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Original Research Article

A study to assess the echocardiographic changes among chronic liver disease in a tertiary care center

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ABSTRACT

Background: Cirrhosis is associated with numerous cardiac abnormalities; however scanty information is available about the changes associated with it in Indian diaspora. which include increased cardiac output, left ventricular diastolic dysfunction, increased wall thickness of cardiac chambers, and pulmonary arterial hypertension. These concomitant cardiac abnormalities in patients with cirrhosis have been termed as 'Cirrhotic Cardiomyopathy'. Objective of this study assess the Echocardiographic Changes among Chronic Liver disease in a tertiary care center.
Method: Thirty patients with cirrhosis (alcoholic and non-alcoholic) were enrolled for the study at Department of Gastroenterology, Command Hospital, Air force, Bangalore from October 2007 to June 2009. Thirty age and sex matched controls without cardiovascular disease were included for comparison. Data collection was done by clinical history, examination and investigations. All subjects underwent Echocardiographic study was at 6 and 12 months and controls at the start of study.
Results: Mean age of the study population was 54.5±15 yrs, males constituted 93% of the study population. Majority of the patients were in Child class B (43.3%) and Child A (40%). Interventricular septal thickness showed significant change compared to Control. There was no evidence of systolic dysfunction noted in the study population. There was no correlation between severity of cirrhosis and echocardiographic Changes.
Conclusion: This study demonstrates that Indian patients with cirrhosis do have diastolic dysfunction. In the absence of other risk factors for cardiac disease, this dysfunction can be attributed only to cirrhotic cardiomyopathy. There is no correlation of cardiac status with severity of liver dysfunction.

Keywords: Cardiac, Child, Cirrhosis, Echocardiography, Liver disease

INTRODUCTION

Until the late 1980s, the patient with liver cirrhosis was considered somehow "protected" against cardiovascular involvement due to the favorable pattern of the main ischemic risk factors (i.e. hypotension, hypolipemia, low platelet count, impaired coagulation). Clear experimental and clinical evidence states that liver cirrhosis is characterized by a sustained peripheral vasodilation due to a wide number of vasoactive substances. The lowered systemic vascular resistance results in a reduction of effective circulating plasma volume and blood pressure, and in an enhancement of heart rate, cardiac output and sympathetic tone ("hyper dynamic" circulation), with an eventual sustained reduction of cardiac after-load.[1]

The cardiovascular abnormalities have been known for centuries, but only until relatively recently did the development of techniques for precisely measuring cardiovascular variables like echocardiography and MRI of heart is used for detecting the extent of these anomalies. Before this, clinicians observed the

tachycardia and bounding pulses of patients with cirrhosis and opined that the circulation was hyper dynamic. In 1953 a seminal study by Kowalski and Abelmann et al, determined that patients with alcoholic cirrhosis have increased cardiac output and decreased arterial pressure and total peripheral resistance, i.e., hyper dynamic circulation. The basal cardiac output is increased, contractile function should, be normal as well. Cardiac output is the product of heart rate and the volume of blood expelled with each contraction, or stroke volume (SV).[2,3]

In 1960 evidence arose that showed this was not the case. Regan et al, studied ten alcoholics with no clinical evidence of cardiac disease, along with eight healthy controls, and intravenously infused both groups with angiotensin.[3] Angiotensin is an eight-amino acid oligopeptide which is produced in the body as part of the renin-angiotensin aldosterone system. Among other roles, it acts on receptors in vascular tissue causing systemic arteriolar vasoconstriction, leading to increased vascular resistance and thereby elevating cardiac after load. After angiotensin infusion, it was observed that although the left ventricular end diastolic pressure of the alcoholic group increased significantly more than the control group, the corresponding rise in stroke output and work was significantly less than the controls.[4,5]

Chronic hepatitis is defined as chronic necroinflammation of the liver of more than 3-6 months' duration, demonstrated by persistently abnormal serum aminotransferase levels and characteristic histologic findings.[6]

The clinical picture of patients with cirrhosis is dominated by the classical complications such as ascites, bleeding from esophageal varices, portal hypertension and encephalopathy. In addition, a considerable number of patients show signs of peripheral vasodilatation with palmar erythema and reddish skin, raised and bounding pulse, and a low systemic blood pressure indicating a hyper dynamic circulation.

The hyper dynamic syndrome comprises an increased heart rate, cardiac output, and plasma volume, and a reduced systemic vascular resistance and arterial blood pressure.

Besides the hepato renal syndrome, this has led to the recognition of new clinical entities, such as cirrhotic cardiomyopathy and the hepato pulmonary syndrome. Cirrhotic cardiomyopathy was initially thought to be of little clinical relevance. However, with the frequent use of invasive procedures like surgical portocaval shunts, trans jugular intrahepatic portosystemic shunt and liver transplantation, the adverse consequences of cardiac dysfunction became evident. These procedures put additional stress on the dysfunctional heart, precipitating overt cardiac failure. Unexpected deaths due to heart failure following these procedures became a cause of concern in centers where these procedures were regularly performed.[7]

There is paucity of data from the Indian subcontinent on cirrhotic Cardiomyopathy. Just as the etiological spectrum of cirrhosis varies in different parts of the world, data from one population may not be valid in a different population.

Authors undertook to study cardiac status in patients with cirrhosis of 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 or not there are significant differences in these parameters between alcoholic and non-alcoholic cirrhosis. Objectives of the study cardiac changes in patients with chronic liver disease using echocardiography.

METHODS

A Longitudinal study was conducted from October 2007 to June 2009 at Department of Gastroenterology, Command Hospital, Air force, Bangalore, Karnataka, India. A total of Thirty Consecutive Patients with Cirrhosis of Liver admitted to the Department of Gastroenterology in the hospital were included in the study.

Diagnosis of cirrhosis of the liver was made on clinical, biochemical, serological, and ultrasound imaging. Liver Biopsy was performed to diagnose cirrhosis when other tests were inconclusive. All patients were ambulatory and hemodynamically stable.

Inclusion criteria

Patients with proven Cirrhosis diagnosed by

- Jaundice for more than 06 month or hematemesis or melena or ascites, or splenomegaly or hepatomegaly and
- Altered LFT for more than six months, with
- Upper gastrointestinal endoscopy showing esophageal varices OR
- Ultrasound showing shrunken or nodular liver with features of portal Hypertension OR
- Biopsy if available showing cirrhosis

Exclusion criteria

Patients with primary cardiac or pulmonary disease, refractory ascites, hypertensive, severe anemia (Hb of less than 8 gm%) were excluded. Patients on recurrent variceal bleed, ascites requiring frequent peritoneocentesis, diuretics and beta blockers were also excluded.

Data collection

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

A Detailed clinical evaluation including history including questioning about risk factors for chronic liver disease, history of hepatitis, alcohol consumption, diabetes mellitus, use of illicit drugs (by injection or inhalation), transfusions, family history of liver disease, travel, and the presence of autoimmune diseases was elicited.

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

American Echocardiography Committee. Echocardiographic evaluations were done on the day of Admission and further follow up of the Echocardiographic findings was done on 6th Month and 12th month after Discharge from the Hospital.

Statistical analysis

The data was entered in MS excel and analyzed using SPSS v 21. The data was presented in the form of Tables and expressed in percentages. Continuous Data was expressed in the form of ME and Standard Deviation. t test was used to find association between continuous variables.

RESULTS

A total of thirty Patients were analyzed in our study.

In our study the age group ranging from 40 to 70 yrs., which included 28 males and two females constituting 93.3% and 6.7%. Maximum age of the patient was 70 yrs. and minimum was 40 yrs. Thirty age and sex matched controls were included for comparison. Majority of the study subjects were male (n-28), and two females. Patients were from various strata of society, including farmers, businessman, housewives and others comprising retired army personnel. Maximum number of patients were farmers (n=12). (Table 1)

The most common presentation was generalized weakness (86.6%), abdominal distension (50.0%), hematemesis and malena in 26.7%.

There were no patients with advanced features of cirrhosis. Among the 30 patient's common clinical signs were icterus (63.3%), edema and Mild ascites (53.3%). Severity of cirrhosis was calculated based on Child Turcotte Pugh criteria; Majority of the subjects were in severity group of Child B (43.3%) or Child A (40.0%).

Table 1: Socio demographic profile of study group.

Socio Demographic		Number	Percentage
Age	40-49	12	40
	50-59	6	20
	60-70	12	40
Gender	Male	28	93.3
	Female	2	6.7
Occupation	Farmer	12	40
	Business	9	30
	Housewife	2	6.7
	Others	7	23.4

Table 2: Clinical features of study group.

Clinical Features		Number	Percentage
Clinical history	Generalized weakness	26	86.6
	Abdominal distension	15	50
	Hematemesis/ Malena	8	26.7
Clinical Signs	Icterus	19	63.3
	Edema	16	53.3
	Clubbing	0	0
	Asterixis	1	3.3
	Ascites	16	53.3
Child Turcotte Pugh score on the day of admission	A	12	40
	B	13	43.3
	C	5	16.7

Table 3: Echocardiographic parameters of the study population and controls.

Echo-cardio graphic parameters	Cases (n=30)	Controls (n=30)	p value
LV systole(mm)	28.17±2.67	27.6±4.0	0.518
LV Diastole (mm)	45.20±3.13	44.0±4.0	0.208
LVEF (%)	64.57±4.97	64.00±4.70	0.618
IVS (mm)	9.80±1.06	8.00±1.00	<0.001**
LVPWT (mm)	10.07±1.14	10.2±2.0	0.758
LA (mm)	32.53±4.66	32.4±2.8	0.900

Among the patients in the study majority of the patients had alcohol has etiology (66.7%). Nonalcoholic etiologies were Hepatitis B (16.7%) and Hepatitis C (16. 7%). None of the patients in the study had other

etiologies like autoimmune, biliary causes. There were no patients with multiple etiologies. (Table 2)

Table 4: Echocardiographic parameters of the study population on follow up.

Variables	0 month (A)	6th month (B)	12th month (C)	p value		
				A-B	A-C	B-C
LV systole(mm)	28.17±2.67	28.23±2.69	28.11±2.69	0.324	0.226	0.222
LV Diastole (mm)	45.20±3.13	45.23±3.11	45.27±3.12	0.328	0.161	0.326
LVEF (%)	64.57±4.97	64.30±3.75	64.47±4.33	0.326	0.825	0.643
IVS (mm)	9.80±1.06	9.87±1.07	10.13±1.01	0.161	0.010*	0.030*
LVPWT (mm)	10.07±1.14	10.13±1.14	10.60±1.16	0.161	0.001*	0.003*
LA (mm)	32.53±4.66	32.60±4.72	32.73±4.88	0.326	0.184	0.326

Echocardiographic parameters of study and control group was evaluated. There was statistically significant difference of IVS (9.80mm±1.06mm) in study population when compared to controls (8.0±1.0 mm), p value was <0.001.other parameters like LVPWT clinical changes were seen, however they were not statistically significant. There was no significant change 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 3)

During the period of observation at 0,6,12 months, echocardiographic parameters like size of LV in systole and diastole, LA size and LVEF did not show statistically significant change. There was significant change in IVS (p <0.030), LVPWT (p <0.003). (Table 4)

Table 5: Doppler echocardiographic parameters.

Doppler Echo cardio graphic parameters	Cases (n=30)	Controls (n=30)	P value
PAP	20.73±2.43	18.26±2.1	<0.001*
DT	223.17±13.93	190.83±14.0	<0.001*
E/A ratio	1.04±0.12	1.10±0.1	0.040*

Doppler echocardiographic parameters of Pulmonary arterial pressure, deceleration time in the study group showed significant change (p <0.001). There was also significant change in E/A ratio (1.10±0.1 vs 1.04±0.12) with a p value of 0.040. (Table 5)

The Echocardiographic parameters showed no statistical difference with severity of liver disease. There was no significant difference in the LV Dimension, systolic function, Diastolic Function, Interventricular Septum, left ventricle posterior wall thickness, Left Atrial thickness when compared with the child Score and Echocardiographic Findings.

Table 6: Echo-cardio graphic parameters according to CHILD grading.

Echo parameters	0 month	6th month	12th month
LV systole(mm)			
Child A	27.50±3.18	27.67±3.14	27.83±3.21
Child B	28.00±2.38	27.80±2.66	27.80±2.66
Child C	30.20±0.45	30.14±0.38	29.38±1.60
p value	0.158	0.117	0.387
LV Diastole(mm)			
Child A	44.25±2.8	44.42±2.71	44.42±2.71
Child B	45.15±3.11	45.00±3.09	44.70±3.23
Child C	47.60±3.29	47.43±3.21	47.25±3.01
p value	0.132	0.112	0.105
LVEF (%)			
Child A	62.17±4.22	63.00±3.62	63.08±4.83
Child B	65.69±3.33	64.60±2.32	63.70±3.83
Child C	67.40±2.61	67.43±2.57	67.50±2.73
p value	0.017*	0.016*	0.060
IVS (mm)			
Child A	9.92±1.00	9.75±1.29	10.42±10
Child B	9.62±1.26	9.90±1.10	9.90±0.99
Child C	10.00±0.71	10.14±0.69	10.00±1.07
p value	0.715	0.760	0.459
LVPWT (mm)			
Child A	9.92±1.24	9.92±1.24	10.83±1.34
Child B	10.00±1.08	10.2±1.14	10.30±1.06
Child C	10.60±1.14	10.57±0.98	10.63±1.06
p value	0.528	0.494	0.578
LA (mm)			
Child A	33.75±3.65	33.42±4.17	33.75±3.65
Child B	31.54±5.13	31.80±5.39	31.20±5.20
Child C	32.2±5.85	32.71±5.38	33.13±6.13
p value	0.504	0.746	0.474

Only Left Ventricular ejection fraction was found to be statistically Significant with CHILD Score and Echocardiographic findings (Table 6).

DISCUSSION

The present study was a prospective descriptive clinical study consisting of thirty patients and controls with cirrhosis who were inpatients in the department of Medicine, Command Hospital, Air force Bangalore from Oct 2007 to June 2009.

In our study male patients outnumbered females (93.3% vs. 6.7%). This is due to the distribution of cirrhosis in between the genders as well as lifestyle difference. The mean age of the patients in our study was around fifty-four years and subjects in the age group 41-70 years were included. Symptoms of overt heart failure is rare because of the peripheral vasodilatation characteristic of cirrhosis, in effect "auto treating" the ventricle by systemic vasodilatation reducing afterload, and compensatory diminution of inhibitory influences such as the cardiac muscarinic system.[8-10]

In our study there was no significant association 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 cirrhotic. However, as the selection criteria of the study excluded advanced hepatic dysfunction. Subtle trends of correlation may not come to light unless entire spectrum of disease is analyzed.

Echocardiographic parameters of Interventricular septal thickness showed significant change compared to control (9.80±1.06mm vs 8.00±1.00mm). LV dimension in systole and diastole showed mild increase, however there was no statistically significant difference. This is concordant with some previous observations by valeriano et al, but discordant with certain other observations which reported smaller left ventricular volumes in pure virus-related cirrhosis compared to alcoholic cirrhosis.[11,12]

Left Ventricular 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.[13] This heterogeneity in the published literature is at least partly due to lack of uniform criteria for diagnosis of cirrhotic cardiomyopathy.

Doppler echocardiography detected 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, and Ali Süner et al.[14]

There were no deaths during the follow up period. With progression of liver dysfunction, the cardiac parameters showed no significant changes. This was discordant with Moller et al, Gaskari et al, who suggested that cardiac dysfunction parallels the severity of liver dysfunction.[15]

As the selection criteria for cirrhotic in our study excluded those with very advanced hepatic dysfunction and as few cirrhotic present in the early stage, our data essentially represents those in the middle of the spectrum of severity of hepatic dysfunction. Subtle trends of correlation may not come to light unless the entire spectrum of disease is analyzed. Echocardiography is an observer dependent procedure. Hence variations are found in various studies. Duration of cirrhosis was not known to predict its relation with cardiac dysfunction.

CONCLUSION

Echocardiography plays a significant role in detecting early cardiac changes in cirrhosis however these changes do not see to be predictor of increased mortality in patients of cirrhosis. Echocardiography should not to be done as a routine investigation in patients with cirrhosis of any child class, as in our study it did not show any correlation of cardiac dysfunction with severity of disease, the etiology of cirrhosis, nor did patients with Echo changes have increased morbidity or mortality compared to controls. However, in these patients where congestive symptoms and signs of cirrhosis especially which may be related to the cardiovascular cause are not adequately controlled with standard measures, an ECHO may play a crucial role in elucidating the cause.

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