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Cirrhotic cardiomyopathy: Correlation with hepatic decompensation severity and hepatorenal syndrome

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Abstract

Background and study aim: *Cirrhotic cardiomyopathy is a cardiac dysfunction that can occur in patients with cirrhosis, independent of other heart conditions. It is linked to the severity of liver disease, portosystemic shunt, and portal hypertension in cirrhosis. Hepatorenal syndrome is directly linked to inadequate cardiac output and circulatory dysfunction. Evaluating subclinical cardiac involvement is crucial for optimizing treatment follow-up. Our study aimed to explore the connection between cirrhotic cardiomyopathy, the severity of liver disease, and complications particularly hepatorenal syndrome.* ***Patient and methods:*** *Sixty cirrhotic patients, matched for sex and age, were selected for the study and divided into three groups. The first group consisted of twenty patients with Child score A, the second group included twenty patients with Child scores B and C, and the third group comprised 20 decompensated cirrhotic patients complicated with HRS. All patients underwent cardiac function assessment through ECG and Doppler study. Cirrhotic cardiomyopathy was diagnosed based on the 2019 criteria, which included systolic dysfunction (left ventricle ejection fraction < 50%) and diastolic dysfunction (meeting at least three of the following criteria: 1. Septal e' velocity < 7 cm/s, 2. E/e' ratio ≥ 15, 3. Tricuspid regurgitation velocity > 2.8 m/second, 4. left atrium volume index (LAVI) > 34 mL/m2).* ***Results and conclusions:*** *The study showed that 14 out of 60 patients (23.33%) exhibited diastolic dysfunction: none in group I, five in group II, and nine in group III. Patients with cirrhotic cardiomyopathy had higher Child scores (p<0.001), serum creatinine levels, and presence of HRS (p=0.009 for both) compared to those without cirrhotic cardiomyopathy. A strong positive correlation between Child score and corrected QT interval (p<0.001, r=0.838) was observed.* ***Conclusion:*** *Cirrhotic cardiomyopathy is prevalent in a significant number of cirrhotic patients and is linked to the severity of liver disease as indicated by the Child-Pugh score and the occurrence of complications particularly hepatorenal syndrome.*

Introduction

Liver diseases cause about 2 million deaths worldwide each year, with liver cirrhosis complications accounting for about half of these deaths[1]. Liver cirrhosis can be asymptomatic in cases of compensated cirrhosis, but complications such as hepatic encephalopathy, gastroesophageal variceal bleeding, ascites, and progression to advanced liver cell failure or death can occur in decompensated cirrhosis[2]. Hepatorenal syndrome (HRS) is a well-known complication of decompensated liver disease characterized by marked kidney dysfunction. It is induced by elevated splanchnic blood flow, vasoconstriction factors activation, and marked renal arteries vasoconstriction without kidney histologic abnormalities[3]. Decompensated cirrhosis with portal hypertension is a major risk factor for HRS-1, a type of acute kidney injury (AKI)[4]. Approximately 20% of patients with significant cirrhosis develop HRS within a year of diagnosis, and 40% develop it within five years. The prognosis for HRS-AKI is the poorest among all types of AKI [5]. The definition of Hepatorenal Syndrome (HRS) has evolved over the past few decades. The International Club of Ascites (ICA) updated the diagnostic criteria for HRS type 1 (HRS-AKI). AKI is characterized by a sudden increase in serum creatinine of at least 0.3 mg/dL within 48 hours or a 50% increase within the past seven days, excluding factors like nephrotoxic drugs, shock, hypovolemia, and kidney injury[6]. Functional kidney injury that does not meet the criteria for HRS-AKI is referred to as HRS-NAKI (non-AKI). An estimated glomerular filtration rate (eGFR) less than 60 mL/min/1.73 m2 for fewer than 3 months is considered HRS-acute kidney disease (HRSAKD), a kind of NAKI, while HRS chronic kidney disease (HRS-CKD) defines when the eGFR stays below 60 mL/min/1.73 m2 for 3 months or more[7]. Cirrhotic cardiomyopathy (CCM) is characterized by abnormalities in heart structure and function. It is believed to be caused by liver dysfunction, the shunting of vasodilators, and cardio-suppressive substances[8]. Cirrhotic cardiomyopathy carries the risk of many complications including HRS, sepsis, refractory ascites, bleeding tendency and poor quality of life which results in increase morbidity and mortality[9]. HRS represents the most severe manifestation of circulatory dysfunction in cirrhosis, with high short-term mortality which makes it crucial to study its relation to CCM[10]. CCM is characterized by a hyperdynamic state, prolonged ventricular depolarization, an inadequate response to stress, and dysfunction in both diastolic and systolic ventricular function[11]. The Cirrhotic Cardiomyopathy Consortium revised its definition of CCM, highlighting the importance of diastolic dysfunction. New guidelines were published in 2019. The proposed criteria now include the assessment of systolic dysfunction (left ventricular ejection fraction < 50%) and several signs of diastolic dysfunction (low septal e' velocity, high E/e' ratio, high left atrial indexed volume, and high tricuspid regurgitation velocity). Additional support for the diagnosis can be provided by

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ECG changes, MRI findings, and biomarker levels[12]. Estimating the prevalence of CCM can be tricky since individuals with nearly normal cardiac function—apart from during stressful situations—are asymptomatic. Research has shown that the pathophysiology of decompensated cirrhosis and hepatorenal syndrome could be linked to the presence of CCM[13]. This study aimed to evaluate the prevalence of cirrhotic cardiomyopathy in patients with liver cirrhosis and its association with hepatic decompensation and the hepatorenal syndrome.

Patients and methods

This cross-sectional study was conducted on 60 cirrhotic patients admitted to the Tropical Medicine and Infectious Diseases department and Internal Medicine department at Tanta University Hospitals from January 2023 to June 2023. The study included adult patients (>18 years) diagnosed with viral induced liver cirrhosis. Hepatorenal syndrome was diagnosed based on The International Club of Ascites criteria. The patients were divided into three groups[6]. ***)** Group I: Involved 20 patients with compensated cirrhosis classified as Child A. ***)** Group II: Involved 20 patients with decompensated cirrhosis classified as Child B or C. ***)** Group III: Involved 20 cirrhotic patients with hepatorenal syndrome. Exclusion criteria: Patients with alcoholic liver cirrhosis, thyroid disease, diabetes, hypertension, dyslipidemia, renal disease, coexisting cardiac conditions (such as ischemic heart disease, dilated cardiomyopathy, rheumatic heart disease, and congenital heart disease), or patients on medications that may affect the heart like beta blockers (discontinued at least seven days before evaluation) and antiviral medications were excluded. Additionally diabetes mellitus under treatment or newly diagnosed (fasting blood glucose >126 mg/dL, postprandial blood sugar >200 mg/dL, HbA1c >6.5%), systemic hypertension under treatment or newly diagnosed (3 consecutive blood pressure readings >140/90 mm Hg), and those with active sepsis requiring organ support (ventilator or inotropic support) were also excluded. All patients were subjected to thorough history taking, complete physical examination, laboratory investigations include (Complete blood picture, liver function tests, renal function tests, prothrombin time and INR, blood glucose, urine analysis, blood electrolytes (sodium and potassium). Abdominal ultrasound was done for all patients to assess liver and kidney conditions.

Sample size

Epi Info version X.X (CDC, Atlanta, GA) was used to calculate the sample size and a K-sample comparison of proportions test was used for detecting significant differences among the proportions. Depending on previously published data, the prevalence of cardiac cardiomyopathy in patients with compensated cirrhosis (Group I) accounts for 20%[14], while the prevalence was 45 % for patients with decompensated cirrhosis (Group II)[15], and it was 60% in patients with HRS (group III)[16,17]. The minum size for the study sample was 18 patients per group with the confidence level of 95% and a power of 80% .To overcome any data loss or patients exclusion , 20 patients were included in each study group with a total 0f 60 patients. *Transthoracic echocardiography (TTE)*: During a standard TTE examination, conventional Doppler echocardiography (vivid GE E9 machine) and tissue Doppler imaging (TDI) were conducted in the lateral decubitus position. Every patient also underwent M-mode and 2D measurements. The left ventricle's internal dimensions and wall thickness were evaluated by means of two-dimensional guided M-mode echocardiographic tracings that were taken in the parasternal long axis view at mid-chordal level. Using the Teichnolz formula, the ejection fraction (EF) and the fractional shortening (FS) percentage were determined[18]. The sample volume was positioned at the tips of the mitral valve leaflets, and pulse-wave Doppler was used to measure the mitral inflow velocities in the apical 4-chamber view. Peak early and late diastolic mitral input velocities were measured during normal breathing and the average across five cardiac cycles was computed. The early-to-late diastolic mitral inflow velocity ratio (E/A) was also measured. A diastolic function ratio of 0.75 to 1.5 is considered normal[19]. **a)** Tricuspid annular systolic plane excursion (TAPSE), as advised by the American Society of Echocardiography, was used to evaluate right ventricular systolic function. The RV apical four-chamber picture aligned an M-mode cursor parallel to the RV free wall where it meets the tricuspid annulus in order to assess the RV systolic function, that decreases when the TAPSE value is less than 16 mm[20]. **b)** The normal pulmonary artery systolic pressure (PASP) is less than 30 mmHg. The tricuspid regurgitation (TR) trace's continuous wave (CW) Doppler was used to measure the pressure differences in the right atrium and right ventricle. Peak TR velocity and the simplified Bernoulli equation (P = 4 [TR max] 2) were used to measure these pressure differences[21]. **c)** Tissue Doppler Imaging (TDI), which was carried out from the apical 4-chamber view with a 2.5-MHz transducer and frame rates of > 80/second, was used to determine the velocity of myocardial motion. Digitization of the images was completed. Commercially available computer software (Echopac, GE-Vingmed) was used to derive and analyze tissue Doppler velocity profiles. **d)** The myocardial velocity was measured by tissue Doppler imaging, a 6-mm sample volume was placed where the mitral annulus and septal myocardial wall meet, and profiles of the septal mitral annulus were obtained. An average of the early diastolic (E'), late diastolic (A'), and peak mitral septal systolic (S') velocities from two consecutive cardiac cycles was determined. While the peak early diastolic mitral inflow velocity was determined using pulse-wave Doppler, the ratio (E/E') of the peak early diastolic mitral annulus velocity was assessed using tissue Doppler imaging. When it comes to predicting normal global left ventricular systolic function, a value of >7.5 cm/s is seen to be both sensitive and specific. **e)** Systolic myocardial velocity (S') at the septal mitral annulus was utilized to evaluate longitudinal systolic function[22]. **f)** Left ventricular filling pressure is measured using (E/E ratio). An average E/E' > 15 was deemed specific for elevated LV filling pressure, and <8 indicated low/normal filling pressures[23].

Electrocardiography

A baseline 12-lead standard electrocardiogram (ECG), calibrated at 1 mV/cm = 10 mm, was performed on each patient while they were supine at a rate of 25 mm/s. Sinus beats were present in all the patients. Three consecutive beats were used for analysis, and each ECG could have at least ten leads.The Qt interval was determined using the QTC = QT/√ RR method, QT interval > 0.44 seconds (or >440 ms) in adult males is usually considered prolonged ;howerever

adult females have slightly higher threshold (>460 ms)[18]. The diagnosis of cirrhotic cardiomyopathy in our study was done according to the 2019 revised CCM criteria[12].

Ethical consideration

Approval was obtained from the Tanta Faculty of Medicine ethical committee (Code: 36264PR13/1/23). Informed consent was obtained from all patients after a full explanation of the benefits and risks. The privacy of all patients' data was ensured, and each patient's file was assigned a unique code number that included all investigations.

Statistical analyses of data

IBM SPSS Statistics, Version 20.0 (IBM Corp., Armonk, NY, USA) were used to analyze data. Categorical data were presented using numbers and percentage representations. The chi-square test was used to explore relationships between categorical variables. The Monte Carlo correlation test was conducted when the expected count was less than five in over 20% of the cells. The Shapiro-Wilk test was used to confirm the normality of continuous data. Descriptive statistics such as mean, standard deviation, median, and range (minimum and maximum) were used for quantitative data. The student t-test was used to compare two sets of normally distributed quantitative data. The Kruskal-Wallis test was employed for non-normally distributed quantitative variables, then Dunn's multiple comparisons test was used for post hoc pairwise comparisons. $p < 0.05$ is considered statistically significant.

Results

Table 1 shows high significant difference was observed in the presence of esophageal varices (p <0.001) and previous episodes of upper gastrointestinal bleeding (p= 0.029) among the three groups. Table 2 presents the laboratory and radiological data of the study groups. Hemoglobin and platelet counts were significantly higher in group 1 compared to groups 2 and 3, with no significant difference between groups 2 and 3. Albumin levels decreased significantly, while prothrombin time and bilirubin levels increased significantly from group 1 to group 3. Serum creatinine levels were significantly higher in group 3 compared to groups 1 and 2 with no significant difference between group 1 and 2. Aspartate transaminase (AST) levels were significantly higher in group 2 compared to group 1, with no significant differences between group 1 and group 3 or between group 2 and group 3. Alanine transaminase (ALT) levels were significantly higher in group 2 compared to groups 1 and 3, with no significant differences between groups 1 and 3. Ultrasonographic findings showed a significant increase in portal vein diameter and splenic size in group 2 and 3 compared to group 1, with no significant differences between groups 2 and 3. Ascites was present significantly in groups 2 and 3, while absent in group 1. Table 3 shows the comparsion of the cardiac condition in the three studied groups. As regarding the corrected QT interval (**QTc**) there was a significant increase from group 1 to group 3 measured by ECG (p<0.001). The echocardiographic evaluation of the studied groups showed a significant decrease in septal velocity (**S'**) from group 1 to group 3. Tricuspid annular systolic plane excrusion (TAPSE), systolic pulmonary artery pressure (SPAP), the ratio of peak early diastolic mitral inflow and peak early diastolic annular velocity (E/E'), and tricuspid regurgitation velocity (TR)) (p value <0.001), the ratio of early diastolic to late diastolic mitral inflow velocity (E/A) ratio also showed a statistically significant difference with p-value 0.017 . Table 4 shows the number and percent of patients with cirrhotic cardiomyopathy (CCM) within each studied group, it was found that in group I, none of the patients had CCM, in group II 5 (25%) patients had CCM, and in group III 9 (45%) had CCM, these findings show significant difference between the three groups (p-value 0.002). Table 5 demonstrates a strong positive correlation between the Child score of the patients and the corrected QT interval (p<0.001, r=0.838). Table 6 indicates that patients with CCM showed a significant increase in Child score (p< 0.001), serum creatinine, and the presence of HRS (p=0.009 for both) compared to patients without CCM. Table 5 also showed the relation between CCM with different parameters, we found that CCM was associated with lower albumin level, higher bilirubin. higher INR, lower hemoglobin level, higher serum creatinine, Child score, prescence of ascites. portal vein diameter, spleen diameter, history of upper gastrointestinal bleeding and the prescence of hepatorenal syndrome.

Table 1. Comparison between the three studied groups regarding different parameters

	Group I (n = 20)	Group II (n = 20)	Group III (n = 20)	p
Sex				
▪ ***Male***	14 (70.0%)	17 (85.0%)	15 (75.0%)	0.641
▪ ***Female***	6 (30.0%)	3 (15.0%)	5 (25.0%)	
Age (years)	51.55 ± 7.07	54.55 ± 7.57	52.65 ± 8.30	0.461
Varices				
▪ ***No varices***	8 (40.0%)	2 (10.0%)	8 (40.0%)	<0.001*
▪ ***Small and medium sized varices***	10 (50.0%)	3 (15.0%)	8 (40.0%)	
▪ ***Large varices***	2 (10.0%)	15 (75.0%)	4 (20.0%)	
History of bleeding				
▪ ***No***	16 (80%)	17 (85%)	10 (50%)	0.029*
▪ ***Yes***	4 (20%)	3 (15%)	10 (50%)	
Child score	5.60 ± 0.50	9.25 ± 1.48	13.65 ± 0.99	p1>0.001 p2>0.001 p3<0.001

p1: *p value for comparing between Group I and Group II,* ***p2:*** *p value for comparing between Group I and Group III,* ***p3:*** *p value for comparing between Group II and Group III.*

Table 2. Comparison between the three studied groups regarding laboratory and ultrasonographic findings

	Group I (n = 20)	Group II (n = 20)	Group III (n = 20)	p
Hemoglobin (mg/dl)	11.23 ± 2.13	9.33 ± 1.06	8.80 ± 0.98	p_1<0.001. p_2<0.001. p_3=0.494
Platelets (×103/mm^3)	127.9 ± 26.12	90.20 ± 25.33	98.80 ± 33.05	p1>0.001, p2=0.006, p3=0.606
Albumin (gm/dl)	3.57 ± 0.29	2.63 ± 0.38	2.22 ± 0.29	p1>0.001, p2>0.001, p3=0.001
INR	1.18 ± 0.13	1.73 ± 0.43	2.93 ± 0.60	p1>0.001, p2>0.001, p3>0.001
Bilirubin (gm/dl)	1.0 (0.95 –1.15)	2.55(1.90 –3.45)	4.05 (3.50 –5.05)	p1=0.001, p2>0.001, p3=0.002
Serum creatinine (gm/dl)	1.02 ± 0.10	0.98 ± 0.10	3.46 ± 0.55	p1=0.913, p2>0.001, p3>0.001
AST (U/L)	51.0 (46.0 –55.0)	63.5(53.50 –80.0)	55.0 (45.0 –60.0)	p_1=0.005, p_2=0.269, p_3=0.088
ALT (U/L)	34.0 (30.0 –45.50)	45.0 (38.0 –52.0)	28.0 (21.0 –45.0)	p_1=0.033, p_2=0.717, p_3=0.013
PV diameter (mm)	12.0 ± 1.69	14.85 ± 1.80	14.60 ± 2.39	p_1<0.001, p_2<0.001, p_3=0.919
Spleen diameter	14.97 ± 3.18	18.16 ± 3.22	19.05 ± 3.48	p_1=0.009, p_2=0.001, p_3=0.668
Ascites				
▪ ***Absent***	20 (100.0%)	1 (5.0%)	0 (0.0%)	<0.001
▪ ***Present***	0%	19% (95%)	20 (100.0%)	

p1: *p value for comparing between Group I and Group II,* ***p2:*** *p value for comparing between Group I and Group III,* ***p3:*** *p value for comparing between Group II and Group III,* ***ALT:*** *alanine aminotransferase,* ***AST:*** *aspartate aminotransferase,* ***PV:*** *portal vein,* ***INR:*** *international normalized ratio*

Table 3. Comparison between the three studied groups regarding cardiological evaluation

	Group I (n = 20)	Group II (n = 20)	Group III (n = 20)	p
QTc (ms)	325.6 ± 9.53	397.5 ± 30.3	418.15 ± 22.68	p_1<0.001*, p_2<0.001*, p_3<=0.014*
S' (cm/sec)	12.53 ± 0.49	8.29 ± 1.80	7.17 ± 0.90	p_1<0.001, p_2<0.001, p_3=0.012*
E.A	0.95 (0.82 –1.33)	0.70 (0.63 –0.87)	0.60 (0.53 –1.15)	p_1=0.055, p_2=0.005*, p_3=0.377
TAPSE (cm)	2.55 (2.10 –3.0)	1.99 (1.90 –2.10)	1.50 (1.40 –1.60)	p_1=0.004*, p_2<0.001*, p_3<0.001*
SPAP (mmHg)	26.0 (24.0 –27.0)	37.50 (33.0 –42.50)	47.50(37.50 – 55.0)	p_1=0.001*, p_2<0.001*, p_3=0.042*
E/E'	7.18 ± 1.08	14.49 ± 1.78	16.03 ± 1.84	p_1<0.001*, p_2<0.001*, p_3=0.010*
TR	2.55 (2.45 – 2.60)	3.06(2.87 – 3.26)	3.44(3.06 – 3.71)	p_1=0.001*, p_2<0.001*, p_3=0.042*

p1: *p value for comparing between Group I and Group II,* ***p2:*** *p value for comparing between Group I and Group III,* ***p3:*** *p value for comparing between Group II and Group III,* ***QTc:*** *corrected QT interval,* ***E:*** *early diastolic transmitral filling,* ***E':*** *early diastolic mitral annular velocity,* ***A':*** *late diastolic velocity,* ***S':*** *peak mitral septal systolic velocity,* ***TAPSE:*** *Tricuspid annular systolic plane excursion (TAPSE):* ***TR:*** *tricuspid regurgitation,* ***SPAP:*** *systolic pulmonary artery pressure,* ***EF:*** *ejection fraction*

Table 4. Comparison between the three studied groups regarding CCM percentage among patients

	Group I (n = 20)	Group II (n = 20)	Group III (n = 20)	p
CCM				
No	20 (100.0%)	15 (75.0%)	11 (55.0%)	$^{FE}p_1$=0.047*, $^{FE}p_2$=0.001*, p_3=0.185
Yes	0 (0.0%)	5 (25.0%)	9 (45.0%)	

p1: *p value for comparing between Group I and Group II,****p2:*** *p value for comparing between Group I and Group III,****p3:*** *p value for comparing between Group II and Group III,* ***CCM :****cirrhotic cardiomyopathy*

Table 5. Correlation between Child score and QTc (ms) in the study patients.

	Child score vs QTc (ms)	
	r	***p***
Total Sample (n= 60)	0.838	<0.001*

r: *Pearson coefficient*

Table 6. Relation between CCM with different parameters in total sample (n= 60)

	CCM		p
	No (n= 46)	**Yes (n= 14)**	
Sex			
▪ ***Male***	35(76.1%)	11(78.6%)	1.000
▪ ***Female***	11(23.9%)	3(21.4%)	
Age (years)	52.46 ± 7.90	54.43 ± 6.74	0.402
Varices			
▪ ***No varices***	15(32.6%)	3(21.4%)	0.689
▪ ***Small varices***	16(34.8%)	5(35.7%)	
▪ ***Large varices***	15(32.6%)	6(42.9%)	
Child score	8.57 ± 3.26	12.57 ± 2.21	<0.001*
Ascites			

▪ *Absent*	21(45.7%)	0(0.0%)	
▪ *Present*	25(54.3%)	14(100.0%)	0.001*
Hemoglobin (mg/dl)	10.12 ± 1.85	8.66 ± 1.02	0.001*
RBCs (×103/mm^3)	3.74 ± 0.76	3.39 ± 0.59	0.118
Platelets (×103/mm^3)	110.39 ± 31.55	90.0 ± 30.72	0.037*
Albumin (gm/dl)	2.97 ± 0.64	2.28 ± 0.34	<0.001*
Bilirubin (mg/dl)	1.70(1.0 – 3.40)	3.95(3.0 – 4.10)	0.003*
sr creat (mg/dl)	1.60 ± 1.10	2.55 ± 1.30	0.009*
INR	1.75 ± 0.80	2.56 ± 0.73	0.001*
AST (U/L)	54.50(48.0 – 64.0)	53.0(45.0 – 64.0)	0.841
ALT (U/L)	38.50(30.0 – 47.0)	32.0(22.0 – 50.0)	0.517
Pv diameter (mm)	13.47 ± 2.34	14.96 ± 2.04	0.036*
Spleen diameter (cm)	16.65 ± 3.63	19.84 ± 2.81	0.004*
History of bleeding			
▪ *1*	33(71.7%)	10(71.4%)	1.000
▪ *2*	13(28.3%)	4(28.6%)	
HRS			
▪ *No*	35(76.1%)	5(35.7%)	0.009*
▪ *Yes*	11(23.9%)	9(64.3%)	

ALT: *alanine aminotransferase,* ***AST:*** *aspartate aminotransferase,* ***pv:*** *portal vein,* ***INR:*** *international normalized ratio,* ***QTc:*** *corrected QT interval, E: early diastolic transmitral filling, E': early diastolic mitral annular velocity. A': late diastolic velocity* ***S':*** *peak mitral septal systolic velocity,* ***TAPSE:*** *Tricuspid annular systolic plane excursion (TAPSE),* ***TR:*** *tricuspid regurgitation,* ***SPAP:*** *systolic pulmonary artery pressure,* ***EF:*** *ejection fraction*

Discussion

Patients with cirrhosis may develop cirrhotic cardiomyopathy (CCM), a kind of heart malfunction marked by an abnormal heart structure, a hyperdynamic circulatory state, and a compromised cardiac response to stress. Because of its stress-induced nature and absence of a standard therapy, it is frequently under estimated[25,26]. Diastolic dysfunction is a common feature of CCM and can be detected using basic echocardiographic measurements like low septal e' velocity, high E/e' ratio, high indexed volume of left atrium, and high tricuspid regurgitation velocity[3,27]. The severity of cirrhosis, including associated portal hypertension and portosystemic shunting, has been linked to the development of cardiac dysfunction in cirrhotic patients. Early detection of subclinical cardiac involvement, such as diastolic dysfunction or prolonged QTc interval, may faciliatate more effective management and improve clinical outcomes[28]. Our objective was to investigate the prevalence of CCM and to examine its association with the severity of liver cirrhosis and its complication HRS. CCM was identified using the 2019 criteria. Among the 60 cirrhotic patients, 14 patients (23.33%) exhibited diastolic dysfunction. None of the patients were classified in group 1, five were in group 2, and nine were in group 3. The prevalence of CCM in the study was consistent with findings from previous studies. For example, Cesari M et al. reported that 29% of cirrhotic patients included in their study had CCM, according to 2019 criteria[27]. While Mansour H .et al, showed systolic dysfunction prevalence of 28% and diastolic dysfunction prevalence of 9 % in the studied cirrhotic patients[29]. Naviqi et al, showed a prevalence of 35% in cirrhotic patients[30] and Behera MK showed a prevalence of 46% in cirrhotic patients and also showed a correlation between diastolic dysfunction and the severity of liver disease[25] while Hammami R et al, showed 65% prevalence of diastolic dysfunction in cirrhotic patients based on 2005 criteria and they showed no correlation with the severity of liver disease. The differences in how CCM is diagnosed between the 2005 and 2019 criteria in these studies lead to the varying prevalence of CCM in the literatures, which range from 46% to 63%. Our findings indicate a positive correlation between the prevalence of CCM and the severity of liver disease, as assessed by the Child score, suggesting a higher incidence of CCM in patients with decompensated cirrhosis. This finding is supported by previous studies, which found that cirrhotic patients with left ventricular diastolic dysfunction had significantly higher Child-Pugh scores[30-32]. However, Hammami R reported no association between the severity of cirrhosis and the prescence of cardiomyopathy[33]. The study compared three groups based on their liver condition and evaluated the corrected QT interval measured by ECG. The results showed a significant difference among the groups, with decompensated cirrhosis patients having a statistically longer QT interval compared to compensated cirrhosis patients. Also, there was a positive correlation between the patients' corrected QT interval and their Child score. This finding is consistent with previous studies by Bhardwaj A and Karki N, which also reported a significant link between QTc prolongation and disease severity measured by the Child-Pugh score[34,35]. A prolonged corrected QT interval (QTc) has been associated with the severity of cirrhosis and its complications, including hepatic encephalopathy and hepatorenal syndrome (HRS), Studies by Scarlatescu et al[36], and Ge et al[37], have demonstrated that monitoring beta-blockers, QTc intervals, and serum sodium levels may help in the early identification of patients at risk for bleed-triggered HRS, therby improving clinical outcomes. Additionally, a study by Rajiv et al[38] suggested that QT interval prolongation in cirrhotic patients with acute variceal hemorrhage may serve as a predictive marker for the development of HRS. The echocardiographic evaluation of the study groups revealed significant differences in septal velocity, tricuspid annular systolic plane excursion (TAPSE), systolic pulmonary artery pressure (SPAP), E/E'

ratio, and tricuspid regurgitation velocity (TR) ($p < 0.001$). The E/A ratio also showed a significant difference ($p = 0.017$, $r = 0.838$). These results indicate a higher prevalence of diastolic dysfunction in patients with HRS and decompensated cirrhosis. The positive correlation between CCM and Child score, serum creatinine, and HRS occurrence suggests that CCM may predict liver disease severity and complications like hepatorenal syndrome. These findings align with Scarlatescu E. et al's study, which linked QTc interval prolongation to severe liver disease complications, including hepatic encephalopathy and hepatorenal syndrome, and cirrhosis severity[36]. Cirrhotic cardiomyopathy is thought to develop in patients with hepatorenal syndrome even without pre-existing cardiac conditions. This condition is characterized by impaired diastolic relaxation, electrophysiological abnormalities, and decreased contractile response to stressors[39]. TAPSE (Tricuspid annular plane systolic excursion) is an echocardiographic tool to assess right ventricular systolic function[40]. It was found to be statistically decreased in decompensated cirrhosis and in patients with hepatorenal syndrome (HRS), suggesting potential unidentified systolic dysfunction in HRS. In compensated cirrhosis, systolic dysfunction may manifest as an inability to increase left ventricular ejection fraction under stress. Echocardiographic stress testing is challenging in cirrhotic patients due to their limited exercise capacity. Advanced cirrhosis with systolic dysfunction is strongly associated with HRS and poor survival rates, as reported by Krag et al[41]. The use of dobutamine stress testing is limited in these patients. However, a study by Donovan et al. in 1996 found that less than 10% of patients who underwent dobutamine stress testing had ventricular dysfunction[42]. An HRS patient with elevated N-terminal pro–B-type natriuretic peptide levels and normal left ventricular ejection fraction was diagnosed in a case report by Mocarzel et al. Speckle tracking echocardiography showed reversible systolic function abnormalities, improved with dobutamine infusion. Following dobutamine treatment, the patient's renal function clinically and in tests improved. The authors emphasized the need for further clinical research on HRS treatment strategies due to the significant impact of cardiac failure on renal dysfunction[43]. When compared to systolic dysfunction in the clinical context, diastolic dysfunction may serve as a valuable prognostic indicator in cirrhotic cardiomyopathy and hepatorenal syndrome (HRS)[44,45]. In a study conducted by Ruíz-del-Árbol et al[45] on cirrhotic patients with portal hypertension and normal level of serum creatinine, left ventricular dysfunction was assessed in relation to circulatory function and prognosis. Ruíz-del-Árbol et al. examined 80 patients using conventional and tissue Doppler echocardiography and also systemic and hepatic hemodynamics and endogenous vasoactive systems activity. Among the 37 patients initially diagnosed with left ventricular diastolic dysfunction (LVDD), 14 subsequently developed HRS. These findings were further supported by Premkumar's 2019 study, which identified a correlation between the severity of LVDD and the risk of renal failure, clinical events, and liver function[46]. We also studied the relation between CCM with different parameters, we found that CCM was associated with lower albumin level, higher bilirubin higher INR, lower hemoglobin level, higher serum creatinine, Child score, prescence of ascites portal vein diameter, spleen diameter, history of upper gastrointestinal bleeding and the prescence of hepatorenal syndrome. The current study has limitations due to its single-center design and limited sample size, which may introduce patient selection bias. Additionally, stress echocardiography was not conducted on the subjects, and B-type natriuretic peptide levels was not measured to detect subclinical heart failure.

Conclusion

We found that cirrhotic cardiomyopathy (ccm) was present in a significant proportion of cirrhotic patients and was associated with the liver disease severity as indicated by the Child score and with complications such as HRS.

Abbreviations

CCM: Cirrhotic cardiomyopathy.
AKI: acute kidney injury.
HRS: Hepatorenal syndrome.
ECG: electrocardiography.
MRI: magnetic resonant imaging.
INR: international normalized ratio.
TTE: Transthoracic echocardiography.
TDI: tissue Doppler imaging.
(E/A): The ratio between the early and late diastolic mitral inflow velocities.
AST: Aspartate transaminase.
ALT: Alanine transaminase.
(E/E'): peak early diastolic mitral annulus velocity
TRV: tricuspid regurgitation velocity.
LAVI: left atrium volume index.
E—early diastolic transmitral filling.
A—late diastolic transmitral filling.
e'—early diastolic mitral annular velocity.

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