



## FREQUENCY OF CARDIOMYOPATHY IN PATIENTS WITH LIVER CIRRHOSIS AT SERVICES HOSPITAL LAHORE

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GE: Conducted the study and wrote the article. MNA: Helped in review the article. SF: Re-arranged data and corrected article. SS: Tables and figures. MAN made corrections and did the proof reading.

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### ABSTRACT

**INTRODUCTION:** Cirrhosis is the end stage liver disease characterized by changes in body metabolism and hemodynamics, which alter the function of virtually every body organ. Cardiac changes in cirrhotic patients include prolongation of QT interval and echocardiographic features, which are hallmarks of cirrhotic cardiomyopathy and can be described on routine electrocardiography and echocardiography respectively. A number of previous studies reported variable frequency of cirrhotic cardiomyopathy among cirrhotic patients depending upon studied population, age, duration of disease and the diagnostic criteria used. The available evidence in local population was limited and required further studies to have an insight into the magnitude of problem.

**OBJECTIVE:** The objective of this study was to assess the frequency of cardiomyopathy in patients with liver cirrhosis.

**MATERIAL AND METHODS:** This cross sectional study was carried out at Gastroenterology Department of Services Hospital Lahore, from 16/12/2016 to 15/06/2017. It included 150 patients with liver disease and included both genders with age between 18-65 years, they all were having liver cirrhosis for at least 6 months. Electrocardiography and echocardiography were performed to see the presence or absence of cardiomyopathy due to liver cirrhosis. The primary outcome was to determine the frequency of cardiomyopathy and were compared among various age, gender and duration of disease groups.

**RESULTS:** The patients were having mean age of  $51.73 \pm 9.97$  years. Majority of the patients were between 51-64 years (54.7%) followed by 35-50 years (45.3%). Males were 92 (61.3%) and females were 58 (38.7%) with a ratio of 1.6 : 1 (male to female). The presence of cirrhosis ranged from 8 - 48 months with a mean of  $21.63 \pm 11.13$  months. Cirrhotic cardiomyopathy was diagnosed in 62 (41.3%) patients with cirrhosis. No significant difference was noted in the frequency of cirrhotic cardiomyopathy across age ( $p=0.483$ ) and gender ( $p=0.993$ ). But it was significantly higher with increasing duration of cirrhosis; <2 years vs. 2-4 years (56.0% vs. 34.0%;  $p=0.010$ ).

**CONCLUSION:** The frequency of cardiomyopathy due to liver cirrhosis was found in 41.3% patients. The more the duration of liver cirrhosis the higher the frequency of cardiomyopathy secondary to liver cirrhosis.

**KEY WORDS:** Cirrhosis, prolong duration, Cardiac Dysfunction, Cirrhotic Cardiomyopathy

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## INTRODUCTION

Cardiomyopathy due to liver cirrhosis is common pathology in which there is cardiac dysfunction both systolic and diastolic. This abnormality is due to presence of abnormal myocardial contractile reserve which is also accompanied by some electrophysiological abnormalities.<sup>1</sup>

In patients with liver cirrhosis systemic vasodilatation secondary to presence of portal hypertension leads to compensation by hyper-dynamic circulation in initial compensatory phasis.<sup>1-5</sup> The systemic vasodilatation is responsible for hypovolemia in central circulation thereby leading to activation of the renin-angiotensin-aldosterone axis, and the circulating levels of anti-diuretic hormone.<sup>2</sup>

The cirrhotic patients develop abnormal intestinal mobility after systemic vasodilatation which leads to bacterial over growth and endotoxemia.<sup>3</sup> Further-more inflammatory cytokines such as tumor necrosis factor  $\alpha$  (TNF- $\alpha$ ), interleukin 6 (IL-6), and interleukin 1b (IL-1b) are produced which leads to increased production of nitric oxide (NO) and further worsens the hyper-dynamic circulation producing strain on cardiac function. Whole sequence of these events lead to development of Cardiomyopathy in patient with liver cirrhosis i.e. "cirrhotic cardiomyopathy" (CC).<sup>1,6-7</sup>

Many previous studies have also determined the presence of Cardiomyopathy in cohort of cirrhosis patients, though with variable results and certain issues. The populations included in such studies have multi-dimensional angles in terms of etiology, concomitant therapies and gender which may affect the results. In addition, certain studies have used only prolongation of corrected QT interval (QTc) and have not taken into account echocardiography findings leading to erroneous results and vice versa.<sup>2,7</sup>

Moreover, some of the studies were retrospective and included only patients with certain severity of disease.<sup>2,7</sup> There is only a single study from Pakistan reporting cirrhotic cardiomyopathy in 44.6% patients from Hyderabad.<sup>4</sup> A recent study by Karagiannakis et al. found cirrhotic cardiomyopathy in 37.8% of the patients, however, the study only used echocardiography findings for the diagnosis and did not take into account QTc.<sup>3</sup>

Another study from India by Patil et al. only used electrophysiological criteria measuring QTc and found that approximately 35-40% patients with liver cirrhosis had prolonged QTc interval.<sup>5</sup> A US

based data reported the presence of Cardiomyopathy in patients with liver cirrhosis to be 51.1% which was diagnosed with ECG and Echocardiographic criteria.<sup>6</sup>

Still another study by Bhatti et al. using QTc interval found that CCM was present in 24.7% of cirrhotic patients in the study.<sup>7</sup>

Keeping in view the different criteria used as well as the difference in frequency ranging from 24.7% to as high as 51.1%, it is imperative that a prospective study be carried out with appropriate sample size to determine the frequency of CCM in cirrhotic patients as CCM may lead to lethal cardiac arrhythmias and sudden cardiac death. Prolonged QTc is also related to Child Pugh score, and a positive correlation with heart rate variability, has been established as prognostic factors.<sup>7</sup> The study would enhance our understanding about cirrhotic cardiomyopathy and enable us to setup protocols for management of such patients.

The objective of our study was to assess the frequency of cirrhotic cardiomyopathy in cirrhotic patients presenting to Services Hospital, Lahore.

## MATERIALS AND METHODS:

It was a cross sectional study, conducted at Department of Gastroenterology, Services Hospital Lahore, from 16/12/2016 to 15/06/2017. Sample size of 150 cases was calculated by Non-Probability, Consecutive Sampling with 95% confidence interval and 8% margin of error while taking expected frequency of cirrhotic cardiomyopathy to be 37.8% in patients with cirrhosis. We included patients after informed consent, of both gender with age range between 18-65 years, diagnosed to have cirrhosis for at least 6 month.

Patients suspected of malignancy of liver as per medical record and history/examination, patients of coronary artery disease, valvular diseases, conduction abnormalities including cardiac arrhythmias and congenital heart defects assessed form medical record and history/examination, those with diabetes (BSR  $\geq$  200mg/dl) and hypertension (BP  $\geq$  160/90 mmHg) assessed form medical record and history/examination and patients with hepatic encephalopathy were not included.

150 patients were included after taking informed consent. ECG was carried out to determine the presence or absence of QT interval abnormalities. QT interval was calculated by using formula.

$$QTc \text{ (Bazett)} = \frac{QT}{\sqrt{RR}}$$



Echocardiography was done in all patients. Diagnosis of CCM was made as per operational definition. Patients of cirrhotic cardiomyopathy were managed as per hospital protocol.

**STATISTICAL ANALYSIS:**

SPSS version 17 was used to analyze the collected data. Variables like age etc. were presented in mean ± SD. Variables i.e., gender and presence of cirrhotic cardiomyopathy were presented as frequencies and percentages. Data was stratified for age, gender and duration of cirrhosis to address effect modifiers. Post-stratification Chi-square test had been applied taking  $p \leq 0.05$  as significant.

**RESULTS:**

The patients ranged from 35 - 64 years with a mean of  $51.73 \pm 9.97$  years. Majority of the patients were between 51 - 64 years (54.7%) followed by 35-50 years (45.3%). Males were 92 (61.3%) and females were 58 (38.7%) with a ratio of 1.6 : 1. The presence of cirrhosis ranged from 8 - 48 months with a mean of  $21.63 \pm 11.13$  months as shown in table 1.

**Table-1: Baseline parameters**

Parameters	n = 150
Age (years)	51.73±9.97
Age Groups	
• 35-50 years	68 (45.3%)
• 51-64 years	82 (54.7%)
Gender	
• Male	92 (61.3%)
• Female	58 (38.7%)
Duration of Disease (months)	21.63±11.13
• ≤2 years	100 (66.7%)
• 2-4 years	50 (33.3%)

**Table-2: Frequency of Cardiomyopathy in Patients with Liver Cirrhosis**

Cirrhotic Cardiomyopathy	Frequencies (n)	Percentages (%)
Yes	62	41.3
No	88	58.7
Total	150	100

**Table-3: Comparison of Frequency of Cirrhotic Cardiomyopathy across Age Groups**

Age	Cirrhotic Cardiomyopathy		Total	P value
	Yes (n=62)	No (n=88)		
35-50 years (n=68)	26	42	68	0.483
	38.2%	61.8%	100.0%	
51-64 years (n=82)	36	46	82	
	43.9%	56.1%	100.0%	
Total	62	88	150	
	41.3%	58.7%	100.0%	

**Table-4: Comparison of Frequency of Cirrhotic Cardiomyopathy across Gender Groups**

Gender	Cirrhotic Cardiomyopathy		Total	P value
	Yes (n=62)	No (n=88)		
Male (n=92)	38	54	92	0.993
	41.3%	58.7%	100.0%	
Female (n=58)	24	34	58	
	41.4%	58.6%	100.0%	
Total	62	88	150	
	41.3%	58.7%	100.0%	

**Table-5: Comparison of Frequency of Cirrhotic Cardiomyopathy across Duration Groups**

Duration of Disease	Cirrhotic Cardiomyopathy		Total	P value
	Yes (n=62)	No (n=88)		
<2 years (n=100)	34	66	100	0.010*
	34.0%	66.0%	100.0%	
2-4 years (n=50)	28	22	50	
	56.0%	44.0%	100.0%	
Total	62	88	150	
	41.3%	58.7%	100.0%	

No statistical significant difference was noted by using Chi-square test

Cirrhotic cardiomyopathy was present in 62 (41.3%) patients with cirrhosis as shown in table 2. There was no significant difference in the frequency of cardiomyopathy across age ( $p=0.483$ ) and gender ( $p=0.993$ ). But it was significantly higher with increasing duration of cirrhosis; <2 years vs. 2-4 years (56.0% vs. 34.0%;  $p=0.010$ ) as shown in tables 3 – 5 respectively.

**DISCUSSION:**

Cirrhosis indicates end stage liver disease characterized by changes in body metabolism and hemodynamics, which alter the function of virtually everybody organ.<sup>1</sup> Cardiac changes in cirrhotic patients include prolongation of QT interval and echocardiographic features, which are hallmarks of cirrhotic cardiomyopathy and can be described on routine electrocardiography and echocardiography.<sup>1-5</sup> A number of previous studies reported variable frequency of cirrhotic cardiomyopathy among cirrhotic patients depending upon studied population, age, duration of disease and the diagnostic criteria used.<sup>3-7</sup> The available evidence in local population was limited and required further studies to prove the importance of cardiac involvement in patients with cirrhosis.

In our study, the mean age was  $51.73 \pm 9.97$  years. Ali et al. in 2008 ( $52 \pm 9$  years), Almani et al. in 2008 ( $53.09 \pm 8.86$  years) and Achakzai et al. in 2016 ( $54 \pm 11$  years) also reported

similar mean age among cirrhotic patients in local population.<sup>8-10</sup> Pentead et al. reported mean age of  $51.4 \pm 7.6$  years which is similar to our results.<sup>11</sup> Mansour-Ghanaei et al. in 2012 reported comparable age group of  $55.03 \pm 12.05$  years in Iranian such patients while much younger age group of  $45.8 \pm 10.45$  years and  $44 \pm 13.7$  years was stated by Bhattacharyya et al. (2016) and Deepika et al. (2015) respectively in Indian patients with liver cirrhosis.<sup>12-14</sup>

There were predominantly males in our study which was also in accordance with a study by Ali et al. conducted at Muhammad Medical College Hospital, Mirpurkhas.<sup>8</sup> A female predominance was however observed by Achakzai et al. in 2016 (M:F, 1:1.5) that such patients presenting at Dow University Hospital, Karachi. Abdel-Fattah El-Feki et al. in 2016 (M: F; 1.5:1) and Mansour-Ghanaei et al. in 2012 (1.9:1) also reported similar male predominance among Egyptian and Iranian such patients respectively.<sup>10,12,15</sup>

Cirrhotic cardiomyopathy was diagnosed in 62 (41.3%) patients with cirrhosis. There was no significant difference in the frequency of cardiomyopathy across age ( $p=0.483$ ) and gender ( $p=0.993$ ). But it was significantly higher with increasing duration of cirrhosis; <2 years vs. 2-4 years (56.0% vs. 34.0%;  $p=0.010$ ). Our results are similar to those of Shaikh et al. (2011) who reported that frequency of cirrhotic cardiomyopathy to be 44.6% among patients presenting at Liaquat University Hospital Jamshoro Hyderabad and Naqvi et al. (2016) who observed it to be

39.32% among such patients at Dow University of Health Sciences, Karachi. Kumar et al. (2017) reported similar frequency of 44.6% among Indian such patients.<sup>4,16-17</sup> A similar frequency of 41.0% has been observed by Karagiannakis et al. (2013) in Korean population.<sup>3</sup> A much lower frequency of 24.7% has been reported by Bhatti et al. (2014) among such patients at Capital Development Authority (CDA) Hospital, Islamabad.<sup>7</sup> A much higher frequency of 61.5% has been reported by Barbosa et al. in Portuguese.<sup>17</sup>

Thus the frequency of cirrhotic cardiomyopathy was found to be 41.3% in patients presenting with cirrhosis at Services Hospital Lahore. In the lights of results of the present study it can be advocated that a considerable proportion of patients with cirrhosis suffer cirrhotic cardiomyopathy. We also noted significantly higher frequency of CCM among patients with increased duration of disease which might suggest a temporal association and can further help in the risk stratification of such patients.

A very important limitation to the present study was that we didn't consider the improvement of cardiac function in response to treatment for liver dysfunction. Such information would enable better patient management in future practice. Therefore such a study is highly recommended in future research.

## CONCLUSION:

The frequency of cardiomyopathy due to liver cirrhosis was found in 41.3% patients. The more the duration of liver cirrhosis the higher the frequency of cardiomyopathy secondary to liver cirrhosis.

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