

ORIGINAL ARTICLE

Cardiomyopathy in Cirrhotic Patients and Its Relationship with the Severity of Cirrhosis

SAIRA KHALID¹, NASIR SHAH², YASIR ABBAS ZAIDI,³ MUHAMMAD SALEEM HASAN,⁴ SAQIB JAHANGIR⁵, SANA REHMAN⁶

¹Postgraduate Resident Internal Medicine Medical unit-1 Sir Ganga Ram Hospital, Lahore

²Senior Registrar Internal Medicine, East Medical Ward Mayo Hospital, Lahore

³Assistant Professor Gastroenterology Nishtar Medical University, Multan

⁴Senior House Officer Internal Medicine Department, Armed Forces Hospital Alkharj, KSA

⁵Primary Care Diabetologist Working at Central Surgery Barton upon Humber DN 185ER, UK

⁶Postgraduate Resident Internal Medicine at Shaukat Khanum Hospital, Lahore

Correspondence to: Dr. Saira Khalid, Email: docsaira111@gmail.com, Ph +92 302 5204769

ABSTRACT

Study Objectives: To determine the frequency of cirrhotic cardiomyopathy in patients with liver cirrhosis and to compare it across varying grades of cirrhosis on Child Turcotte Pugh classification.

Study Design and Settings: It was a descriptive cross-sectional study carried at Department of Medicine, Lahore General Hospital Lahore over 1 year from Jan 2018 to Dec 2018.

Patients and Methods: The present research involved 100 male and female patients aged between 16-70 years having liver cirrhosis diagnosed at least 6 months ago. These patients underwent echocardiographic screening of cardiomyopathy which was diagnosed by the presence of diastolic dysfunction (i.e. increased E/A ratio >1). An informed written consent was obtained from every patient.

Results of the Study: There was a male predominance (M:F, 1.6:1) among cirrhotic patients with a mean age of 51.9±9.8 years. The mean BMI was 26.5±3.7 Kg/m² while the mean duration of cirrhosis was 22.0±10.9 months. Majority (49.0%) of the patients belonged to CTP Class C followed by Class-B (39.0%) and Class-A (12.0%). Cirrhotic cardiomyopathy was observed in 41.0% patients with cirrhosis. There was statistically insignificant difference in the observed frequency of cirrhotic cardiomyopathy among various subgroups of cirrhotic patients depending upon patient's age (p-value=0.928), gender (p-value=0.997), BMI (p-value=0.983) and duration of disease (p-value=0.782). However, it increased considerably with worsening of disease on CTP Classification; Class-A vs. Class-B vs. Class-C (8.3% vs. 35.9% vs. 53.1%; p-value=0.013).

Conclusion: Cirrhotic cardiomyopathy was observed in a substantial proportion of cirrhotic patients and was more frequent in patients with more severe disease which warrants routine echocardiographic screening of cirrhotic patients so that timely recognition and anticipated treatment of this complication may improve the case outcome in future medical practice.

Keywords: Cirrhosis, Cardiomyopathy, Child Turcotte Pugh Class

INTRODUCTION

Cirrhosis is the end result of chronic liver injury which may result from a number of causes with autoimmune hepatitis and viral hepatitis to name a few leading to necroinflammation and fibrogenesis.¹ It is more frequently seen in men than women. Due to associated morbidity requiring repeated hospital admissions and management as well as loss of work days, the economic burden of cirrhosis is very high. It is also a frequent cause of early death in adults where it has been reported as the 10th leading cause of adult mortality in men and 12th in women in USA responsible for approx. 27,000 deaths annually.^{2,3}

Cirrhosis is associated with a wide array of local as well as systemic complications like ascites, spontaneous bacterial peritonitis, coagulopathy, vascular and hemodynamic alterations and portosystemic shunts leading to variceal bleed and poor quality of life.⁴ Due to changes in systemic as well as splanchnic circulation, as well as higher levels of lipopolysaccharide binding proteins, cirrhosis is also accompanied by deranged cardiac function where the heart is both hyperdynamic as well as dysfunctional.⁵ Collectively this contributes to the development of diastolic dysfunction or cirrhotic cardiomyopathy, the incidence of which varies from 49% to 63.7%.^{6,7} Timely identification and appropriate management of cardiac dysfunction in

cirrhotic patients is important as it not only improves the overall survival of the patient with cirrhosis but also improves the life expectancy of patients undergoing liver transplantation⁸⁻¹⁰.

The reported frequency of cirrhotic cardiomyopathy varied among already published studies. Moreover there were only few such studies in local population which compelled the current study. We aimed to correlate the cardiac dysfunction in cirrhotic patients with the severity of cirrhosis on Child Turcotte Pugh classification with a hope that it may help in the risk classification and management planning of such cases in future medical practice.

PATIENTS AND METHODS

This was a descriptive cross-sectional study which was carried out at the Department of Medicine Lahore General Hospital Lahore over a period of 1 year from Jan to Dec 2018. Sample size of 100 patients was estimated with 95.0% confidence level, 10.0% margin of error and taking anticipated percentage of cirrhotic cardiomyopathy i.e. 49% in patients with liver cirrhosis⁶. 100 cases of cirrhosis diagnosed in the preceding 6 months period were included in the study. Pregnant females, patients already diagnosed of cardiomyopathy or ischemic heart disease and those suffering from hypertension (BP ≥160/90 mmHg) and

diabetes (BSR ≥ 200 mg/dl) were excluded from the study. Severity of liver cirrhosis was classified according to Child Turcotte Pugh (CTP) classification. Each patient underwent ECG and echocardiography and cardiomyopathy was diagnosed upon presence of diastolic dysfunction (i.e. increased E/A ratio >1). Patients diagnosed with cardiomyopathy were managed according to hospital protocol. All this information was recorded in a pre-designed proforma (attached). Age, BMI and duration of cirrhosis have been described by mean \pm SD. Gender, obesity, CTP class and cirrhotic cardiomyopathy have been described by frequency as well as percentage. Data has been stratified for age, gender, obesity, duration of cirrhosis and Child Turcotte Pugh class to control effect modifiers. Following stratification, chi-square test has been used to compare frequency of cardiomyopathy across each strata taking $p \leq 0.05$ as statistically significant.

STUDY RESULTS

The age of the patients ranged from 35 years to 65 years with a mean of 51.9 ± 9.8 years. There were 61 (61.0%) male and 39 (39.0%) female patients with a male to female ratio of 1.6:1. Patient's BMI varied from 21.1 - 33.9 Kg/m² with a mean of 26.5 ± 3.7 Kg/m². The mean duration of disease was 22.0 ± 10.9 months (ranged from 8 months to 48 months). Majority ($n=49$, 49.0%) of the patients belonged to Child Turcotte Pugh (CTP) Class C followed by Class-B (39.0%) and Class-A (12.0%) as presented in Table 1.

Table 1: Demographic features of studied patients

Demographics	Participants n=100
Age (years)	51.9 ± 9.8
• 35-50 years	42 (42.0%)
• 51-65 years	58 (58.0%)
Gender	
• Male	61 (61.0%)
• Female	39 (39.0%)
BMI (Kg/m ²)	26.5 ± 3.7
• 20-25 Kg/m ²	45 (45.0%)
• 25-30 Kg/m ²	31 (31.0%)
• 30-35 Kg/m ²	24 (24.0%)
Duration of Disease (months)	22.0 ± 10.9
• ≤ 2 years	65 (65.0%)
• 2-4 years	35 (35.0%)
CTP Class	
• Class-A	12 (12.0%)
• Class-B	39 (39.0%)
• Class-C	49 (49.0%)

Table 2: Frequency of Cirrhotic Cardiomyopathy in Patients with Cirrhosis

Cirrhotic Cardiomyopathy	Frequency (n)	Percent (%)
Yes	41	41.0
No	59	59.0
Total	100	100.0

Cirrhotic cardiomyopathy was observed in 41 (41.0%) patients with cirrhosis as presented in Table 2. There was statistically insignificant difference in the frequency of cirrhotic cardiomyopathy among various subgroups of cirrhotic patients depending upon patient's age (p-

value=0.928), gender (p-value=0.997), BMI (p-value=0.983) and duration of disease (p-value=0.782). However, it increased considerably with worsening of disease on CTP Classification; Class-A vs. Class-B vs. Class-C (8.3% vs. 35.9% vs. 53.1%; p-value=0.013) as presented in Table 3.

Table 3: Stratification of Cirrhotic Cardiomyopathy across various Subgroups

Subgroups	n	CCM n (%)	P-value
Age			
• 35-50 years	42	17 (40.5%)	0.928
• 51-65 years	58	24 (41.4%)	
Gender			
• Male	61	25 (41.0%)	0.997
• Female	39	16 (41.0%)	
BMI (Kg/m ²)			
• 20-25 Kg/m ²	45	18 (40.0%)	0.983
• 25-30 Kg/m ²	31	13 (41.9%)	
• 30-35 Kg/m ²	24	10 (41.7%)	
Duration of Disease			
• ≤ 2 years	65	26 (40.0%)	0.782
• 2-4 years	35	15 (42.9%)	
CTP Class			
• Class-A	12	1 (8.3%)	0.013*
• Class-B	39	14 (35.9%)	
• Class-C	49	26 (53.1%)	

Chi-square test, * observed difference was statistically significant, CCM; Cirrhotic Cardiomyopathy

DISCUSSION

Chronic injury of the hepatic tissue leads to necroinflammation and fibrosis regardless of the etiology which may be alcoholic hepatitis, viral hepatitis or autoimmune hepatitis. Cirrhosis is the end stage of chronic liver damage and is associated with a wide range of systemic disturbances as liver is central organ in many vital physiological processes.^{1,2} Moreover, due to integrated bodily processes, derangement of one physiological process leads to another abnormality, cumulatively resulting in multiorgan dysfunction which is the hallmark of cirrhosis.^{3,4} Cirrhosis therefore adversely affects the patient's quality of life with high morbidity and mortality.⁵⁻⁷ Liver transplantation is the only definitive treatment option for such patients. Even after transplant, the remnants of cirrhotic systemic disturbances may continue to affect patient's quality of life.⁸ One such complication is cirrhotic cardiomyopathy^{6,7} which not only complicates the course of cirrhosis but also affects patient's quality of life after liver transplant.⁸⁻¹⁰ A number of studies have reported that a substantial proportion of cirrhotic patients suffer cirrhotic cardiomyopathy and advised routine screening for timely identification and optimal management of such cases^{6,7}. However, the reported frequency of cardiomyopathy varied among existing studies while there was only limited local such published material which necessitated the present study.

In the present study, the mean age of the patients was 51.9 ± 9.8 years. This finding is comparable to that of Hussain et al.¹¹ (2014) who conducted a similar study at Services Hospital Lahore and observed similar mean age of 51.12 ± 6.03 years among patients presenting with chronic liver disease. Ali et al.¹² (2008) in another similar

study at a tertiary care hospital of Mirpurkhas reported a comparable mean age of 52 ± 9 years among cirrhotic patients. In two other local studies, Achakzai et al.¹³ (2016) and Almani et al.¹⁴ (2008) also observed comparable mean age of 54 ± 11 years and 53.09 ± 8.86 years individually. Mansour-Ghanaei et al.¹⁵ (2012) reported a similar mean age of 55.03 ± 12.05 years in Iranian patients with liver cirrhosis while Penteado et al.¹⁶ observed it to be 51.4 ± 7.6 years in such patients in Brazil. A relatively lower mean age of 45.8 ± 10.45 years and 44 ± 13.7 years has been observed by Bhattacharyya et al.¹⁷ (2016) and Deepika et al.¹⁸ (2015) in Indian cirrhotic patients.

We observed that there were 61 (61.0%) male and 39 (39.0%) female patients with a male to female ratio of 1.6:1. Our observation matches with that of Ali et al.¹² who described comparable male predominance (m:f; 1.5:1) among cirrhotic patients at a tertiary care hospital of Mirpurkhas. However, a female predominance has been observed by Achakzai et al.¹³ who reported a male to female ratio of 1:1.5 in another local study. El-Feki et al.¹⁹ and Mansour-Ghanaei et al.¹⁵ also reported similar male predominance with male to female ratio of 1.5:1 and 1.9:1 among Egyptian and Iranian such patients respectively.

In the present study, majority (49.0%) of the patients belonged to CTP Class C followed by Class-B (39.0%) and Class-A (12.0%). Our observation is in line with that of Shaikh et al.²⁰ (2011) who observed comparable rate of CTP Class-A, Class-B and Class-C and reported it to be 12.2%, 39.2% and 48.6% respectively among such patients coming to medical outdoor of Liaquat Hospital Jamshoro. In another local study, Naqvi et al.²¹ (2016) reported similar frequency of 11.4%, 31.4% and 57.2% for the Class-A, Class-B and Class-C respectively. Kumar et al.²² (2017) also reported similar distribution of CTP Class-A (12.2%), Class-B (38.9%) and Class-C (48.9%) in Indian patients with liver cirrhosis undergoing evaluation for cardiomyopathy.

We observed that cirrhotic cardiomyopathy was present in 41.0% patients with cirrhosis. Shaikh et al.²⁰ (2011) in a similar study reported the frequency of cirrhotic cardiomyopathy to be 44.6% among patients presenting at Liaquat Hospital Jamshoro. A comparable frequency of 39.3% has been described by Naqvi et al.²¹ in another local study at Karachi. A comparable frequency of 44.6% has been described by Kumar et al.²² among Indian cirrhotic patients. Karagiannakis et al.²³ (2013) observed it to be 41.0% in Korea. Nisar et al.⁶ (2011) reported much higher frequency of 49.0% at Services Hospital, Lahore while Bhatti et al.²⁴ (2014) observed much lower frequency of 24.7% among such patients in Islamabad.

In the present study, we observed that the frequency of cirrhotic cardiomyopathy increased significantly with increasing CTP class. This observation coincides with that of Naqvi et al.²¹ (2016) who conducted a similar study in cirrhotic patients in local population and observed similar higher frequency of cardiomyopathy in patients with more severe disease; CTP Class A versus B versus C (17.8% vs. 24.7% vs. 57.5%; $p < 0.001$).

Thus cirrhotic cardiomyopathy is a frequent complication observed in cirrhosis occurring in approximately half of the patients and is related with the severity of disease. In the light of this evidence, it is

advocated that patients with cirrhosis should be routinely screened for cardiac dysfunction. As far other cirrhotic complications, CTP classification can also help in the risk stratification of patients for cardiomyopathy with patients having higher CTP class having higher risk of cardiomyopathy and more suitable for echocardiographic screening. This anticipated echocardiographic screening may enable timely recognition of patients with cirrhotic cardiac dysfunction. The subsequent timely management may in turn improve the outcome of such patients before and after liver transplantation.

A very important limitation to the present study was that we didn't consider the improvement of cardiac function in relation to optimization of liver function as suggested by our own findings where we observed increased frequency of CCM with higher CTP class. It could help in the appropriate management planning of such patients. Such a study is highly recommended in future research.

CONCLUSION

Cirrhotic cardiomyopathy was observed in a substantial proportion of cirrhotic patients and was more frequent in patients with more severe disease which warrants routine echocardiographic screening of cirrhotic patients so that timely recognition and anticipated treatment of this complication may improve the case outcome in future medical practice.

REFERENCES

1. Milic S, Lulic D, Stimac D, Ruzic A, Zaputovic L. Cardiac manifestations in alcoholic liver disease. *Postgrad Med J* 2016;92(1086):235-9. doi: 10.1136/postgradmedj-2015-133755.
2. Heron MP. Deaths: leading causes for 2015. *Natl Vital Stat Rep* 2017;66(5):1-76.
3. Smith A, Baumgartner K, Bositis C. Cirrhosis: diagnosis and management. *Am Fam Physician* 2019;100(12):759-70.
4. Wang X, Wu B. Critical issues in the diagnosis and treatment of liver cirrhosis. *Gastroenterol Rep (Oxf)* 2019;7(4):227-30. doi: 10.1093/gastro/goz024.
5. Berzigotti A. Advances and challenges in cirrhosis and portal hypertension. *BMC Med* 2017;15(1):200. doi: 10.1186/s12916-017-0966-6.
6. Nisar S, Qazi S, Ashraf Y. To assess the frequency of cirrhotic cardiomyopathy among patients with cirrhosis of liver. *Pak J Med Health Sci* 2013;7(3):851-4.
7. Rodina AS, Shubina ME, Dudanova OP. Diagnosis and clinical manifestations of cirrhotic cardiomyopathy. *EKSP Clin Gastroenterol* 2015;17(11):34-7.
8. Zardi EM, Zardi DM, Chin D, Sonnino C, Dobrina A, Abbate A. Cirrhotic cardiomyopathy in the pre- and post-liver transplantation phase. *J Cardiol* 2016;67(2):125-30. doi: 10.1016/j.jjcc.2015.04.016.
9. Sonny A, Ibrahim A, Schuster A, Jaber WA, Cywinski JB. Impact and persistence of cirrhotic cardiomyopathy after liver transplantation. *Clin Transplant* 2016;30(9):986-93. doi: 10.1111/ctr.12778.
10. Liu H, Jayakumar S, Traboulsi M, Lee SS. Cirrhotic cardiomyopathy: Implications for liver transplantation. *Liver Transpl* 2017;23(6):826-35. doi: 10.1002/lt.24768.
11. Hussain A, Nadeem MA, Nisar S, Tauseef HA. Frequency of gallstones in patients with liver cirrhosis. *J Ayub Med Coll Abbott* 2014;26(3):341-3.
12. Ali M, Abbas SZ, Sultana F, Akhtar W, Shaw S, Abbas SQ. Non-B, Non-C Hepatitis as a cause of Advanced Chronic

- Liver Disease requiring medical admission at a rural centre in Pakistan. *Pak J Med Sci* 2008;24(2):278-82.
13. Achakazi MS, Shaikh H, Mobin A, Majid S, Javed A, Khalid AB, et al. Factors leading to hepatic encephalopathy in patients with liver cirrhosis at a tertiary care hospital in Karachi, Pakistan. *Gomal J Med Sci* 2016;14(2):71-4.
14. Almani SA, Memon AS, Memon AI, Shah I, Rahpoto Q, Solangi R. Cirrhosis of liver: Etiological factors, complications and prognosis. *J Liaquat Uni Med Health Sci* 2008;7(2):61-6.
15. Mansour-Ghanaei F, Mehrdad M, Mortazavi S, Joukar F, Khak M, Atrkar-Roushan Z. Decreased serum total T3 level in hepatitis B and C related cirrhosis by severity of liver damage. *Ann Hepatol* 2012;11(5):667-71.
16. Penteado KR, Coelho JC, Parolin MB, Matias JE, Freitas AC. The influence of end-stage liver disease and liver transplantation on thyroid hormones. *Arq Gastroenterol* 2015;52(2):124-8. doi: 10.1590/S0004-28032015000200009.
17. Bhattacharyya M, Barman NN, Goswami B. Clinical profile of cirrhosis of liver in a tertiary care hospital of Assam, North East India. *IOSR J Dent Med Sci* 2016;5(1):21-7. doi: 10.9790/0853-151102127.
18. Deepika G, Veeraiah N, Rao PN, Reddy DN. Prevalence of hypothyroidism in liver cirrhosis among Indian patients. *Int J Pharm Med Res* 2015;3(3):4-7.
19. El-Feki MAF, Abdalla NH, Atta MI, Ibrahim AA. Serum level of thyroid hormones in patients with chronic hepatitis c virus infection. *Open J Endocr Metab Dis* 2016;6:126-34. doi: 10.4236/ojemd.2016.63017.
20. Shaikh S, Abro M, Qazi I, Yousfani A. Frequency of cirrhotic cardiomyopathy in patients with cirrhosis of liver: a tertiary care hospital experience. *Pak J Med Sci* 2011;27(4):744-8.
21. Naqvi IH, Mahmood K, Naeem M, Vashwani AS, Ziaullah S. The heart matters when the liver shatters! Cirrhotic cardiomyopathy: frequency, comparison, and correlation with severity of disease. *Prz Gastroenterol* 2016;11(4):247-56. doi: 10.5114/pg.2016.57962
22. Kumar SS, Rajasigamani A, Socrates D. Prevalence of cirrhotic cardiomyopathy in patients with cirrhosis of liver: a tertiary hospital experience. *Int J Pharm Bio Sci* 2017;8(1):298-303. doi: 10.22376/ijpbs.2017.8.1.b298-B303.
23. Karagiannakis DS, Vlachogiannakos J, Anastasiadis G, Vafiadis-Zouboulis I, Ladas SD. Frequency and severity of cirrhotic cardiomyopathy and its possible relationship with bacterial endotoxemia. *Dig Dis Sci* 2013;58(10):3029-36. doi: 10.1007/s10620-013-2693-y.
24. Bhatti B, Ali F, Akbar SS. Prolonged QTc interval is an electrophysiological hallmark of cirrhotic cardiomyopathy. *Open J Intern Med* 2014;4:33-9. doi: 10.4236/ojim.2014.41006.