PREVALENCE OF CARDIOMYOPATHY IN PATIENTS WITH LIVER CIRRHOSIS, CROSS-SECTIONAL STUDY.

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ABSTRACT

Introduction: Dysfunction of the liver gives rise to many complications, one of which is "cirrhotic cardiomyopathy". Its prevalence in the United States population is >40%. In Pakistan, the prevalence is not well documented however; some studies estimated it to be 20-45%. The results of this study will provide baseline data on the burden of cardiomyopathy in cirrhotic patients which will help in the early management of cardiomyopathy among patients of cirrhosis. **Methods:** This descriptive study was conducted at the medical intensive care unit of Jinnah Postgraduate Medical Centre Karachi, Pakistan from 16-1-2018 to 15-1-2019 taking a sample of 95 patients of either sex, 25-60 years of age, diagnosed cirrhotic for >5 years and with Child-Pugh classification C. Patients with prior history of heart diseases and drug intake (such as calcium channel blockers, antiarrhythmics, and digoxin) were excluded. **Results:** 83 were males (87.36%) with a male-female ratio of 6.9:1. The mean age was 47±9.1 years. E/A ratio <1 was present in 80 (84.20%) cases, QT interval >0.44 seconds present in 87 (91.60%) cases and ejection fraction >55% in 83 (87.40%) cases. Cirrhotic cardiomyopathy was detected in 72 (75.78%) cases. Age and gender were non-significant (p= 0.218 & 0.321 respectively) while Child-Pugh class, E/A ratio, QT interval, and ejection fraction were significant effect modifiers on the frequency of cardiomyopathy among cirrhotic patients (p<0.0001). **Conclusion:** Pakistani 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.

Keywords: Cirrhosis, Cardiomyopathy, Child-Pugh class, QT interval, Ejection fraction.

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INTRODUCTION

Dysfunction of the master gland of the human body- the liver due to its fibrosis (Cirrhosis), gives rise to many complications of other major and important organs. One of these complications is "cirrhotic cardiomyopathy"[1].This term refers to the group of clinical features depicting abnormal heart structure and function in patients with cirrhosis. The combined liver dysfunction and portosystemicshunting lead to cardiac abnormalities likeincreased cardiac output, decreased systemic vascular resistance & arterial pressure, electrophysiological changes, macroscopic, and microscopic structural changes. Simultaneously; despite the increased basal cardiac output, cardiac response to physiologic or pharmacologic stimuli remain below normal giving the term cirrhotic cardiomyopathy (CC)[2].

After 1953, Kowalski and Abelmann first described the condition in patients presenting with clinical manifestations of hyperdynamic circulations include warm skin, spider angioma, palmar erythema, and bounding pulse[3]. With the advancing cirrhotic disease, tachycardia, high ejection fraction, and increased cardiac output develop as manifestations of hyperdynamic circulation. This systolic dysfunction becomes evident when there is physical or pharmacological stress on the circulation like bacterial infection such as spontaneous bacterial peritonitis[4,5]. This inability to mount a sufficient cardiac output further worsens when the patient develops hepatorenal syndrome as its result. The negative inotropic cytokines such as TNF-α and interleukin-1β produced by infection also contribute to their negative role in the presence of HRS[6].

A recent study from the United States population revealed that the prevalence of CC is >40%. In

Pakistan, the prevalence of CC is not well documented however, some studies estimated it to be between 20-45%[7,8].Addressing the lack of evidence in our population, the current study was conducted to measure the magnitude of the burden of cardiomyopathy in patients presenting with liver cirrhosis. The results of this study will provide baseline data that will be helpful in the future for other healthcare professionals as well as these will help in the early management of cardiomyopathy among patients of cirrhosis.

MATERIALS AND METHODS

This descriptive cross-sectional study was conducted at the medical intensive care unit-4 of Jinnah Postgraduate Medical Centre (JPMC), Karachi, Pakistan for six months from 16-1-2018 to 15-1-2019. The sample size calculation was based on the single proportion of cirrhotic cardiomyopathy @ 44% with a 95% confidence interval and a 10% margin of error, which came out to be 95. The sample was enrolled through a non-probability consecutive sampling of patients of age25-60 years, either gender,andthose diagnosed withlivercirrhosis and a Child-Pugh class C.Patient with prior history of myocardial infarction, valvular heart disease, conduction abnormalities, cardiac failure, hypertension, electrolyte imbalance, and history of drug intakes such as calcium channel blockers, antiarrhythmic, and digoxin were excluded. Ethical approval was granted by the ethical review committee of JPMC while valid written consent was taken from all enrolled patients.

Data was collected by the primary investigator on bio data, age, gender, weight, and the grade of cirrhosis. Relevant investigations like liver functions test, prothrombin time, electrocardiogram, echocardiogram (E/A ratio, ejection fraction, and cardiomyopathy status), protein profile, and ultrasound abdomen were done from the respective JPMC departments. A proforma was filled accordingly by the primary investigator. Outcome variable i.e. cirrhotic cardiomyopathy was noted on the radiological investigation.

Data analysis was conducted using IBM Statistical Package for the Social Sciences (SPSS) Statistics for Windows, version 21.0. (IBM Corp., Armonk, NY, US). Frequency and percentages were computed for qualitative variables. Mean and the standard deviation were calculated for quantitative variables. Effect modification was controlled by stratification and the Chi-square test was applied to see the effect of these on the outcome variable. P-value $\leq$0.05 was taken as significant.

RESULTS

There was a wide variety of age ranging from a minimum of 25 years to 60 years as shown in Table 1. The mean age was 47±9.1 years. Out of 95 patients included in this study, 83 (87.36%) were male and 12 (12.63%) patients were female with a male-female ratio of 6.9:1.

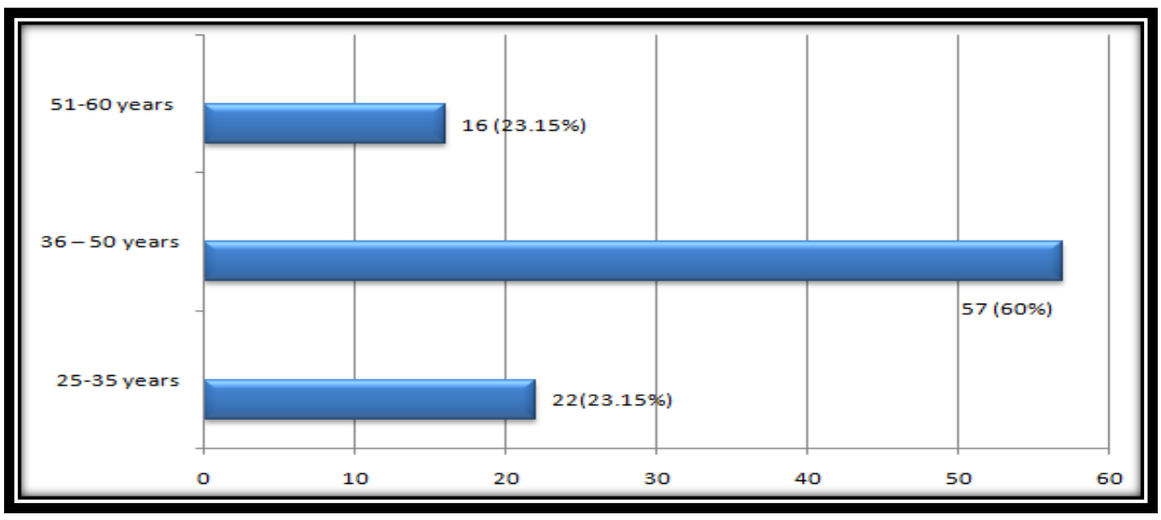

Figure 1: Age distribution

When cardiovascular parameters were assessed, the E/A ratio <1 was present in 80 (84.20%) cases, QT interval >0.44seconds was detected in 87 (91.60%) cases, and ejection fraction of >0.55 was found in 87.40% (n=83) cases. In the current study, cirrhotic cardiomyopathy was detected among 72 (75.78%) cases while 23 (24.21%) cases of cirrhosis were free from it.

	Frequency	Percentage (%)
E/A ratio		
<1	80	84.20
>1	15	15.80
QT interval		
>0.44 sec	87	91.6
<0.44 sec	8	8.42
Ejection fraction		
>0.55	83	87.40
<0.55	12	12.60
Cardiomyopathy		
Yes	72	75.78
No	23	24.21

Table 1: Cardiovascular parameters

The stratified analysis revealed that increasing age and male gender were associated with increased frequency of cardiomyopathy but these were statistically non-significant. However, Child-Pugh class C, lower E/A ratio (<1), increased QT Interval (>0.44 sec), and raised ejection fraction (>0.55) were statistically very significantly associated with cardiomyopathy among cirrhotic patients (p< 0.0001).

	Cirrhotic cardiomyopathy		Total	P-Value
	Yes (n=72)	No (n=23)		
Age				
25-35 Years	16 (66.7%)	8 (33.3%)	24	0.218
36- 50 Years	39 (75.0%)	13 (25.0%)	52	
51- 60 Years	17 (89.5%)	2 (10.5%)	120	
Gender				
Male	64 (77.1%)	19 (22.9%)	83	0.321
Female	8 (66.7%)	4 (33.3%)	12	
E/A Ratio				
<1	72 (90.0%)	8 (10.0%)	80	0.0001
>1	0	15 (100.0%)	15	
Child-Pugh Class				
B	19 (52.8%)	17 (47.2%)	36	0.0001
C	53 (89.8%)	6 (10.2%)	59	
QT interval				
<0.44 seconds	72 (82.8%)	15 (17.2%)	87	0.0001
>0.44 seconds	0	8 (100.0%)	8	
Ejection Fraction				
>0.55	72 (86.7%)	11 (13.3%)	83	0.0001
<0.55	0	12 (100.0%)	12	

Table 2: Effect of age, gender, and cardiovascular parameters on the frequency of cardiomyopathy among cirrhotic patients

DISCUSSION

Patients living with chronic liver disease or cirrhosis are prone to and affected with multisystem disorders which in turn increases their morbidity. Cardiomyopathy is one of the most significant yet least investigated complications of cirrhosis in our part of the world. The resulting chronic cardiac dysfunction along with electrophysiological abnormalities leads to compromised yet hidden contractile responsiveness to the increased demand for blood circulation[9]. Only when there is physical or pharmacological stress or increased demand for cardiac output for example in bacterial infection such as spontaneous bacterial peritonitis, the condition of cirrhotic cardiomyopathy is unveiled[10]. The development of hepatorenal syndrome further worsens it[4,11].

The current study found that cirrhotic cardiomyopathy was present in 72(75.78%) cases. This is much lower than what was earlier reported by other studies like that by Samiullah Shaikh and coworkers who reported 44.6% prevalence of cirrhotic cardiomyopathy[12]. The important difference, however, in the current study was that the male gender was dominant (87.36%) while Samiullah Shaikh and coworkers noted no significant gender difference. Mimicking to our results, male preponderance (>90%) was found in a study by Saha M[13]. There was a wide variety of age ranging from a minimum of 25 years to 60 years. We noted that the mean age of patients was 47±9.1 years while other studies reported a wider range age varying from 14 years to 75 years (mean: 39.68 years)[13].

Statistical analysis revealed a strong relation of severity of cirrhosis with the parameters of cardiomyopathy i.e. QT>0.44 seconds ($p<0.004$), ejection fraction > 55% ($p<0.004$) and E/A ratio <1 ($p<0.005$)[10].Studieshave found that on one hand there is a prolongation of deceleration time and higher mean E/A ratio (reflecting disturbance in ventricular function) while on the other hand the E/A ratio becomes paradoxically normal despite diastolic dysfunction (reflecting pseudonormalization)[14]. In our study, out of 95 patient's E/A ratio of<1 was found in 33.68%of cases while >1 in 66.31%. Some of the studies found a reduced E/A ratio in the cirrhotics having ascites compared to those without ascites. Similarly, they also found a decreased ratio in cirrhotics with non-viral etiologies compared to those with viral [15,16]. These studies also commented on uncertainty regarding the phenomenon of pseudonormalization of E/A ratio and its role in reflecting the diastolic dysfunction.

There is much variation in finding studies on prolongation of repolarization i.e. QT interval. Some found that nearly 60% of cirrhotic patients had QT interval >0.44 seconds while others reported a much lower rate of 5% has prolonged QT interval[17–19].But overall, it was a general notion that cirrhotic subjects report QT interval abnormalities to a much larger extent, and these patients compared to the normal controls are indeed much more prone to develop polymorphic ventricular tachyarrhythmias[20].

Regarding left ventricular functions, it is well documented that cirrhotic patients tend to have raised ejection fraction, although, some studies do not agree with this and found that ejection fraction is slightly but significantly reduced[21,22]. The current study like these studies noted that a vast majority of patients i.e. 71.57% had <55% ejection fraction leaving only 28.42% in whom ejection fraction was >55%. However, this finding did not include the pre-ascites patients and was only limited confound to patients with ascites. On the other hand, studies report that cirrhosis of viral etiology had higher ejection fraction than the normal individuals and alcoholic cirrhosis (in whom subclinical alcoholic cardiomyopathy may be a cause)[23]. We document here that none of our study participants had a history of alcoholism while the single centered, small sample size and uniform diagnostic criteria may be considered as factors responsible for the noted variability of ejection fraction.

CONCLUSIONS

This study demonstrates that Pakistani 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. Echocardiography plays a significant role in detecting early cardiac changes in cirrhosis however these changes do not seem to be a predictor of increased mortality in patients of cirrhosis.

DECLARATIONS

The authors declare that there are no conflicts of interest to disclose

REFERENCES

1. Voiosu AM, Daha IC, Voiosu TA, Mateescu BR, Dan GA, Baicus CR, et al. Prevalence and impact on survival of hepatopulmonary syndrome and cirrhotic cardiomyopathy in a cohort of cirrhotic patients. Liver Int. 2015;35(12):2547–55.
2. Wiese S, Hove JD, Bendtsen F, Moller S. Cirrhotic cardiomyopathy: pathogenesis and clinical relevance. Nat Rev Gastroenterol Hepatol. 2014;11(3):177–86.
3. Pudil R, Praus R, Hulek P, Safka V, Fejfar T, Vasatova M, et al. Transjugular intrahepatic portosystemic shunt is associated with significant changes in mitral inflow parameters. Ann Hepatol. 2013;12(3):464–70.
4. Ruiz-del-Árbol L, Serradilla R. Cirrhotic cardiomyopathy. World J Gastroenterol. 2015;21(41):11502–21.
5. Somani PO, Contractor Q, Chaurasia AS, Rathi PM. Diastolic dysfunction characterizes cirrhotic cardiomyopathy. Indian Heart J. 2014;66(6):649–55.
6. 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.
7. Kumar A, Riaz S, Rajesh, Kazmi S, Kumar R, Ghauri M. Prolongation of QT interval in ECG: a hidden complication in cirrhotic liver disease. Ann ASH KM&DC. 2019;24(1):20.
8. Ali M, Shahzad A, Khan I, Alam S, Noor H, Imran A, et al. Frequency of corrected qt interval in patients with cirrhosis. J Rawalpindi Med Coll. 2016;20(2):79–91.
9. Fede G, Privitera G, Tomaselli T, Spadaro L, Purrello F. Cardiovascular dysfunction in patients with liver cirrhosis. Vol. 28, Annals of gastroenterology. Greece; 2015. p. 31–40.
10. Karagiannakis DS, Papatheodoridis G, Vlachogiannakos J. Recent advances in cirrhotic cardiomyopathy. Dig Dis Sci. 2015;60(5):1141–51.
11. Chayanupatkul M, Liangpunsakul S. Cirrhotic cardiomyopathy: review of pathophysiology and treatment. Hepatol Int. 2014;8(3):308–15.
12. 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 July - Sept 2011 Vol 27 No 4 744-748. 2011;27.
13. Saha M, Saha S, Asaduzzaman K, Banik R. Cirrhotic cardiomyopathy in Bangladeshi patients: a pilot study. Euroasian J Hepato-Gastroenterol. 2013;3(1):42–5.
14. Sampaio F, Lamata P, Bettencourt N, Alt SC, Ferreira N, Kowallick JT, et al. Assessment of cardiovascular physiology using dobutamine stress cardiovascular magnetic resonance reveals impaired contractile reserve in patients with cirrhotic cardiomyopathy. J Cardiovasc Magn Reson. 2015;17(1):61.
15. Rahman S, Mallett S V. Cirrhotic cardiomyopathy: Implications for the perioperative management of liver transplant patients. World J Hepatol. 2015;7(3):507–20.
16. Gassanov N, Caglayan E, Semmo N, Massenkeil G, Er F. Cirrhotic cardiomyopathy: a cardiologist's perspective. World J Gastroenterol. 2014;20(42):15492–8.
17. Zuberi BF, Ahmed S, Faisal N, Afsar S, Memon AR, Baloch I, et al. Comparison of heart rate and QTc duration in patients of cirrhosis of liver with non-cirrhotic controls. J Coll Physicians Surg Pak. 2007;17(2):69—71.

18. Hammami R, Boudabbous M, Jdidi J, Trabelsi F, Mroua F, Kallel R, et al. Cirrhotic cardiomyopathy: is there any correlation between the stage of cardiac impairment and the severity of liver disease? Libyan J Med. 2017;12(1):1283162.
19. Genovesi S, Prata Pizzala DM, Pozzi M, Ratti L, Milanese M, Pieruzzi F, et al. QT interval prolongation and decreased heart rate variability in cirrhotic patients: relevance of hepatic venous pressure gradient and serum calcium. Clin Sci (Lond). 2009;116(12):851–9.
20. Lee Y Bin, Lee J-H. Cirrhotic cardiomyopathy: An independent prognostic factor for cirrhotic patients. Vol. 24, Clinical and molecular hepatology. 2018. p. 372–3.
21. Sampaio F, Pimenta J. Left ventricular function assessment in cirrhosis: Current methods and future directions. World J Gastroenterol. 2016;22(1):112–25.
22. Senni M, Paulus WJ, Gavazzi A, Fraser AG, Diez J, Solomon SD, et al. New strategies for heart failure with preserved ejection fraction: the importance of targeted therapies for heart failure phenotypes. Eur Heart J. 2014;35(40):2797–815.
23. Maisch B. Alcoholic cardiomyopathy : The result of dosage and individual predisposition. Herz. 2016;41(6):484–93.