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Original research article

A study on echocardiographic changes in chronic liver disease patients attending to a tertiary care hospital

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Abstract

Background: A hyperdynamic state in cirrhosis patients is distinguished by increased Cardiac Output (CO), plasma volume, and decreased Systemic Vascular Resistance (SVR) and blood pressure [1]. Initially, decreased LV performance in cirrhotic patients was assumed to be caused by alcohol's direct toxic action.

Aim: To study cardiac changes in patients with chronic liver disease using echocardiography.

Objectives:

1. To evaluate the LV dysfunction.
2. To assess pulmonary hypertension.
3. To evaluate pericardial effusion in CLD.

Material & Methods:

Study Design: Hospital-based, cross-sectional study.

Study Area: The study was conducted in the Department of General Medicine, Narayana Medical College and Hospital, Nellore. A.P.

Study Period: April 2023 to March 2024.

Sample Size: The study consisted of a total of 30 subjects and 30 controls.

Sampling Technique: Simple Random technique.

Study Tools and Data Collection Procedure: A total of thirty patients with cirrhosis were included in the study. A proforma was prepared which included a detailed history, clinical examination and requisite investigations. Complete clinical evaluation including history including questioning about risk factors for chronic liver disease, history of hepatitis, alcohol consumption, diabetes mellitus, use of illicit drugs, transfusions, family history of liver disease, travel, and the presence of autoimmune diseases The review of systems including questioning related to fatigue, easy disability, lower extremity oedema, fever, weight loss, pruritus, increasing abdominal circumference and sleep disturbance suggestive of encephalopathy.

Results: The most common presentation was a Generalised weakness (86.6%) and abdominal distension (86.6%), hematemesis and Malena in 23.3%. There were no patients with advanced features of cirrhosis. In the study, among the 30 patients common clinical signs were icterus (63.3%), oedema and ascites (53.3%). Ascites were minimal to moderate; refractory ascites was not included in the study.

Conclusion: This study demonstrates that Indian patients with cirrhosis do have diastolic dysfunction. If other risk factors for cardiac disease are lacking, this dysfunction can be attributed only to cirrhotic cardiomyopathy. There is no correlation between cardiac status with the severity of liver dysfunction. Echocardiography plays a significant role in detecting early cardiac changes in cirrhosis however these changes do not seem to be a predictor of increased mortality in patients of cirrhosis.

Keywords: Chronic liver disease, echocardiography, hepatic

Introduction

A hyperdynamic state in cirrhosis patients is distinguished by increased Cardiac Output (CO), plasma volume, and decreased Systemic Vascular Resistance (SVR) and blood pressure [1]. Initially, decreased LV performance in cirrhotic patients was assumed to be caused by alcohol's direct toxic action [2].

Cirrhotic cardiomyopathy refers to a set of symptoms that indicate structural and functional cardiac abnormalities caused by liver cirrhosis. These include systolic and diastolic function issues, electrical alterations, and macroscopic and microscopic structural abnormalities. Alcoholic cardiomyopathy is a

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kind of acquired dilated cardiomyopathy that results from excessive alcohol consumption over time. Hepatic cirrhosis leads to hyperdynamic circulation, which causes cardiac structural and function dysfunctions, resulting in the Cirrhotic Cardiomyopathy (CCM) syndrome. This syndrome includes hyperdynamic circulation, systolic and diastolic dysfunctions, enhanced ventricular repolarisation, and sinus node abnormalities that cause the heart rate (HR) to rise during increasing exercise [3-9].

Cardiac dysfunction in the cirrhotic population occurs in the context of circulatory dysfunction and is distinguished by dilated splanchnic vasculature. In the early stages of cirrhosis, the circulatory dysfunction is compensated for by hyperdynamic circulation. Later, the advancement of liver illness and portal hypertension induces increasing vasodilation, resulting in a decrease in effective arterial blood volume and activation of the Renin-Angiotensin-Aldosterone System (RAAS) and the Sympathetic Nervous System (SNS) [10]. These changes in the circulation might cause cardiac dilatation of the left chambers and the onset of functional cardiovascular abnormalities. High norepinephrine levels can impair β-adrenergic receptor activity [11].

Aside from sympathetic nerve activity and the aldosterone system, other factors have been proposed as potential causes of cardiac dysfunction in cirrhosis. These include nitric oxide (NO), carbon monoxide (CMO), and endogenous cannabinoids [6]. Aggregation of these compounds along portosystemic shunts may cause a negative inotropic impact, and they may also play a role in the aetiology of Left Ventricular Diastolic Dysfunction (LVDD) in Cardiomyopathy (CCM) [12]. Inflammation is linked to the development of heart dysfunction, particularly in decompensated cirrhosis. Cytokines can alter myocardial function in two ways: by affecting both myocyte contractility and the extracellular matrix [13]. Not only can cytokines affect myocardial remodelling, but they also directly and indirectly affect myocardial function.

The present study seeks to evaluate cardiac status in patients with cirrhosis of the liver in comparison to healthy controls to assess the occurrence of cirrhotic cardiomyopathy, to study if echocardiographic parameters of cardiac dysfunction correlate with the severity of liver dysfunction, and to appraise whether there are significant differences in these parameters.

Aim: To study cardiac changes in patients with chronic liver disease using echocardiography.

Objectives

1. To evaluate the LV dysfunction,
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Material & Methods

Study Design: Hospital-based, cross-sectional study.

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Sampling Technique: Simple Random technique.

Inclusion Criteria

1) Patients with proven Cirrhosis diagnosed by
a) Jaundice for more than 06 months or haematemesis or melaena or ascites, or splenomegaly or hepatomegaly.
b) Altered LFT for more than six months.
c) Upper gastrointestinal endoscopy showing oesophageal varices.
d) Ultrasound showing shrunken or nodular liver with features of portal Hypertension.
e) Biopsy if available showing cirrhosis.

Exclusion criteria

Patients with primary cardiac or pulmonary disease, refractory ascites, hypertensives, severe anomia (Hb of less than 8 gm%) were excluded.

Patients on recurrent variceal bleed, ascites requiring frequent peritoneocentesis, Diuretics and Beta blockers were also excluded.

Thirty age and sex-matched healthy subjects from the relatives or patients admitted with other diseases were selected as controls. Alcoholics, Hypertensives, those with primary cardiac or pulmonary disease, Diabetes Mellitus, and those on cardiac medications were excluded.

Study tools and data collection procedure

A total of thirty patients with cirrhosis were included in the study. A proforma was prepared which included a detailed history, clinical examination and requisite investigations. Complete clinical evaluation including history including questioning about risk factors for chronic liver disease, history of hepatitis, alcohol consumption, diabetes mellitus, use of illicit drugs, transfusions, family history of liver disease, travel, and the presence of autoimmune diseases The review of systems including questioning related to fatigue, easy bruisability, lower extremity oedema, fever, weight loss, pruritus, increasing

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abdominal circumference, and sleep disturbance suggestive of encephalopathy. Clinical signs including spider naevi, gynaecomastia, anaemia, low-grade fever, opaque white nails, clubbing of nails, foetor hepaticus, jaundice, ascites, encephalopathy, Prominent veins over the abdomen, caput medusa, hepatomegaly, splenomegaly.

Two-dimensional, pulsed Doppler, M-mode and colour flow Doppler echocardiographic studies were performed by an experienced cardiologist using a commercially available cardiac ultrasound machine (Philips Sonos 5500). Echocardiographic images were procured from the parasternal and apical windows with the patient reclining on the left side, according to the recommendations of the American Echocardiography Committee.

Mitral inflow velocity pattern was recorded by placing the pulsed wave Doppler sample volume between the mitral valvular endings. Left ventricle outflow pattern was recorded from the apical five space window by placing the pulsed wave Doppler sample volume just under the aortic valve.

In Doppler echocardiography accompanied by electrocardiogram, peak early filling velocity (E wave), peak atrial systolic velocity (A wave), early and late mitral diastolic flow ratio (E/A), ratio of E and A velocity time integrals and the time period between the peak level of early mitral diastolic flow and its termination as E deceleration time (EDT) were measured. With M-mode measurements, interventricular septum (IVS) and left ventricle posterior wall (LVPW) thicknesses separately at diastole and systole and left ventricle end-diastolic (LVED) and end-systolic (LVES) diameters were determined.

In the echocardiographic evaluation, flow characteristics and rates of mitral, tricuspid, aortic and pulmonary valves were evaluated with Doppler studies Pulmonary arterial pressure (PAP) was calculated on the tricuspid regurgitation flow.

Follow-Up: Patients were followed up regularly in the Out-Patient Department for the development of new signs and symptoms.

Statistical analysis

Results of demographic and biochemical characteristics were expressed as a range and mean standard deviation. The severity of cirrhosis was graded using Child pughs criteria, Echocardiographic measurements of the controls and cirrhotic groups were compared. Statistical analysis was made using the SPSS 15.0 trail version.

Statistical methods

Analysis of variance (ANOVA) was used to identify the significance of study parameters between three or more groups of patients, Student t-test (two-tailed, independent) and Student t-test (two-tailed, dependent) was used to identify the significance of study parameters on a continuous scale within each group.

Observations & Results

Table 1: The age distribution of patients studied

Age in years	Cases	%	Controls	%
20-40	12	40.0	12	40
41-60	15	50.0	15	50
61-80	3	10.0	3	10
Total	30	100.0	30	100

In this study, thirty patients were included, with age groups ranging from 20 to 80 yrs., which included four males and 26 females constituting 13.3% and 86.6%. The maximum age of the patient was 80 yrs. And the minimum was 24 yrs. Thirty age and sex-matched controls were included for comparison.

Table 2: Sex distribution of patients studied

Gender	Cases	%	Controls	%
Female	26	86.6	26	86.6
Male	4	13.3	4	13.3
Total	30	100.0	30	100.0

Majority of the study subjects were female (n-26), and four males.

Patients were from various strata of society, including Homemakers, farmers, businessman comprising a maximum number of patients were Homemakers (n=26).

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Table 3: Spectrum of symptoms at presentation

Clinical history	(n=30)		(n=30)	
	cases	%	Controls	%
Generalized weakness	26	86.6	0	0
Abdominal distension	26	86.6	0	0
Hematemesis/Malena	7	26.7	0	0
Altered sensorium	0	0.0	0	0

The most common presentation was a generalised weakness (86.6%) and abdominal distension (86.6%), hematemesis and Malena in 23.3%. There were no patients with advanced features of cirrhosis.
In the study, among the 30 patients common clinical signs were icterus (63.3%), oedema and ascites (53.3%). Ascites were minimal to moderate; refractory ascites were not included in the study.

Table 4: Child Turcotte Pugh score of the study population

Child	(n=30)		(n=30)	
	cases	%	Controls	%
A	19	63.3	30	0
B	11	36.6	0	0
C	0	0	0	0

The severity of cirrhosis was calculated based on Child Turcotte Pugh's criteria. The majority of the subjects were in the severity group of Child A (63.3%) or Child B (36.6%), There was no mortality recorded during the period of study.
Among the patients most of the patients had Hepatitis B (20%), Hepatitis C (13.3%) and autoimmune aetiology (20%).

Table 5: Echocardiographic parameters of the study population and controls

Echo-cardio graphic	Controls	Cases	P value	Significance
LV systole(mm)	25.46 ±2.27	30.36 ± 5.32	<0.001**	High
LV Diastole (mm)	47.2 ±7.49	57.9 ± 5.31	<0.001**	High
LVEF (%)	55.8± 2.26	62.96± 6.13	<0.001**	High
IVS (mm)	10.03±0.96	13 ± 2.08	<0.001**	High
LVPWT (mm)	8.96±2.73	10 ±0.83	>0.05	No
LA (mm)	33.9 ± 5.86	44.96 ±3.03	<0.001**	High

The echocardiographic parameters of the study and control group are as in Table 09. There was a statistically significant difference of IVS (9.80mm±1.06mm) in the study population when compared to controls (8.0 ± 1.0 mm), the p-value was <0.001. Other parameters like LVPWT clinical changes were seen. However, they were not statistically significant. There was no significant difference noted in the LV dimensions during systole and diastole between controls and the study population. The LV ejection fraction was found to be increased in the study group (64.57 ± 4.97% vs 64.00 ± 4.70%). However, it was not statistically significant. (p<0.618).

Table 6: Doppler echocardiographic parameters

Doppler Echo cardio	Controls (n=30)	Cases(n=30)	P value	significance
PAP	11.8±1.97	23.5 ± 2.73	<0.001**	High
DT	182.8±17.56	226 ±9.50	<0.001**	High
E/A ratio	1.03±0.10	1.03± 0.123	>0.05	No

Doppler echocardiographic parameters of Pulmonary arterial pressure, deceleration time in the study group showed significant change (p <0.001) as in table 10. There was also a significant change in the E/A ratio (1.10±0.1 vs 1.04 ± 0.12) with a p-value of 0.040.

Table 7: Echocardiography parameters (structural)

Study	Cases	%	Controls	%
TR	26	86.6	0	0
RWMA	2	6.6	0	0
Pericardial	3	10	0	0

The study objects were found to have TR (10%) (26 of thirty subjects), 2 of 30 patients had RWMA, and three of the subjects had pericardial effusion (10%). There was no progression of the above parameters during the study period noted.

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Table 8: Echo-cardio graphic parameters according to CHILD grading

Echo parameters		
LV systole(mm)		Significance
CHILD A	30.42±5.40	
CHILD B	30.72±5.42	
CHILD C	0	
P-VALUE	>0.05	No
LV Diastole(mm)		
CHILD A	46.89±8.42	
CHILD B	47.72±5.90	
CHILD C	0	
P-VALUE	>0.05	No
LVEF (%)		
CHILD A	61.15±6.75	
CHILD B	66.09±3.17	
CHILD C	0	
P-VALUE	<0.05	Moderately
IVS (mm)		
CHILD A	10.31±1.60	
CHILD B	10.72±2.05	
CHILD C	0	
P-VALUE	>0.05	No
LVPWT (mm)		
CHILD A	10±0.942	
CHILD B	10.00±0.63	
CHILD C	0	
P-VALUE	>0.05	No
LA (mm)		
CHILD A	34.05±6.45	
CHILD B	34.36 ±6.63	
CHILD C	0	
P-VALUE	>0.05	No

Echocardiographic parameters showed no statistical difference with the severity of liver disease. There was no significant difference in the LV Dimension or systolic function.

Discussion

The patients in this study were estimated for the presence of cirrhotic cardiomyopathy. Cirrhotic cardiomyopathy is defined as chronic cardiac dysfunction in patients with cirrhosis, characterised by declined contractile responsiveness to stress and altered diastolic relaxation with electrophysiological abnormalities in the absence of known cardiac disease.[14]

In this study, female patients outnumbered males (86.6% vs 13.3%). This difference is due to the distribution of cirrhosis between the genders and alcohol being included in the exclusion criteria. The mean age of the patients was found to be around 47 years and subjects in the age group 20-80 years were included. The majority presented with a history of generalised weakness (86.6%), and abdominal distension (50%) as the chief complaint. Out of 30 patients, 26 (approximately 86.6%) presented with generalised weakness and fifteen (50%) had presented with abdominal distension.

Symptoms of apparent heart failure are rare because of the peripheral vasodilatation characteristic of cirrhosis, in effect "auto-treating" the ventricle by systemic vasodilatation reducing afterload, and the compensatory decrease of inhibitory effects such as the cardiac muscarinic system.[15] Even though patients had complaints of dyspnoea, reduced exercise capacity, peripheral fluid retention and ascites, these symptoms are mutual to both heart failure and advanced cirrhosis. It is thus difficult to determine by symptoms alone if patients are suffering from symptomatic heart failure. The only discriminating feature is that dyspnoea in cirrhosis is usually connected with hydrothorax from ascitic fluid tracking into the pleural cavity and not with pulmonary congestion or pulmonary oedema. The existence of such pulmonary congestion strongly points to a diagnosis of heart failure, whether due to cirrhotic cardiomyopathy or additional causes.

Clinically icterus was found in 13 members of this study patients (43.3%), probably secondary to ongoing hepatitis, oedema was detected in 8 (26.6%), due to activated RAAS, hypoproteinaemia and ascites compressing the abdominal inferior vena cava, Ascites was detected in 26 (86.6%) of the study population, this was due to the inclusive criteria used in the study.

Cirrhotic patients in this study had liver dysfunction of early or intermediate severity (Twelve patients (40%) were in Child-Pugh class A, and 13 Patients (43.3%) were in severity class B. Detection of child class A was due to the aggressive investigation, Child B presented with symptoms suggestive of liver dysfunction. Child C patients presented with features of gross ascites or recent GI bleeding, which can

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cause hemodynamic alterations or features of cardiac dysfunction. Only ambulated patients were enrolled to remove the effect of cardiac decondition due to rest. During the study period, all cases were reviewed monthly in Medicine OPD, all class A patients remained stable, and no patients of class B progressed to class C. This was due to poor adherence to dietary and drug compliance.

The study showed no significant correlation between the severity of hepatic dysfunction and cardiac changes in contrast to few reports in the literature that cardiac changes parallel the severity of hepatic dysfunction in cirrhotics [16]. However, the selection criteria of the study excluded advanced hepatic dysfunction. Subtle trends of correlation may not come to light unless the entire spectrum of disease is analysed-also, the use of medication which can improve cardiac dysfunction in Class C like spironolactone, furosemide and ß blockers. These may diminish any change in cirrhotic patients in this class C patients.

The cardiac changes in this study patients are due to cirrhosis. There was a significant difference in this series in cardiac parameters between patients with cirrhotics and those with controls. Cirrhotics in this series had features of diastolic dysfunction. Alcoholic cardiomyopathy, conversely, is characterised by systolic dysfunction. In this study, ejection fraction, the marker of systolic function, was, in fact, higher in cirrhotics compared to controls. These are the classic features described in cirrhotic cardiomyopathy. Thus, cardiac changes, even in patients with non-alcoholic cirrhosis, are rather due to cirrhosis.

Echocardiographic parameters of Interventricular septal thickness exhibited significant change compared to control (9.80 ± 1.06mm vs 8.00 ± 1.00mm). LV dimension in systole and diastole displayed a mild increase. However, there was no statistically significant difference. This is concordant with some previous observations by Valeriano *et al*. and J Alexander *et al*. but discordant with specific other observations which reported smaller left ventricular volumes in pure virus-related cirrhosis [17, 18].

An indicator of diastolic dysfunction, Deceleration time was found to be extended in the study group compared to controls (223.17 ± 13.93 ms vs 190.83 ±14.0ms). There was evidence of diastolic dysfunction in cirrhotics as indicated by a significant prolongation of deceleration time compared to the controls. The E: A ratio, the other parameter of diastolic dysfunction, display a statistically significant difference. Both the E: A ratio and deceleration time reflect impedance to ventricular filling. However, the E: A ratio, but not deceleration time, is subject to the phenomenon of 'pseudo normalisation' whereby the E: A ratio becomes paradoxically normal regardless of diastolic dysfunction [19]. This might have led to fewer changes in E: A ratio in some patients with diastolic dysfunction in this study. However, in literature demonstrates a decrease in the E: A ratio in cirrhotics, with observations of a considerable decrease in the E: A ratio in cirrhotics with ascites compared to cirrhotics without ascites [20]. and decreased E: A ratio in cirrhotics with non-viral aetiologies related to virus-related cirrhosis [21]. LV ejection fraction was found to be increased in patients (64.57 ±4.07 vs 64.00 ±4.70). However, it was not statistically significant. There have been reports of higher ejection fraction in pure virus-related cirrhosis than in alcoholic cirrhosis and controls, which has been attributed to the presence of subclinical alcohol cardiomyopathy in alcoholic patients [22]. This heterogeneity in the literature is at least partly due to the lack of universal criteria for the diagnosis of cirrhotic cardiomyopathy.

Three of the 30 patients had pericardial effusion (all three had associated ascites). 26 (86.6%) of these patients had TR (21 with grade 1, 4 with grade 2 and one with grade 3). The exact cause cannot be attributed to cardiac dysfunction as these patients had diastolic dysfunction along with ascites and portal hypertension. Doppler echocardiography spotted significant changes in the study population in Pulmonary arterial pressures (PAP) compared to control (20.73 ±2.43 vs 18.26 ± 2.1mm Hg). This was similar to Yasemin Soyoral, Ali Süner *et al*. [23].

Mechanics of increased PAP is not described yet; previous studies suggested that increased levels of vasoactive substances in the pulmonary circulation and the probable toxic effects of these substances on endothelial cells. Krowka *et al*. indicated that microthrombi can travel to pulmonary vascular bed along portosystemic shunts and lead to an increase in vascular resistance [24].

It must be noted that even normal echocardiographic parameters do not rule out the presence of cardiac dysfunction in cirrhosis. Patients with cirrhosis have increased production of nitric oxide which, apart from its contribution to the pathogenesis of myocardial contractile dysfunction, produces systemic arterial vasodilatation by its vasodilator properties. The reduction in afterload thus allows the heart to maintain a normal cardiac output even with the presence of contractile dysfunction and a decreased preload.

The follow-up period did not show any mortality. With the progression of liver dysfunction, the cardiac parameters did not show significant changes. This was discordant with Moller *et al*., and Gaskari *et al*. who suggested that cardiac dysfunction parallels the severity of liver dysfunction [25].

Echocardiography should be done as a routine investigation in patients with cirrhosis of any Child class, as this study did not show a correlation of cardiac dysfunction with the severity of disease, but not with the aetiology of cirrhosis and also patients with Echo changes did not have increased morbidity or mortality compared to controls. However, in these patients where congestive symptoms and signs of cirrhosis especially those that may be related to the cardiovascular cause are inadequately controlled with standard measures, an ECHO may play an important role in delineating the cause. All patients being

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planned for liver transplant should undergo an Echocardiography as such a patient who demonstrates Echocardiographic change may be a candidate for cardioactive drugs. Despite all measures to control the progression of chronic liver disease the patients eventually will end up with complications, in a scenario like India where the transplant is a far away option in the future the importance of palliative care cannot be undermined.

Conclusion

This study demonstrates that Indian patients with cirrhosis do have diastolic dysfunction. If other risk factors for cardiac disease are lacking, this dysfunction can be attributed only to cirrhotic cardiomyopathy. There is no correlation between cardiac status with the severity of liver dysfunction. Echocardiography plays a significant role in detecting early cardiac changes in cirrhosis however these changes do not seem to be a predictor of increased mortality in patients of cirrhosis. Future pathophysiological and clinical research is needed to assess the prognostic implications of cirrhotic cardiomyopathy.

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