 45.7% and 42.9% patients, respectively, ( $P=0.032$ ) reflecting the presence of vasodilatation. Cirrhotic patients show higher values of CI, SVI, and Cardiac Cycle Efficiency on standing posture. This study was conducted by Tarquini et al.<sup>6</sup> LVEF was more than 65% in 42% of the patients and decreased in 23% cases and suggests that this may be an indicator of cirrhotic cardiomyopathy. Ascites may also contribute to low EF, and it may increase after drainage of peritoneal fluid. The changes in LVEF in a series were increased with increasing severity of liver disease and were statistically significant ( $P=0.047$ ). In a study by Kwon et al.,<sup>7</sup> LVEF <60% is strongly associated with higher post liver transplantation mortality in advanced liver disease indicating the need to appraise both LVEF and liver disease severity simultaneously.

On analyzing diastolic function, 60% of patients met two out of the three criteria of dysfunction as mentioned, 45.7% had increased LVMI and 51.4% had increased LA size.<sup>8</sup> All the values showed association with higher severity of CLD and was statistically significant ( $P=0.012$ ). Thus, in line with other studies, including a study by De et al.,<sup>9</sup> at IPGMER Kolkata 2003, our study also showed presence of DD as a marker of cardiac dysfunction. The importance lies in the fact that though not usually clinically manifest, it is more easily measured. The study at IPGMER also confirmed presence of the abnormalities in pre-ascitic as well as ascitic groups of cirrhotic patients and also in NCPF. In another study by Karki et al.,<sup>10</sup> DD was seen in 61.9% patients, particularly more common in alcoholics and cirrhotic cardiomyopathy<sup>11</sup> in 51.4% patients.

In our study, paracentesis was done in 15 patients, and improvement in EF was seen in five, and improvement in diastolic function in six of these patients. Similar findings were found in Sembiring et al., study.<sup>12</sup> After paracentesis, there was a significant improvement in diastolic function, decrease of four chambers of heart and increase of EF insignificantly. This is postulated to be due to elevation of the diaphragm and compression of the cardiac structures from below by the ascitic fluid, which is relieved by drainage of the fluid.

Thus it was seen that both systolic and DD were demonstrated in this study of patients of CLD, and there

was good overall correlation with Child-Pugh Score and Class of severity. DD was the commonest abnormality seen. Speckle Tracking Analysis by Kockritz et al., reveals increased LV deformation.<sup>13</sup> Reversal of some abnormalities after paracentesis shows that mechanical problems exacerbate the CV dysfunction already present in these patients.

### Limitations of our study

It was an observational cross-sectional study. A follow-up of the patients would give a better assessment of the progression of CV dysfunction in these patients, and their ultimate outcome and prognosis.

## CONCLUSION

The previous studies and the current investigations show CV dysfunction is an important, but often subtle, complication of CLD. However, it may become overt when the patient is exposed to stress. Thus, a high index of suspicion should be there to identify CV dysfunction and cirrhotic cardiomyopathy in these patients, to be aware of possible adverse cardiac events. Further study to find specific treatment modalities are needed to improve the outcome in these patients.

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**SB-** Concept and design of the study, manuscript preparation, data collection, statistically analyzed, and interpreted; **PKK-** Manuscript preparation, statistically analyzed, and interpreted, critical revision of the manuscript

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