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INCIDENCE OF CARDIOVASCULAR DYSFUNCTION IN PATIENTS WITH LIVER CIRRHOSIS - A HOSPITAL BASED OBSERVATIONAL STUDY

General Medicine

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ABSTRACT

Background: Liver cirrhosis is a chronic condition marked by scarring of liver tissue, leading to significant functional impairment. Cardiovascular dysfunction, often referred to as cirrhotic cardiomyopathy, is a known complication in liver cirrhosis patients, characterized by altered cardiac structure and function. Our study aimed to elucidate the incidence and nature of cardiovascular abnormalities in this patient population. **Aim:** To study the incidence of cardiovascular dysfunction in patients with liver cirrhosis and its correlation with the severity of liver disease as classified by the Child-Pugh score. **Material and Methods:** An observational study was conducted at Mahatma Gandhi Medical College & Hospital, Jaipur, including 101 patients with liver cirrhosis, without any pre-existing cardiac ailments. Demographic data, liver disease severity (Child-Pugh classification), and various cardiac function parameters were recorded. Cardiac assessments included measurements of LV ejection fraction (EF), global longitudinal strain (GLS), septal e', E/e' ratio, TR velocity, systolic and diastolic function, QTc interval, and BNP levels. **Results:** Age and Gender:Patients ranged from 22 to over 50 years, with the majority (41.6%) over 50 years old. The cohort included 71 males (70.3%) and 30 females (29.7%). Child-Pugh Class: 62.4% of patients were in Class A, 23.8% in Class B, and 13.9% in Class C. Cardiac Function: 28.7% had an LV EF <50%, and 24.8% had GLS <18%, 23.8% had septal e'<7cm/second, 30.7% had E/e' >15, 28.7% had TR velocity >280cm/second. Systolic dysfunction was present in 23.8%, and diastolic dysfunction in 22.8%. Elevated QTc intervals (>440 ms) were found in 45.5%, and 60.4% had elevated BNP levels (>100 pg/mL). Associations: Significant associations were found between higher Child-Pugh classes and both systolic and diastolic dysfunction (p-value = 0.001). **Conclusion:** This study highlights a significant incidence of cardiovascular dysfunction in liver cirrhosis patients, particularly among those with more severe liver disease (Child-Pugh Classes B and C). Comprehensive cardiovascular assessment is crucial in this population for early detection and management of cardiac complications, potentially improving overall patient outcomes.

KEYWORDS

INTRODUCTION

Liver cirrhosis is a progressive disorder that disrupts the normal structure and function of the liver. Up to 90% of the liver parenchyma experiences damage before clinical manifestations of liver failure become apparent[1]. In developing nations, cirrhosis is predominantly attributed to Hepatitis B and C, while in developed nations, Alcoholic Liver Disease (ALD) and Non-Alcoholic Steatohepatitis (NASH), alongside Hepatitis C, are recognized as the primary culprits for the development of cirrhosis.[1]

The assessment of liver cirrhosis severity can be conducted using both the Child-Pugh score and the Model for End-Stage Liver Disease (MELD) score. Notably, the Child-Pugh score exhibits a higher sensitivity compared to the MELD score. This scoring system relies on factors such as jaundice, ascites, encephalopathy, serum albumin levels, and prothrombin time[2]. Despite being a concern often overlooked, cardiac dysfunction in cirrhosis, situated on the 'blind side of the heart,' presents a significant issue. Cirrhosis is associated with a spectrum of cardiovascular abnormalities, including hyperdynamic circulation, portal hypertension, hepato-pulmonary syndrome, and alterations in various vascular territories, such as the renal and cerebral vasculature.[3]

	Child-Pugh Classification (CPC)		
	1	2	3
Encephalopathy	None	Grades 1 - 2 (or precipitant-induced)	Grades 3 - 4 (or chronic)
Ascites	None	Mild/moderate (diuretic-responsive)	Severe (diuretic-refractory)
Bilirubin (mg/dL)	< 2	2 - 3	> 3
Albumin (g/dL)	> 3.5	2.8 - 3.5	< 2.8
PT (s)	< 4	4 - 6	> 6
INR	< 1.7	1.7 - 2.3	> 2.3

Figure 1; Child Pugh Scoring system

Liver cirrhosis is associated with a wide range of cardiovascular abnormalities. This was first described by Kowalski and Abelmann who noted a higher resting cardiac output and decreased systemic vascular resistance in patients with cirrhosis[1,2]. However, despite the hyperdynamic circulation, impaired ventricular contractility in response to stimuli was described in cirrhotic patients.[3] These abnormalities were initially thought to be a manifestation of latent alcoholic cardiomyopathy. But in the mid-1980s, studies in nonalcoholic patients and in experimental animal models showed a similar pattern of blunted cardiac contractile responsiveness.[4]

These cardiovascular changes are now termed 'cirrhotic cardiomyopathy'.[6] The prevalence of cirrhotic cardiomyopathy remains unknown at present. Features include structural, histological, electrophysiological changes, systolic and diastolic dysfunction. Multiple factors are considered which includes impaired beta-adrenergic receptor signal transduction, abnormal membrane biophysical characteristics, and increased activity of cardio-depressant systems mediated by cGMP.[7]

Overt heart failure is not generally a feature of cirrhotic cardiomyopathy because the associated marked vasodilatation accompanying the hyperdynamic circulation significantly reduces ventricular afterload. However, major stresses on the cardiovascular system such as liver transplantation, infections and insertion of transjugular intrahepatic portosystemic shunts (TIPS) can unmask the presence of cirrhotic cardiomyopathy and thereby convert latent to overt heart failure.[8]

Cirrhotic cardiomyopathy may also contribute to the pathogenesis of hepatorenal syndrome and circulatory failure in liver cirrhosis.[9] This condition represents a multifactorial cardiac dysfunction characterized by alterations in both systolic and diastolic function. The exact mechanisms contributing to cirrhotic cardiomyopathy are complex and not entirely understood, involving a combination of hemodynamic, neurohormonal, chronic inflammatory milieu and structural changes.

Key features of cirrhotic cardiomyopathy include:[10-12]

Systolic Dysfunction:

- Impaired contractility of the heart muscle, leading to reduced ejection fraction and/or a normal resting ejection fraction with blunted contractile responsiveness to stress,.
- Inotropic incompetence, chronotropic incompetence.

Diastolic Dysfunction:

- Abnormalities in the relaxation phase of the cardiac cycle, affecting the heart's ability to fill with blood.
- Increased stiffness of the myocardium, contributing to impaired ventricular filling.

Electrocardiographic Changes:
- Prolongation of the QT interval on electrocardiograms (ECGs).
- Altered repolarization and increased susceptibility to arrhythmias.

Autonomic Dysfunction:
- Dysregulation of the autonomic nervous system, with increased sympathetic tone and decreased parasympathetic activity.
- Altered response to stress and exercise.

Hemodynamic Disturbances:
- Increased cardiac output at rest, known as hyperdynamic circulation.
- Reduced systemic vascular resistance.

Implications for Liver Transplantation:
- Cirrhotic cardiomyopathy may have significant implications for patients undergoing liver transplantation, as alterations in cardiac function can affect perioperative outcomes.

The exact prevalence of cirrhotic cardiomyopathy remains eluded, and its diagnosis can be challenging due to the absence of specific diagnostic criteria. Furthermore, the clinical manifestations may not be apparent until the heart is subjected to stressors such as surgery, infection, or volume overload.[11]

Management of cirrhotic cardiomyopathy primarily involves addressing the underlying liver disease. Optimization of fluid balance, cautious use of vasoactive medications, and close monitoring of cardiac function as essential components of care. Current guidelines for heart failure management may be considered, including the use of beta adrenergic receptor blockers, although their use is often approached with caution.[12]

Diastolic dysfunction is present in the vast majority of patients with cirrhotic cardiomyopathy, echocardiographic indices such as the E/A ratio may help detect diastolic dysfunction, even at rest. This may therefore represent the best available screening test to diagnose cardiac dysfunction.[13]

Due to the limited number of human studies, the management of cirrhotic cardiomyopathy remains largely empirical. Treatment of this condition is mainly supportive. Orthotropic liver transplantation appears to improve or normalize the condition, generally after a period of several months.[14] If overt heart failure develops in these patients, the general treatment principles of non cirrhotic congestive heart failure may be applied, including salt restriction, diuretics, and careful preload and afterload reduction[15]

The relationship between liver cirrhosis and cardiac dysfunction is complex, involving intricate interactions between hemodynamic changes, neurohormonal activation, and the presence of cirrhotic cardiomyopathy. Understanding the cardiac implications of liver cirrhosis is crucial, as it may have implications for both the prognostication and management of patients with this condition.[16-17]

The Child-Pugh score, a well-established clinical tool for assessing the severity of liver cirrhosis, incorporates objective measures of liver function, such as bilirubin, albumin, prothrombin time, ascites, and hepatic encephalopathy. While it has been extensively used for prognostication and treatment decisions in liver disease, its potential correlations with cardiac parameters in cirrhotic patients have not been fully elucidated.

Through our study, we endeavored to study the incidence of Cardiovascular Dysfunction in patients with Liver Cirrhosis. By employing comprehensive cardiac assessments alongside established clinical grading systems, this study aims to contribute valuable insights into the cardiovascular implications of liver cirrhosis and pave the way for improved risk stratification and management strategies for this complex patient population.

MATERIALS AND METHODS

We conducted a hospital based observational study, in Mahatma Gandhi Medical College & Hospital, Jaipur. For a duration of 18 months, from September 2022 to March 2024. Assessing all clinically diagnosed cases of Liver Cirrhosis in this duration. With the aim of studying the incidence of Cardiovascular Dysfunction in patients with Liver Cirrhosis. The objectives of our study were, to help show incidence thus association of Cardiovascular Dysfunction in patients with Liver Cirrhosis without pre-existing cardiovascular ailments; and to highlight the need for a rigorous cardiovascular risk assessment in patients with liver cirrhosis. Our inclusion criteria was; Patients giving consent for the study; Patients above the age of 18years; Patients diagnosed with Liver Cirrhosis. And exclusion criteria was; Patients with pre existing cardiovascular ailments.

All the patients diagnosed with liver cirrhosis, meeting inclusion criteria were explained about the study; its components, the aim and relevance. They were also intimated that their non participation would not in any way alter or affect the quality of treatment they were receiving. Consent was then recorded of the ones willing and consenting to participate.

Detailed clinical history was sought, history for co-morbidities, any pre-existing cardiovascular ailments was solicited, and if present, such patients were excluded from the study.

Thorough clinical examination was conducted, the necessary and relevant to the study obligatory investigations were carried out including; Total Serum Bilirubin, Serum Albumin, Prothrombin Time, Ultrasonography Abdomen, Electrocardiography, 2-D Echocardiography, Speckle-Tracking Echocardiography, Tissue Doppler, Pulsed Wave Doppler, Continuous Doppler And Serum Brain Natriuretic Peptide.

Based on results of the investigations, patients were first categorised into Child Pugh classes A,B and C; based on the parameters set forth by the Child Pugh scoring system.

Data was then recorded for each patient, in keeping with the parameters set forth by cirrhotic cardiomyopathy diagnostic criteria proposed by the Cirrhotic Cardiomyopathy Consortium, 2019.

All the collected data was entered in Microsoft Excel sheet and then transferred to SPSS software ver. 26 for analysis. Qualitative data was presented as frequency and percentages and analysed using chi-square test. P-value < 0.05 was taken as level of significance.

RESULTS

Gender Distribution

The study population consists of 101 patients, with a gender distribution of 30 females (29.7%) and 71 males (70.3%).

Age group Distribution

Among the 101 patients, 14.9% are aged 22 to 30 years, 20.8% are aged 31 to 40 years, 22.8% are aged 41 to 50 years, and the largest age group is those older than 50 years, comprising 41.6%.

Child Pugh Class

In terms of liver disease severity, 62.4% of the patients fall into Child-Pugh Class A, 23.8% are in Class B, and 13.9% are in Class C, indicating that the majority have less severe liver disease.

LV EF %

For cardiac function, 28.7% of the patients have an LV ejection fraction (EF) less than 50%, while 71.3% have an LV EF greater than 50%, indicating better systolic function in the majority.

Absolute GLS %

The absolute GLS values show that 24.8% of the patients have a GLS of less than 18%, and 75.2% have a GLS of more than 18%, suggesting better myocardial function in most patients.

Systolic Dysfunction

Regarding systolic dysfunction, 23.8% of the patients exhibit systolic dysfunction, while 76.2% do not, indicating that the majority of patients have preserved systolic function.

Septal e' cm/second

Septal e' velocity measurements reveal that 23.8% of the patients have a septal e' velocity of less than 7 cm/second, whereas 76.2% have a

velocity greater than 7 cm/second, indicating better diastolic function in the majority.

E/e' ratio

The E/e' ratio shows that 30.7% of the patients have a ratio greater than 15, while 69.3% have a ratio less than 15, suggesting that the majority have better left ventricular filling pressures.

TR velocity cm/second

In terms of TR velocity, 28.7% of patients have a TR velocity greater than 280 cm/second, while 71.3% have a TR velocity less than 280 cm/second, indicating lower pulmonary pressures in most patients.

Diastolic dysfunction

Regarding diastolic dysfunction, 22.8% of the patients exhibit diastolic dysfunction, while 77.2% do not, suggesting that the majority have normal diastolic function.

Qtc interval milisecond

For the QTc interval, 45.5% of the patients have a QTc interval greater than 440 milliseconds, while 54.5% have a QTc interval less than 440 milliseconds, indicating that the majority have normal QTc intervals.

BNP pg/mL

The BNP levels show that 60.4% of the patients have BNP levels greater than 100 pg/mL, indicating elevated cardiac stress in the majority, while 39.6% have BNP levels less than 100 pg/mL.

Table no 1 Systolic Dysfunction vs Child Pugh Class

			Systolic Dysfunction		Total
			No	Yes	
Child Pugh Class	A	Count	60	3	63
		%	77.90%	12.50%	62.40%
	B	Count	17	7	24
		%	22.10%	29.20%	23.80%
	C	Count	0	14	14
		%	0.00%	58.30%	13.90%
Total		Count	77	24	101
		%	100.00%	100.00%	100.00%

Chi square test, P value- 0.001

There is a significant association between systolic dysfunction and Child-Pugh class (p-value = 0.001). Among patients without systolic dysfunction, 77.9% fall into Class A, 22.1% into Class B, and none into Class C. Conversely, among patients with systolic dysfunction, only 12.5% are in Class A, 29.2% in Class B, and a significant 58.3% in Class C. Overall, 62.4% of the total patients are in Class A, 23.8% in Class B, and 13.9% in Class C. This indicates that higher Child-Pugh classes are more prevalent in patients with systolic dysfunction.

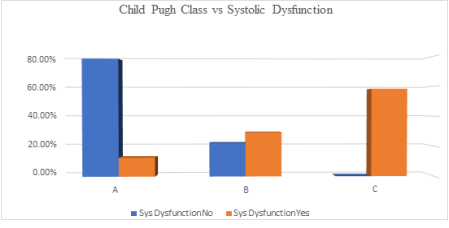


Table no 2 Diastolic Dysfunction vs Child Pugh Class

			DD		Total
			No	Yes	
Child Pugh	A	Count	62	1	63
		%	79.50%	4.30%	62.40%
	B	Count	15	9	24
		%	19.20%	39.10%	23.80%
	C	Count	1	13	14
		%	1.30%	56.50%	13.90%
Total	Count		78	23	101
	%		100.00%	100.00%	100.00%

Chi square test, P value- 0.001

There is a significant association between DD and Child-Pugh class (p-value = 0.001). Among patients without DD, 79.5% fall into Class A, 19.2% into Class B, and only 1.3% into Class C. In contrast, among patients with DD, 4.3% are in Class A, 39.1% in Class B, and 56.5% in Class C. Overall, 62.4% of the total patients are in Class A, 23.8% in Class B, and 13.9% in Class C. This indicates that higher Child-Pugh classes are more prevalent in patients with DD.

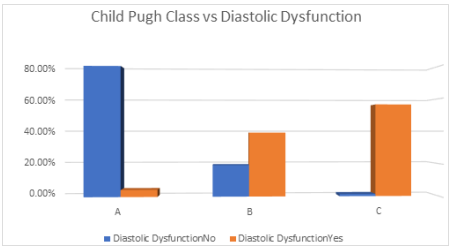
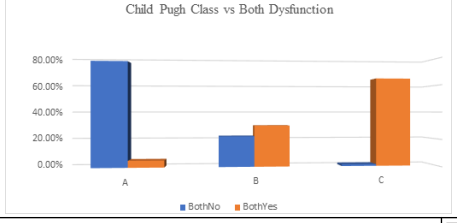


Table no 3 Both Dysfunction vs Child Pugh Class

			BOTH		Total
			no	yes	
Child Pugh Class	A	Count	62	1	63
		%	76.50%	5.00%	62.40%
	B	Count	18	6	24
		%	22.20%	30.00%	23.80%
	C	Count	1	13	14
		%	1.20%	65.00%	13.90%
Total		Count	Count	20	101
		%	%	100.00%	100.00%

Chi square test, P value- 0.001

There is a significant association between the presence of both systolic dysfunction and diastolic dysfunction and the Child-Pugh class (p-value = 0.001). Among patients without both conditions, 76.5% fall into Class A, 22.2% into Class B, and only 1.2% into Class C. Conversely, among patients with both conditions, 5.0% are in Class A, 30.0% in Class B, and a significant 65.0% in Class C. Overall, 62.4% of the total patients are in Class A, 23.8% in Class B, and 13.9% in Class C. This indicates that higher Child-Pugh classes are more prevalent in patients with both conditions.



CCM	Frequency
Patients with systolic dysfunction	24
Patients with diastolic dysfunction	23
Patients with both dysfuncton	20
Total number of unique patients with cardiomyopathy	**27**
Total number of patients in the study	101
Incidence of Cirrhotic Cardiomyopathy	**26.73%**

Total Cardiomyopathy Patients = (24+23) −20 = 27

DISCUSSION

Liver cirrhosis is a chronic, progressive disease marked by the replacement of healthy liver tissue with scar tissue, leading to impaired liver function. Patients with liver cirrhosis often experience a range of complications, including cardiovascular dysfunction. The cardiovascular system's involvement in liver cirrhosis is complex and multifaceted, encompassing alterations in cardiac structure and function. This condition, often referred to as cirrhotic cardiomyopathy, is characterized by blunted cardiac responses to stress, systolic and diastolic dysfunction, and electrophysiological abnormalities such as prolonged QTc intervals. These cardiovascular issues can significantly impact patient prognosis and quality of life. The Child-Pugh classification system, which assesses the severity of liver disease, often correlates with the extent of cardiovascular dysfunction. Understanding the incidence and nature of cardiovascular abnormalities in liver cirrhosis patients is crucial for early diagnosis and intervention, potentially improving clinical outcomes and reducing morbidity and mortality in this vulnerable patient population.

The present study aimed to investigate the incidence of cardiovascular dysfunction in patients with liver cirrhosis.

The study participants had a wide age distribution, with the largest age group being those older than 50 years, comprising 41.6% of the total population. The remaining participants were distributed across the 22-30 years (14.9%), 31-40 years (20.8%), and 41-50 years (22.8%) age groups.

The age distribution observed in the present study is consistent with the epidemiology of liver cirrhosis, which typically affects individuals across a broad age spectrum, with an increasing prevalence in the older adult population.

The studies reviewed also included participants with similar age distributions. For instance, the study by Karki et al[72]. (2023) reported a mean age of 48.29 years, with 54.3% of the participants falling between 40-60 years of age. Similarly, the study by Chandey et al[73]. (2020) did not provide the mean age but included participants with cirrhosis of varying etiologies.

The preponderance of liver cirrhosis in the older age groups can be attributed to the cumulative effects of various risk factors, such as chronic viral hepatitis, alcohol consumption, and metabolic disorders, which typically accumulate over time. The consistent age distribution across these studies highlights the importance of considering the specific needs and management strategies for the older adult population in the context of liver cirrhosis and its associated cardiovascular complications.

The present study had a male predominance, with 70.3% of the participants being male and 29.7% being female. This gender distribution is in line with the higher prevalence of liver cirrhosis observed in the male population in various epidemiological studies.

The studies reviewed did not consistently report the gender distribution of the participants, as their primary focus was on the evaluation of cardiovascular dysfunction in the context of liver cirrhosis, rather than the specific gender-based epidemiology of the condition. The observed male predominance in liver cirrhosis may be attributed to several factors, including higher rates of alcohol consumption, occupational exposures, and genetic susceptibility among men compared to women. However, it is important to note that the gender distribution of liver cirrhosis can vary across different populations and geographic regions, as environmental, socioeconomic, and cultural factors may influence the epidemiology of this condition.

The present study categorized the participants based on the Child-Pugh classification, which is a widely used system for assessing the severity of liver disease. The majority of the participants (62.4%) were in Child-Pugh Class A, indicating less severe liver disease, followed by Class B (23.8%) and Class C (13.9%).

The distribution of participants across the Child-Pugh classes in the present study is consistent with the findings reported in some of the reviewed studies. For instance, the study by ieranu et al.[75] (2018) found that 10% of their participants were in Class A, 46.67% in Class B, and 43.33% in Class C.

The predominance of participants with less severe liver disease (Class A) in the present study may be related to the fact that patients with advanced liver cirrhosis (Class C) often have a poorer prognosis and may not have been included in the study due to various clinical factors or higher mortality rates.

The stratification of participants based on the Child-Pugh classification allows for a more comprehensive understanding of the relationship between the severity of liver disease and the development of cardiovascular dysfunction, which is a key objective of this investigation.

The present study evaluated various parameters of cardiac function in the participants, including left ventricular ejection fraction (LVEF), global longitudinal strain (GLS), systolic dysfunction, diastolic function, and pulmonary pressures.

The study found that 28.7% of the participants had an LVEF less than 50%, indicating the presence of systolic dysfunction, while 71.3% had an LVEF greater than 50%, suggesting better systolic function.

The study assessed the absolute GLS values and found that 24.8% of the participants had a GLS of less than 18%, indicating impaired myocardial function, while 75.2% had a GLS of more than 18%, suggesting better myocardial function. The use of GLS as a measure of myocardial function in the setting of liver cirrhosis is less commonly reported in the reviewed studies, as this parameter is a relatively newer echocardiographic technique for the evaluation of cardiac dysfunction.

The study found that 23.8% of the participants exhibited systolic dysfunction, while 76.2% did not, indicating that the majority of the participants had preserved systolic function.

The study evaluated diastolic function using parameters such as septal e' velocity and E/e' ratio. It found that 23.8% of the participants had a septal e' velocity of less than 7 cm/second, indicating impaired diastolic function, and 30.7% had an E/e' ratio greater than 15, suggesting elevated left ventricular filling pressures.

The assessment of diastolic function in the setting of liver cirrhosis is a common theme in the reviewed studies. For instance, the study by Patil et al. (2016) reported that diastolic dysfunction, as assessed by the E/A ratio, correlated with the severity of liver cirrhosis.

The study examined the tricuspid regurgitation (TR) velocity and found that 28.7% of the participants had a TR velocity greater than 280 cm/second, suggesting elevated pulmonary pressures, while 71.3% had a TR velocity less than 280 cm/second, indicating lower pulmonary pressures.

QT Interval and BNP The present study also evaluated the QTc interval and brain natriuretic peptide (BNP) levels in the participants. The study found that 45.5% of the participants had a QTc interval greater than 440 milliseconds, indicating a prolonged QTc, while 54.5% had a QTc interval less than 440 milliseconds, suggesting a normal Qtc.

The findings on QTc interval prolongation in the present study are consistent with the observations reported in the reviewed literature. Several studies, such as Karki et al[72]. (2023), Chandey et al[73]. (2020), Dhoat et al[74]. (2019), and Bhatti et al[80]. (2014), have also demonstrated a correlation between the severity of liver cirrhosis, as assessed by the Child-Pugh classification, and the prolongation of the QTc interval.

The study found that 60.4% of the participants had BNP levels greater than 100 pg/mL, indicating elevated cardiac stress, while 39.6% had BNP levels less than 100 pg/mL.

The evaluation of BNP levels in the context of liver cirrhosis and its association with cardiovascular dysfunction is less frequently reported in the reviewed studies, as the primary focus was often on the assessment of QT interval and other echocardiographic parameters.

The findings on QTc interval prolongation and elevated BNP levels in the present study are relevant, as they suggest the presence of subclinical cardiac dysfunction in a significant proportion of the participants with liver cirrhosis. These parameters can serve as valuable markers for the early detection and monitoring of cardiovascular complications in this patient population. One of the key findings of the present study was the observed association between the severity of cardiovascular dysfunction and the severity of liver disease, as assessed by the Child-Pugh classification.

The study found a significant association between the presence of systolic dysfunction and higher Child-Pugh classes. Among patients without systolic dysfunction, 77.9% were in Class A, 22.1% in Class B, and none in Class C. In contrast, among patients with systolic dysfunction, only 12.5% were in Class A, 29.2% in Class B, and 58.3% in Class C.

Similarly, the study observed a significant association between the presence of diastolic dysfunction and higher Child-Pugh classes. Among patients without diastolic dysfunction, 79.5% were in Class A, 19.2% in Class B, and only 1.3% in Class C. Conversely, among patients with diastolic dysfunction, only 4.3% were in Class A, 39.1% in Class B, and 56.5% in Class C.

The study also found a significant association between the presence of both systolic and diastolic dysfunction and higher Child-Pugh classes.

Among patients without both conditions, 76.5% were in Class A, 22.2% in Class B, and only 1.2% in Class C. In contrast, among patients with both conditions, only 5.0% were in Class A, 30.0% in Class B, and a significant 65.0% in Class C.

These findings suggest that as the severity of liver disease, as assessed by the Child-Pugh classification, increases, the prevalence of cardiovascular dysfunction, including both systolic and diastolic abnormalities, also increases.

The reviewed studies provide supporting evidence for this association. For instance, the study by Chandey et al[73]. (2020) reported a linear increase in the QTc interval with the severity of liver cirrhosis, as classified by the Child-Pugh score. Similarly, the study by Dhoat et al[74]. (2019) found a statistically significant prolongation of the QTc interval in patients with Child-Pugh Class B and C compared to Class A.

The study by Patil et al[78]. (2016) also observed a correlation between diastolic dysfunction, as assessed by the E/A ratio, and the severity of liver cirrhosis, as evidenced by proportional changes in left ventricular dimensions and wall thickness.

The underlying mechanisms that contribute to the development of cardiovascular dysfunction in the setting of liver cirrhosis are multifactorial and may involve factors such as hemodynamic changes, neurohumoral alterations, oxidative stress, and the direct effects of cirrhosis on myocardial structure and function.

The strong association between the severity of liver disease and the prevalence of cardiovascular dysfunction observed in the present study highlights the importance of a comprehensive assessment and close monitoring of cardiac function in patients with advancing liver cirrhosis. This information can guide the development of appropriate management strategies and assist in the identification of high-risk individuals who may benefit from more targeted interventions or specialized care.

The study by Karki et al[72]. (2023) focused on the correlation between the QT interval and the severity of liver dysfunction, as assessed by the Child-Pugh and MELD scores. Their findings were consistent with the present study, demonstrating a higher prevalence of prolonged QTc intervals in patients with more advanced liver disease.

The study by Chandey et al[73]. (2020) also evaluated the electrocardiographic and echocardiographic signs of cardiovascular dysfunction in patients with liver cirrhosis and found a linear increase in the QTc interval with the severity of cirrhosis, as classified by the Child-Pugh score. This observation aligns with the present study's findings on the association between the severity of liver disease and the prevalence of cardiovascular dysfunction.

The studies by Dhoat et al[74]. (2019) and Bhatti et al[80]. (2014) further corroborated the association between the prolongation of the QTc interval and the severity of liver cirrhosis, as categorized by the Child-Pugh classification.

The study by ieranu et al[75]. (2018) reported that despite variations in Child-Pugh classes, the mean QT interval values did not significantly differ among their study participants. This finding contrasts with the observations in the present study, where a clear association was found between the severity of liver disease and the presence of cardiovascular dysfunction.

The study by Tsiompanidis et al[76]. (2018) focused on the impact of liver cirrhosis on the QT interval and cardiac autonomic neuropathy (CAN), finding significant associations between QT interval prolongation and factors such as diabetes mellitus and diuretic treatment, but not the Child-Pugh score.

The studies by Sukhwani et al[77]. (2016) and Naik et al[79]. (2014) emphasized the presence of diastolic dysfunction in patients with liver cirrhosis, with the latter study also reporting various clinical and laboratory parameters associated with the condition.

The study by Patil et al[78]. (2016) demonstrated a correlation between diastolic dysfunction, as assessed by the E/A ratio, and the severity of liver cirrhosis, which is in line with the findings of the present study.

The observed differences in the strength of the association between the severity of liver disease and the prevalence of cardiovascular dysfunction across the reviewed studies may be attributed to factors such as variations in study populations, differences in the assessment methods employed, and the potential influence of comorbidities and other confounding factors.

CONCLUSION

The present study provides valuable insights into the incidence of cardiovascular dysfunction in patients with liver cirrhosis. A significant proportion of the participants exhibited impairments in cardiac function, including systolic dysfunction (23.8%), diastolic dysfunction (22.8%), and elevated pulmonary pressures (28.7%). Prolongation of the QTc interval, a marker of cardiac electrical instability, was observed in 45.5% of the participants, suggesting the presence of subclinical cardiac abnormalities. There was a strong association between the severity of liver disease, as classified by the Child-Pugh score, and the prevalence of cardiovascular dysfunction. Patients with more advanced liver cirrhosis (Child-Pugh Class B and C) had a higher incidence of systolic dysfunction, diastolic dysfunction, and the presence of both conditions compared to those with less severe liver disease (Child-Pugh Class A). These findings highlight the importance of comprehensive cardiovascular assessment and monitoring in patients with liver cirrhosis, as the severity of the liver disease appears to be a significant contributor to the development of cardiac abnormalities. Early identification and management of these cardiac complications may have important implications for the overall care and prognosis of individuals with liver cirrhosis.

Strengths of the Study:

1. Comprehensive evaluation of various parameters of cardiac function, including systolic and diastolic indices, as well as the assessment of pulmonary pressures, in a well-characterized cohort of liver cirrhosis patients.
2. Exploration of the association between the severity of liver disease, as classified by the Child-Pugh score, and the prevalence of cardiovascular dysfunction.
3. Inclusion of both electrocardiographic (QTc interval) and biomarker (BNP) assessments to provide a more holistic evaluation of cardiac status.

Limitations of the Study:

1. Cross-sectional design, which limits the ability to establish causal relationships and determine the temporal sequence of events between the development of liver cirrhosis and the onset of cardiovascular dysfunction.
2. Lack of long-term follow-up to assess the progression of cardiovascular dysfunction and its impact on clinical outcomes in the study population

Recommendations for Future Research:

1. Conduct prospective, longitudinal studies with extended follow-up periods to better understand the causal relationships and the long-term impact of liver cirrhosis on the development and progression of cardiovascular dysfunction.
2. Incorporate advanced cardiac imaging techniques, such as cardiac magnetic resonance imaging and speckle-tracking echocardiography, to provide a more comprehensive assessment of myocardial structure and function in patients with liver cirrhosis.
3. Explore the influence of specific etiologies and complications of liver cirrhosis on the development of cardiovascular dysfunction, to identify high-risk subgroups and tailor management strategies accordingly.

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