Original Article

Frequency of Cardiomyopathy in Patients with Hepatic Cirrhosis

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ABSTRACT

OBJECTIVE: To determine the frequency of cardiomyopathy and its manifestations in patients with liver cirrhosis presenting at Tertiary Care Hospital, Karachi.

METHODOLOGY: This cross-sectional study was carried out in Medical unit I of Jinnah Postgraduate Medical Center, Karachi, from July-December 2017. The sampling technique employed was nonprobability consecutive samplings. 95 patients with liver cirrhosis diagnosed earlier on clinical and investigations were included. Systolic dysfunction of the heart on Echocardiography was considered at EF<55% while decreased diastolic dysfunction was labeled when the E/A ratio was found to be <1. QTc and heart rate were calculated from lead II of ECG. proBNP levels were determined. Descriptive statistics were analyzed by software SPSS 20.

RESULTS: Total 61 male and 34 female patients were registered. The mean age was 48.20±8.77 years. EF <55% was in 51.6% cases and E/A ratio <1 was in 42.1% cases. QTc>0.44 was in 47.4% cases and heart rate >100 was in 33.7% cases. The proBNP>93 pg/ml was observed in 77.4% male patients and >144 pg/ml in 87.5% female patients. Cirrhotic cardiomyopathy was observed in 69.5% of patients and was not significantly associated with gender, age, duration of disease, and child Pugh class.

CONCLUSION: Although there is a considerably high frequency of cardiomyopathy in cirrhotic patients, its presence, generally, is not realized and, thus, due attention is not given. Highlighting its high frequency, its need for workup and treatment may improve the quality of life of these patients.

KEYWORDS: Liver Cirrhosis, Cirrhotic Cardiomyopathy, proBNP

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INTRODUCTION

Liver cirrhosis is characterized by liver fibrosis causing disfigured architecture along with regenerative nodule formation[1]. Cirrhotic cardiomyopathy, a condition due to liver cirrhosis is known for causing poor cardiac contractility as seen by reduced Ejection fraction, disturbed diastolic function, QT interval prolongation, high level of Atrial Natriuretic Peptide (ANP) and\or high level of B-Type Natriuretic Peptide (BNP)[2].

The decreased cardiac function causes low blood pressure which leads to the situation that the autonomic sympathetic system is activated. Low cardiac output also activates the rennin angiotensin system and causes the release of sodium and fluid retaining hormone, aldosterone[3,4],

The observation of the decreased quality of life and feeling of weakness in cirrhotic patients could be said to be due to cirrhotic cardiomyopathy and decreased cardiac function[5,6].

The objective of this study was to determine the frequency of cardiomyopathy and its various manifestations in patients with liver cirrhosis presenting at Tertiary Care Hospital, Karachi and to compare the results with international studies and contribute to the literature by locally produced data in a public sector hospital in the metropolitan city of Pakistan.

METHODOLOGY

This cross-sectional study was carried out in Medical unit I of Jinnah Postgraduate Medical Center, Karachi, from July - December 2017. Approval of the study was taken from the ethical review board of JPMC. By taking the prevalence of cirrhotic cardiomyopathy 44.6%, margin of error = 10%, and confidence level CI=95%, sample size after calculating by WHO software, came out to be 95 patients.

The sampling technique employed was nonprobability consecutive samplings. Informed consent was taken from patients. 95 patients among patients attending OPD of Medical Unit of either gender with age between 30 years to 60 years diagnosed as Liver Cirrhosis earlier, at least more than 6 months before on clinical grounds and on ultrasound, S. Albumen, Ascitic fluid examination findings, and with (if done) or without Endoscopic findings suggestive of cirrhotic portal hypertension, ie. Portal hypertensive gastropathy & esophageal Varices and having calculated for Child-Pugh score (A/B/C) were registered using a nonprobability consecutive sampling technique.

Ultrasound scan of the abdomen of all patients was repeated by senior radiologist having experience of three years after post-graduation.

Finding of reduced liver size (i.e. < 90 mm right lobe

and <70 mm left lobe maximum measurable diameter), nodularity of liver surface, coarsening of liver echotexture, transudative ascites, dilated portal vein ie more than 14mm were noted and on the presence of any 3 or more of these findings patients were considered as having liver cirrhosis[1].

Known patients of diabetes mellitus, valvular heart disease (known or discovered during Echocardiography) hypertension, conduction abnormalities, electrolyte imbalance, hypo or hyperthyroidism, heart failure, ischemic heart disease, chronic or new renal failure due to hepatorenal syndrome, COPD, stroke, and patients on cardiac drugs were excluded.

Echocardiography was performed by a senior radiologist having more than 3 years of experience in the Echocardiography section of the Radiology Department of JPMC. Systolic impairment was labeled when the Ejection fraction was <55% and diastolic impairment was labeled on finding reversed E/A ratio[7]. ECG was also obtained and corrected QT as well as heart rate was calculated from lead II. QTc of > 0.44 and heart rate >100 were taken as abnormal. proBNP levels were obtained from blood samples. proBNP levels in Male > 93-pg/ml and in Female > 144-pg/ml were considered higher[2]. Cirrhotic cardiomyopathy was labeled as positive by the presence of any two among i) abnormal echocardiography (systolic impairment and/ or diastolic impairment), ii) abnormal ECG (Prolonged QTc and or increased heart rate as described above), and iii) raised proBNP[2,7].

Patients' data were collected and processed through Statistical Package for Social Sciences (SPSS 20). Mean as well as standard deviations were computed for age, QTc, heart rate, proBNP, E/A ratio, and duration of disease. Frequencies and percentages were determined for gender, duration of disease, Child -Pugh score (A/B/C), and presence or absence of cirrhotic cardiomyopathy was concluded and all data recorded. The outcome was compared using the Chi-Square test. Stratification of gender, Child-Pugh Score (A/B/C), and duration of disease was done to see the effect of these on outcome variables ie cardiomyopathy. The post-stratification chi-square test was applied. P-value ≤ 0.05 as a standard values, was taken statistically significant with CI 95%.

RESULTS

The mean age of subjects was 48.20±8.77 years**.** Among patients having liver cirrhosis, 64.2% were male and 35.8% were female. Among these in 43.3% of patients, child Pugh class A was found, while class B was seen in 32.6% patients, and 24.2% patients had class C. The mean duration of being a known disease was 10.19±2.65 months. 30 patients were aged ≤45 years and 65 patients were aged >45 years. Duration of disease in 54 patients was ≤10 months and > 10 months in 41 patients.

The echocardiography evaluation showed that 51.6% of cases had EF <55% and reversed E/A ratio were observed in 42.1% cases. The electrocardiographic evaluation showed that QTc more than 0.44 was in 47.4% cases and a heart rate of more than 100 was observed in 33.7% cases. The proBNP level >93 pg/ml was seen in 77.4% of male patients and 87.5% of female patients had >144 pg/ml (more than normal as female normal value is higher). The main focus i.e. cirrhotic cardiomyopathy was determined to be present in 69.5% of patients as on fulfilling conditions given in material and methods.

The association of cirrhotic cardiomyopathy was observed with gender, age, duration of disease, and child Pugh class. The results showed that cirrhotic cardiomyopathy was not significantly associated with gender (p=0.451), age (p = 0.377), child-pugh class (p=0.567) and duration of disease (p = 0.264) Table III - VI.

TABLE I: DESCRIPTIVE STATISTICS OF AGE (YEARS) (n=95)

	Age (years)
Mean ±SD	48.20±8.77
95%CI (LB – UB)	46.41 – 49.99
Median (IQR)	50.00 (15)
Range	30
Minimum	30
Maximum	60

TABLE II: FREQUENCY DISTRIBUTION OF ECHOCARDIOGRAPHY EVALUATION, ELECTROCARDIOGRAPHIC EVALUATION, PROBNP OUTCOME, AND CIRRHOTIC CARDIOMYOPATHY. TOTAL PATIENTS: (n=95)

		Present/ not present	**Frequency (n)**	**Percentage (%)**
Echocardiography Evaluation	EF <55%	Yes	49	51.6%
		No	46	48.4%
	E/A Reversal	Yes	40	42.1%
		No	55	57.9%
Electrocardiographic Evaluation	QTc>0.44	Yes	45	47.4%
		No	50	52.6%
	Heart Rate >100	Yes	32	33.7%
		No	63	66.3%
proBNP Outcome	Among 61 Male Patients (>93 pg/ml)	Yes	44	72.1%
		No	17	27.9%
	Among 34 Female Patients (>144 pg/ml)	Yes	22	64.7%
		No	12	35.3%
Cirrhotic Cardiomyopathy	--	Yes	66	69.5%
		No	29	30.5%

TABLE III: FREQUENCY AND ASSOCIATION OF CIRRHOTIC CARDIOMYOPATHY ACCORDING TO AGE GROUP (n=95)

	Cirrhotic Cardiomyopathy			P-Value
	Yes (n=66)	No (n=29)	Total	
≤ 45 years (n=30)	19	11	**30**	0.377**
> 45 years (n=65)	47	18	**65**	
Total	**66**	**29**	**95**	

*Chi-Square Test was applied; P-value ≤0.05 is considered a significant; ** Not Significant at 0.05 levels*

TABLE IV: FREQUENCY AND ASSOCIATION OF CIRRHOTIC CARDIOMYOPATHY ACCORDING TO GENDER (n=95)

	Cirrhotic Cardiomyopathy			P-Value
	Yes (n=66)	No (n=29)	Total	
Male (n=61)	44	17	**61**	0.451**
Female(n=34)	22	12	**34**	
TOTAL	**66**	**29**	**95**	

*Chi-Square Test was applied; P-value ≤0.05 considered a significant; ** Not Significant at 0.05 levels*

TABLE V: FREQUENCY AND ASSOCIATION OF CIRRHOTIC CARDIOMYOPATHY ACCORDING TO DURATION OF DISEASE (Months) (n=95)

	Cirrhotic Cardiomyopathy			P-Value
	Yes (n=66)	No (n=29)	Total	
≤ 10 months (n=54)	40	14	**54**	0.264**
> 10 months (n=41	26	15	**41**	
TOTAL	**66**	**29**	**95**	

*Chi-Square Test was applied; P-value ≤0.05 is considered a significant; ** Not Significant at 0.05 levels*

TABLE VI: FREQUENCY AND ASSOCIATION OF CIRRHOTIC CARDIOMYOPATHY ACCORDING TO CHILD PUGH CLASS (Months) (n=95)

	Cirrhotic Cardiomyopathy			P-Value
	Yes (n=66)	No (n=29)	Total	
A-Class (n=23)	18	5	**23**	0.567**
B-Class (n=31)	21	10	**31**	
C-Class (n=41)	27	14	**41**	
TOTAL	**66**	**29**	**95**	

*Chi-Square Test was applied; P-value ≤0.05 is considered a significant; ** Not Significant at 0.05 levels*

DISCUSSION

Cardiomyopathy in cirrhotic patients was known since the 1960s, but the cardiac defect was wrongly attributed to alcoholism[7,8]. However, in the last 20 years, cardiac dysfunction was found in patients with liver cirrhosis even in non-alcoholics. To recognize this finding separately a term "cirrhotic cardiomyopathy" was coined. It covers impaired cardiac function as well as ECG abnormalities provided there is no prior cardiac disease history or evidence and therefore attributable confidently to liver cirrhosis only[7,9-10].

Cardiomyopathy is a group of myocardial diseases that affects the mechanical or electrical function of the heart[11]. Cirrhotic cardiomyopathy entity has been put forward in the past twenty to thirty years when impairment of systolic or diastolic function in hepatic cirrhosis has been observed and there is no other explainable cardiac disease[12]. Cirrhosis has many well -known complications[13]. But usually, Cirrhotic cardiomyopathy is silent or mild clinically, although it was postulated that it has a role in causing hepatorenal syndrome[14]. This cardiomyopathy can be diagnosed by the presence of features like systolic or diastolic disorders, ECG, or abnormal serum biomarkers i.e. NTproBNP[4].

In our study, more cases of cirrhosis were of male gender (64.2% male vs 35.8% female) and cardiomyopathy among these was found more prevalent in males compared to female patients although statistically not significant (p=0.451). Most of the patients were aged >45 years. The mean duration of liver cirrhosis was 10.19±2.65 months. Among child -pugh classes for our study group, the 'A' class was found more frequent followed by 'B' and 'C' with frequencies 43.3%, 32.6%, and 24.2% respectively.

EF <55% was observed in more than half of the study subjects. The QTc>0.44 was seen in 47.4% of the patients and heart rate >100 was observed in 33.7% of cases. The proBNP outcome was more positive in female than male patients. The cirrhotic cardiomyopathy was determined to be present in 66 (69.5%) patients on fulfilling conditions given in material and methods.

Its presence concerning gender, age, duration of disease, and the child-pugh class was also statistically analyzed but it was seen these are not statistically significant. Similar studies on analyzing the presence of 'Cardiomyopathy in cirrhosis' were also done in past. A study[15] reported that the degree of liver cirrhosis had a direct effect on cardiomyopathy along with electrophysiological, ECG, and biomarker levels. In addition to it also reported a concomitant increase in the frequency of cirrhotic cardiomyopathy with

advancing child-Pugh class which represented the severity of the stages of liver cirrhosis[15]. In other studies too, it has been reported that "cirrhotic cardiomyopathy is seen with increasing frequency with advancing Child-Pugh class"[16,17]. Cardiomyopathy was reported as 25% in class A, 51% in Child-Pugh class B and 60% in class C and it was mainly seen with the finding of prolonged QT-interval" [16,17]. Yildiz R 2005[18] reported that "with advancing stage of liver cirrhosis, presence of cirrhotic cardiomyopathy increases as assessed by levels of pro-BNP". The hepatologists universally agree that cirrhotic cardiomyopathy causes electrophysiological changes, ECG abnormalities, and variability in Natriuretic peptides levels[19].

Electrophysiological abnormalities are manifested as prolonged repolarization i.e. prolonged QT interval. A study by Genovesi S et al.[20] reported "21.62% of cirrhotic patients with prolonged QTc interval" while Zuberi BF et al.[21] "reported that frequency was 19.2%". Wong F 2009[4] reported "higher frequency of 45% of prolonged QTc interval". Prolonged QT intervals are associated with cardiac rhythm disorders, a factor to be kept in mind.

On Echocardiographic examination, less than normal ejection fraction ie < 55 at rest was seen in 49(51.6%) patients and was normal in 46 (48.4%) patients. Echocardiographic abnormalities present were divided into two subtypes i.e; systolic and diastolic impairment[7], although a study of Baik SK 2007[22] also used stress during the Echocardiographic examination, this, however, was not feasible to be determined in our setup. As Diastolic dysfunction is determined by reversed E/A ratio, our study reported 42.1% of patients with reversed E/A ratio at rest as compared to 50% reported by Pozi M 2006[23] and Henriksen JH et al.[24] suggested that the drainage of ascitic fluid caused betterment in E/A ratio, which however still did not reach the level of that of a healthy individual. An Indian study reported the presence of diastolic dysfunction in the majority of cirrhotic patients[25]. Regarding biomarkers, our study reported elevated levels of proBNP in 69.47% of the patients which was similar to the percentage given by Henriksen JH et al.[24].

It was thought that "increased values of proBNP were attributable to alcoholic cardiomyopathy, therefore labeling it as cirrhotic cardiomyopathy may be a misnomer".[16] But as in our setup, Hepatitis B and C are major causes of cirrhosis, elevated levels of pro-BNP may be suggested to be considered as an indicator of cardiomyopathy irrespective of the cause. Cirrhotic cardiomyopathy is still underdiagnosed and thus remains untreated, especially in developing countries like Pakistan due to a lack of awareness of this condition.

The main limitations of the present study included its single-center study with an unequal gender representation (greater number of males) and the application of a non-randomized study design. The limited sample size and the inclusion of only one center may generalize the study to the general population less favored.

CONCLUSION

Although there is a considerably high frequency of cardiomyopathy in cirrhotic patients, its presence, generally, is not realized and, thus, due attention not given. Highlighting its high frequency, its need for workup and treatment may improve the quality of life of these patients.

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AUTHOR CONTRIBUTIONS

Jafri M: Conceived & designed the manuscript
Haider S: Study design, analysis
Tabassum S: Drafting of manuscript, Echo/ultrasound
Ansari N: Data entry, patient inclusion, revision of manuscript
Talpur MT: Data entry, patient inclusion, revision of manuscript

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