Original Article

Echocardiographic Alterations in Liver Cirrhosis

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ABSTRACT

Objective: To determine echocardiographic alterations in patients of liver cirrhosis.

Study Design: Cross-sectional descriptive study

Place and Duration of Study: This study was conducted at the Indus medical college and hospital, Tando Muhammad Khan from 11 October, 2019 to 11 March, 2020.

Materials and Methods: Study participants were the already diagnosed cases of liver cirrhosis. Liver cirrhosis been identified on the grounds of clinical history, systemic examination, laboratory investigations as well as ultrasonographic changes. On the basis of ultrasound findings, ascites graded clinically, conferring to 'The International Ascites Club grading system'; Ascites considered as Grade I, when there was mild ascites noticeable by ultrasound only; Grade II, when there was moderate ascites and modest symmetrical distention of abdomen; Grade III, when there was gross ascites and also noticeable distention of abdomen. Severity of illness graded by Child Pugh Scoring system. All study participants screened for both hepatitis C & B with thorough history and then undertook two dimensional transthoracic echocardiography with color Doppler. The cardiac variables measured by echo cardiography were left atrial diameter, left ventricular systolic and diastolic diameters, left ventricular posterior wall, right ventricular diameter, intervenetricular septum and ejection fraction. Sampling technique was non probability purposive. Diagnosed patients of liver cirrhosisaged > 18 years and <75 years of any gender, included in this study. Confounding factors like previous heart disease (valvular heart disease, coronary heart disease, hypertension, congestive heart failure); chronic respiratory disease; chronic kidney disease; anemia; thyroid disease; hyperlipidemia or diabetes mellitus; previous GI bleeding wiin last 4 weeks excluded from this study.

Results: The liver cirrhosis patients with mean age of 48.52 years±8.1participated in the study. Out of total 79, 58 and 21 were males and females respectively, while 63 found having hepatitis B and 16 with hepatitis C. According to Child Pugh scoring based disease severity, patients separated in three sets, i.e., A, B and C. Regarding echocardiographic alterations, means±sd of LVIDD.Ed, LVIDD.Es, left atrium, interventricular septum, aortic root and posterior wall among study population were 50.72cm ±8.42, 41.03±11.63, 35.45±4.8, 9.08±2.13, 25.41±3.92 and 9.17±1.66 respectively. While, ejection fraction (Ef) revealed as 30.46%±8.61& the E/A ratio of 1.07. Out of total 79, 37 (46%) identified as the cirrhotic cardiomyopathy. Echocardiographic alterations were statistically significant($p < 0.05$) in cirrhotic patients related with Child-Pugh scoring based disease severity.

Conclusion: This study revealed significant echocardiographic alterations in patients of liver cirrhosis. That's why, liver disease patients should be investigated by mean of echocardiography to avert under diagnosis of liver disease related cardiomyopathy for better prognosis.

Key Words: Liver cirrhosis, Child Pugh Scoring, cardiomyopathy, Echocardiographic

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INTRODUCTION

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Hepatic cirrhosis is one of the main reasons of death globally and is defined as diffuse and general fibrosis of hepatic parenchyma and regenerative nodules.[1,2] Alterations in cardiac physiology has been reported due to underlying mechanisms of liver disease.[3,4] Liver cirrhosisis diagnosed with distinctive clinical and histopathologic findings. Altered cardiac physiology can distress the liver and can expand to cardiac cirrhosis. Meanwhile, liver cirrhosis might disruptcardiac functions and so may culminate to cirrhotic cardiomyopathy.[5] Cirrhotic cardiomyopathy is defined as manifestation of altered systolic and diastolic functions with electrophysiologic deviations. These findings built on current doppler/ echocardiography or quantitative MRI.[6] Patients of liver cirrhosis mainly had altered diastolic functions with no changes in systolic variables during rest. Theses altered

diastolic functions occur due to thickening of myocardial walls, which began because of left ventricular hypertrophy, changes in collagen, subendothelial edema and fibrosis, culminating in increased left ventricle filling pressures.[7]

Suspected cases of cirrhotic cardiomyopathy should undertake echocardiography as crucial step for early diagnosis of diastolic disfunctions; as this might affect prognosis in patients of liver cirrhosis, however, either liver was transplanted or not. Patients of liver cirrhosis, should be assessed for cardiovascular function, specifically, if cirrhotic patient is acandidate for somewhat intervention that might cause alterations in hemodynamic parameters.[9] It is of great value to identify and manage cirrhotic cardiomyopathy timely as this might contribute to augmented heart related morbidity as well as also mortality. This study designated to evaluate the association of liver cirrhosis with cardiac structure and function among the patients of liver cirrhosis with help of echocardiography**.**

MATERIALS AND METHODS

Study participants were the already diagnosed cases of liver cirrhosis. This cross sectional descriptive study was done at Indus medical college and hospital, Tando Muhammad Khan from 11 October 2019 to 11 March 2020.The sampling technique adopted was non probability purposive. Liver cirrhosis been identified on the grounds of clinical history, systemic examination, laboratory investigations as well as ultrasonographic changes. On the basis of ultrasound findings, ascites graded clinically, conferring to 'The International Ascites Club grading system'; Ascites considered as Grade I, when there was mild ascites noticeable by ultrasound only; Grade II, when there was moderate ascites and modest symmetrical distention of abdomen; Grade III, when there was gross ascites and also noticeable distention of abdomen. Severity of illness graded by Child Pugh Scoring system. All study participants screened for both hepatitis C & B with thorough history and then undertook two-dimensional transthoracic echocardiography with color Doppler. The cardiac variables measured by echo cardiography were diameters of left atrium, left ventricular in both systolic and diastolic phases, left ventricle posterior wall, right ventricle, inter-ventricular septum and ejection fraction. Sampling technique was non probability purposive. Diagnosed patients of liver cirrhosisaged > 18 years and <75 years of any gender, included in this study. Confounding factors like previous heart disease (valvular heart disease, coronary heart disease, hypertension, congestive heart failure); chronic pulmonary condition; chronic kidney condition; anemia (Hb less than 9 gm/dL); thyroid disease; hyperlipidemia or diabetes mellitus; previous GI bleeding within last 4 weeks and alcohol abusers excluded from this study. Cirrhotic cardiomyopathy was demarcated as cardiac dysfunction in patients with severe liver disease in the absence of prior cardiac disease.[10]In echo, E/A ratio is the indicator of left ventricular function and it embodies ratio of early diastolic peak velocity flow (the E wave) to late diastolic peak velocity flow produced by contraction of atria (the A wave). Data filled in predesigned proforma and analyzed on software IBM SPSS version 22.0.Mean and standard deviation measured for quantitative variables while frequency (%) for qualitative variables like gender, disease severity by child Pugh scoring, grades of ascites and cirrhotic cardiomyopathy. Echocardiographic findings compared according to Child-Pugh class severity by applying one way ANOVA. P- value less than 0.05 considered as significant statistically**.**

RESULTS

This study conducted on 79 patients of liver cirrhosis (n=79). Their mean age was 48.52 years±8.1 and out of them, 58 and 21 were males and females respectively, while 63 found having hepatitis B and 16 with hepatitis C. According to Child Pugh scoring based disease severity, patients separated in A, B and C groups. (As shown in Table I)

Table No. 1: Descriptive statistics of liver cirrhosis patients (n=79)

	Frequency (%)
Age (Mean± Sd)	48.52 years±8.11
Gender	
Male	58(73.4%)
Female	21(26.6%)
Hepatitis B positive	63(80%)
Hepatitis C positive	16(20%)
Child-Pugh Score based severity of liver disease	
A	32(40.5%)
B	27(34.2%)
C	20(25.3%)
Ascites	
Grade II	25(32%)
Grade III	19(24%)
Grade I	35(44%)

Table No. 2:Echocardiographic findings in patients of liver cirrhosis (n=79)

	Mean	**Std. Deviation**
LVIDD. ed (cm)	50.72	8.42
LVIDS. es(cm)	41.03	11.63
Left Atrium	35.45	4.84
Ejection fraction (%)	30.46	8.61
Aortic root	25.41	3.92
Posterior wall	9.17	1.66
EA ratio	1.07	.56
Pulmonary artery pressure	15.86	1.17
Interventricular septum	9.08	2.13
Valid N (list wise)		

LVIDD.ed stands for Left Ventricular Internal Dimension-diastole. end-diastolic

LVIDS.es stands for Left Ventricular Internal Dimension-systole. end systolic

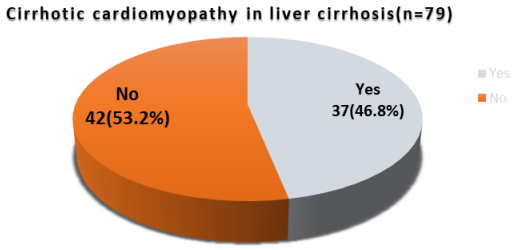

Figure No. 1 Cirrhotic Cardiomyopathy among liver cirrhosis patients

Table No 3: Association of Echocardiographic findings with severity of liver disease by child Pugh scoring

Echocardiographic findings	Child Pugh scoring		
LVIDD.ed	A(n=32)	43.47±6.8	
	B(n=27)	54.48±6.5	<0.01
	C(n=20)	57.25±1.6	
LVIDS.es	A(n=32)	31.84±8.5	<0.01
	B(n=27)	46.07±10.3	
	C(n=20)	48.95±6.8	
LA	A(n=32)	32.8±3.4	
	B(n=27)	36.77±4.7	<0.01
	C(n=20)	37.90±5.0	
Inter-ventricularseptum	A(n=32)	9.34±2.3	0.65
	B(n=27)	9.00±2.1	
	C(n=20)	8.80±1.8	
Ejection Fraction	A(n=32)	34.31±10.8	
	B(n=27)	28.00±6.1	<0.01
	C(n=20)	27.65±4.2	
Heart rate(beats/ minute)	A(n=32)	66.68±7.2	<0.01
	B(n=27)	75.37±7.0	
	C(n=20)	75.30±8.2	
Posterior wall	A(n=32)	9.06±1.4	.040
	B(n=27)	8.74±1.7	
	C(n=20)	9.95±1.6	
E/A ratio	A(n=32)	0.65±0.4	<0.01
	B(n=27)	1.20±0.4	
	C(n=20)	1.55±0.3	
Aortic Root	A(n=32)	23.54±2.3	
	B(n=27)	27.33±4.4	<0.01
	C(n=20)	25.7±4.0	
Pulmonary artery pressure	A(n=32)	15.34±1.1	<0.01
	B(n=27)	16.07±1.1	
	C(n=20)	16.40±0.9	

**statistically highly significant

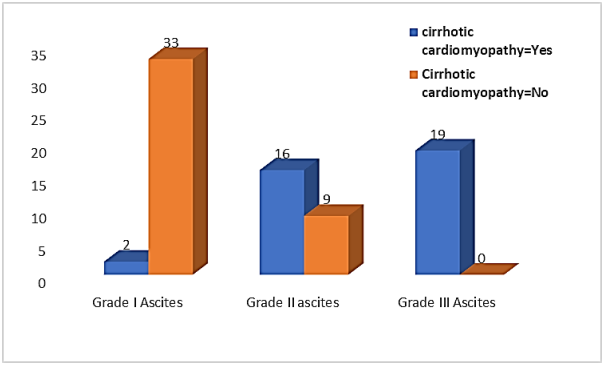

Figure No.2: Association of Cirrhotic cardiomyopathy with grade of ascites (n=37)

Regarding echocardiographic alterations, means±sd of LVIDD.Ed, LVIDD.Es, left atrium, interventricular septum, aortic root and posterior wall among study population were 50.72cm ±8.42, 41.03±11.63, 35.45±4.8, 9.08±2.13, 25.41±3.92 and 9.17±1.66 respectively. While, ejection fraction revealed as 30.46%±8.61. (As shown in Table 2)

Out of total 79, 37 (46.8%) identified as the cirrhotic cardiomyopathy. As shown in figure No. 1 and out of 37 patients of cirrhotic cardiomyopathy, 19 patients had been suffering from grade III ascites while 16 had grade II ascites. As shown in figure 2

Echocardiographic alterations were statistically significant($p < 0.05$) in cirrhotic patients related with Child-Pugh scoring based disease severity. As shown in table 3.

DISCUSSION

Liver cirrhosis has displayed principal part to global morbidity as well as mortality. Cirrhotic cardiomyopathy was first defined 13 years backin world congress of gastroenterology, Criterion for cirrhotic cardiomyopathy was described as early identifying altered echocardiographic parameters to diagnose subclinical cardiac dysfunctions in liver cirrhosis patients in absence of other prior diseases.[10]In this study (n=79) , liver cirrhosis is more predominant in male patients and 37(46%) revealed with cirrhotic cardiomyopathy. Joshi N et al. also concluded with similar findings, they conducted study on 133 patients of chronic liver illness, having mean age 45.7 +14.0 years. [11] Bokarvadia R, et al revealed proportion of cirrhotic cardiomyopathy as 33.8%with male predominance and this proportion of cirrhotic cardiomyopathy was revealed independent of the etiology of cirrhosis, comorbidity as well as severity of liver ailment. Diastolic dysfunctions were frequent finding in such patients. [12] W.Ouechtati ben Attia also detected 46% occurrence of cardiomyopathy among cirrhotic patients.[13]

In patients of liver cirrhosis, systemic circulation becomes hyperdynamic with increase in heart rate, cardiac output and decrease in vascular resistance. The

associated cardiac disfunction has been considered as cirrhotic cardiomyopathy, that is distinct from alcoholic myocardial disease. [14,15] Additionally, circulating vaso-dilators as well as cardio-depressive constituents cause hyperdynamic circulation with altered structure as well as functions of myocardium among the cirrhotic patients. [6] Underlying pathogenic mechanisms involve gut bacterial translocation and endotoxemia that stimulates cardio-depressant agents (like nitric oxide, endocannabenoids). Biochemical as well as biophysical alterations in myocardial cell plasma membrane might had role in underlying pathogenesis. They also cause reduced beta-adrenergic function. Projected recent echocardiography bases criteria for diagnosis of cirrhotic cardiomyopathy comprise indices of diastolic disfunction and this further may lead to hepatorenal syndrome and culminating to increased ratio of morbidity and mortality, infection, hemorrhage and surgery, countinghepatic transplantation. There is no exact treatment, although β-adrenergic blockade and supportive management are proposed for better outcomes, but yet this needs further study.[14]On the grounds of pathophysiological mechanisms, augmented levels of vasodilators in such cases, leads to portosystemic shunting, bacterial translocation enhance central hypovolemia and also to hyperdynamic alterations in circulation. These hyperdynamic alterations lead to hyperdynamic multi-organ syndrome that alters functions of multiple systems of body and disturbs cardiacfunctions by developing cirrhotic cardiomyopathy, renal disturbance and autonomic dysfunctions as portion of cardiorenal syndrome. Such hemodynamic alterations might affect the survival of patients but still this revealed as reversible and changeable after hepatic transplantation. Numerous drugs used in the treatment of portal hypertension including non-selective beta-blockers and terlipressin enhance hyperdynamic circulation.[15]

In presents study, cirrhotic cardiomyopathy is more prominent among those who had grade III as cites and severity of disease in Child Pugh score C. Jyotirmayi B, et al.[16]revealed that patients having ascites are more expected to develop diastolic dysfunctions. Yuan W, et al.[17] and also Moller, Bedtesen F[15] revealed positive association of cirrhotic cardiomyopathy with severity of liver disease as well as ascites and meanwhile no association with underlying etiology of hepatic cirrhosis either hepatitis B or C. Results of this as well as other research report sendorse that function of hyperdynamic left ventricle in cirrhotic patients is connected to severity of liver disease as well as stimulation of sympathetic nervous system and beta blockers that play meaningfully affect cardiac systolic function. Taking vasoconstrictors like terlipressin decrease heart rate and also cardiac output, an effect which might be thought an enhancement in hyper dynamic circulation. Furthermore, terlipressin might employ negative inotropic effect on left ventricle and consequently the over-all effects on the cardiovascular structure are multifaceted.[15] Features of cirrhotic cardiomyopathy include hyperdynamic circulatory status, diminished contractility with transformed diastolic relaxationand electrophysiologic changes, specifically QT interval prolongation. Underlying pathogenicmechanisms comprise diminished function of betareceptors, transformed transmembrane currents and increased production of cardio-depressants like nitric oxide, endogenous cannabinoids and cytokines. [7]

In present study echocardiographic variables are increased among cirrhotic patients as the liver disease becomes more severe on the basis of Child Pugh Scoring i.e., LVIDD. Ed, LVIDD.Es, left atrium, E/A ratio and decrease in ejection fraction but no noteworthy change in interventricular septum. Marconi C, et al [18] also found noteworthy dilatation of left atrium with increases in left atrium, aortic root, interventricular septum, E/A ratio and posterior wall in patients of liver cirrhosis. in connotation with increase in left ventricular diameters. Left atrial enlargement might be considered diagnostic feature for diastolic dysfunction in progression to cirrhotic cardiomyopathy. Merli et al.[19] also displayed enlargement of left atrium enlargement among the patients of hepatic cirrhosis. Barbosa et al. [8] mentioned that echocardiography should be acquired necessarily among the patients with doubt of worsening to cirrhotic cardiomyopathy. Diastolic impairment is an obvious and initial feature of cirrhotic cardiomyopathy and this might worsen the prognosis in patients of cirrhosis, regardless of transplanted liver or not. Kazan K and his coworkers [20] also revealed decreased ejection fraction during diastole at rest. Among the patients of hepatic cirrhosis, stress echocardiography is suggested as ideal investigation as this may detect sub clinical systolic and diastolic dysfunctions before decline in ejection fraction**.**

CONCLUSION

This study revealed significant echocardiographic alterations in patients of liver cirrhosis. That's why, liver disease patients should be examined by mean of echocardiography to avert under diagnosis of liver disease related cardiomyopathy for better prognosis**.**

Author's Contribution:

Concept & Design of Study:	Keenjhar Rani
Drafting:	Zaman Baloch, Ramesh Kumar
Data Analysis:	Ramesh Kumar, Kavita Bai
Revisiting Critically:	Keenjhar Rani, Zaman Baloch
Final Approval of version:	Keenjhar Rani

Conflict of Interest: The study has no conflict of interest to declare by any author.

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