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A STUDY OF CARDIAC DYSFUNCTION AND CONDUCTION DISTURBANCES IN NON ALCOHOLIC CIRRHOTIC PATIENTS

Gastroenterology

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ABSTRACT

Liver Cirrhosis is associated with wide range of cardiac abnormalities in the form of structural and hemodynamic alterations. These changes are reported mainly in alcoholic patients and are collectively termed as Cirrhotic cardiomyopathy. Cirrhotic cardiomyopathy can manifest with an increased cardiac output, systolic and diastolic dysfunction and electrophysiological abnormalities.

AIMS : This study is aimed to evaluate the cardiac dysfunction and conduction disturbances in non alcoholic cirrhotic patients and to assess their relationship with the severity of cirrhosis and ascites.

Methods: This is a retrospective study study of 30 patients done at The Department of Digestive Health and Diseases, Government Peripheral Hospital, Anna Nagar, Chennai. All patients with non alcoholic cirrhosis of liver were subjected to electrocardiography and echocardiography. The results were interpreted and analyzed for their association with severity of cirrhosis.

Results: Out of the total 30 cases, cirrhosis due to hepatic B and Hepatitis C viral infections were 12 and 1case respectively. 1case of primary biliary cirrhosis, 10 were due to non-alcoholic fatty liver disease and in 6 patients the cause was Not known. Of the 30 patients included in the study, 20 cases (66.67%) had Class A CTP and 10 cases (33.3%) had Class B CTP. Echocardiography study showed, 14 patients had end diastolic volume above 90 and 3 patients had end systolic volume above 38. Around 26 patients showed features of cirrhotic cardiomyopathy, of which 16 patients had CTP Class A and 10 patients had CTP Class B. 4 patients with CTP Class A did not have cirrhotic cardiomyopathy at all. Electrocardiogram study showed a QTc prolongation in 16 patients (53.3%).

Conclusion: Non alcoholic Cirrhotic patients also have evidence of cirrhotic cardiomyopathy in the form of diastolic dysfunction and prolonged QTc interval. The severity of cirrhosis does not correlate with the presence of diastolic dysfunction. Prolongation of QTc interval is influenced by the sex of the cirrhotic individuals. Ventricular end diastolic volume, end systolic volume and ejection fraction are not significantly affected in cirrhotic individuals. Cirrhotic cardiomyopathy in these patients is independent of the etiology of cirrhosis and Ascites is a significant feature of all cases with diastolic dysfunction.

KEYWORDS

INTRODUCTION

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[3-7]. These cardiovascular changes are now termed 'cirrhotic cardiomyopathy'[8-11]. Cirrhotic cardiomyopathy includes structural, histological, electrophysiological, systolic and diastolic dysfunction. Multiple factors responsible are impaired beta-adrenergic receptor signal transduction, abnormal membrane characteristics, and increased activity of cardiodepressent systems mediated by cGMP[12].

Overt heart failure is not generally a feature of cirrhotic cardiomyopathy, However, major stresses such as liver transplantation, infections and insertion of transjugular intrahepatic portosystemic shunts (TIPS) can unmask existing cirrhotic cardiomyopathy to overt heart failure. Cirrhotic cardiomyopathy may also contribute to the pathogenesis of hepatorenal syndrome and circulatory failure [12].

Simple echocardiographic indices such as the E/A ratio may detect diastolic dysfunction even at rest. Decreased E/A ratio i.e the ratio of early to late (atrial) phases of ventricular filling and delayed early diastolic transmitral filling with prolonged deceleration and isovolumetric relaxation times[13,14]. Therefore diastolic dysfunction is simple screening test to diagnose cardiac dysfunction[15]. Diastolic filling consists of two parts normally: rapid, early diastolic (active) relaxation and late diastolic (passive) filling. The first phase depends on the rate of ventricular relaxation, elastic ventricular recoil, the atrio-ventricular pressure gradient, and the passive elastic features of the left atrium and ventricle [16,17].The second phase is based on the strength of left atrial contraction and the stiffness of the left ventricle.

Treatment of cirrhotic cardiomyopathy is mainly supportive. Orthotropic liver transplantation appears to improve or normalize the condition, generally after a period of several months[18]. If overt heart failure develops, management includes bed rest, salt restriction, oxygen, diuretics, and careful preload and afterload reduction [11].

MATERIALS AND METHODS

Patients included in the study were from the Department of Digestive Health and Diseases, Government Peripheral hospital, Anna Nagar, Chennai.

Inclusion criteria: Patients diagnosed to have cirrhosis of nonalcoholic etiology formed the study group.

Exclusion criteria : Alcoholics patients, both past and active drinkers were excluded from the study. Patients who had features of decompensated liver disease like tense ascites, history of recent bleed, severe anemia were also also excluded from the study. Those patients who had risk of cardiomyopathy other than cirrhosis like hypertension and diabetes or any h/o coronary artery disease were not considered in the study group.

All patients were subjected for complete blood count, liver function test, ultrasound scan of the abdomen along with Doppler scan, viral markers, ascitic fluid analysis, liver biopsy, electrocardiography and echocardiography. The parameters that were assessed in echocardiography are E/A ratio, end diastolic volume (EDV), end systolic volume (ESV), ejection fraction.

Qtc interval more than 440 msec and E/A ratio less than 1 were considered diagnostic of cirrhotic cardiomyopathy in this study. End diastolic volume of 90, end systolic value of 38 and ejection fraction of 60% were considered mean of the normal values while doing statistical analysis. The statistical analysis was done using SSPS software version 15. Univariate and multivariate analysis were done with Chi Square test. P value of < 0.05 was found to be significant.

Results

The total number of cases included in this study was 30. Of these, there were 8 males and 22 females. Of the 30 cases included in this study 10 patients were below 40 years of age, 11 cases were between 40 and 50

years of age and 9 cases were above 50 years of age. In 12 cases, cirrhosis was due to hepatic B viral infection, 1 due to hepatitis C, 1 due to primary biliary cirrhosis , 10 due to non-alcoholic fatty liver disease and in 6 patients it was cryptogenic.

Clinical findings

Child Turcotte Pugh Class:

Of the 30 cases included in the study, 20 cases (66.67%) had Class A CTP. 10 cases (33.33%) had Class B CTP. Of the 30 cases included in the study, 24 cases had ascites (80%) and 25 had varices (83.33%).

Conduction disturbances:

Out of the 30 cases who were included in the study, 16 patients had QTc interval of more than 440 msec. Of these 16 patients 11 were males and 5 were female patients

Left Ventricular Dysfunction:

Out of the 30 cases, the ratio of early diastolic and late diastolic filling velocity (E/A ratio) was less than 1 in 25 cases. Of these 25 cases 19 were females and 6 were males.Out of the 30 cases included in this study 26 patients had features cirrhotic cardiomyopathy. These cases had a prolonged QTc interval of more than 440 msec or an E/A ratio of less than 1. Of these 26 cases, 8 were males and 18 were females.

Cirrhotic Cardiomyopathy: Of the 30 patients included in this study, 14 patients had end diastolic volume above 90. 3 patients had end systolic volume above 38. 29 patients had ejection fraction above 60%. The distribution of End Diastolic Volume in study population observed as follows. Below 90 groups, 16 (53.33%) cases; above 90 group, 14(46.67%) cases were observed. The distribution of End Systolic Volume in study population observed as follows. Below 38 group, 27(90%) cases and Above 38 group, 3(10%) cases were observed.

The distribution of ejection Fraction in study population was as follows. Below 60 group, 1 (3.3%) case, Above 60 group, 29(96.67%) cases were observed.

Out of the 30 cases, 26 showed features of cirrhotic cardiomyopathy. 16 patients with cirrhotic cardiomyopathy had Class A Child Turcotte Pugh score. 10 patients with cirrhotic cardiomyopathy had Class B Child Turcotte Pugh score. 4 patients with Class A Child Turcotte Pugh score did not have cirrhotic cardiomyopathy. The 'p' value of this association between Child Turcotte Pugh score and cirrhotic cardiomyopathy is 0.128 and it is not significant (Table 1). This implies that cirrhotic cardiomyopathy is not influenced by the class of Child Turcotte Pugh score.

The QTc interval was more than 440 msec in 11 females and 5 males. It was below 440 msec in 11 females and 3 males. 68% of those who had QTc above 440 msec were females. Similarly 78% of those who had QTc below 440 msec were females. 50% of the 22 females had QTc above 440 msec. 62.5% of the 8 males had QTc above 440 msec. These associations have a 'p' value of 0.543 which is not significant (Table 2). This implies prolongation of QTc interval is not a significant finding in patients who are cirrhotics. Similarly the prolongation of QTc interval is not influenced by sex.

14 patients had end diastolic volume above 90. 16 patients had EDV below 90. 12 patients with diastolic dysfunction had EDV above 90. 14 patients with diastolic dysfunction had EDV below 90. 2 patients with EDV above 90 did not have diastolic dysfunction. The 'p' value of this association between EDV and diastolic dysfunction is 0.885 and it is not significant(Table 3). This implies that abnormality of EDV is not a significant feature of cirrhotic cardiomyopathy.

3 cases had end systolic volume above 38. 27 cases had ESV below 38. 2 cases with diastolic dysfunction had ESV above 38. 24 cases with diastolic dysfunction had ESV below 38. 1 case with ESV above 38 did not have diastolic dysfunction. 3 cases without diastolic dysfunction had ESV below 38. The 'p' value of this association between ESV and diastolic dysfunction is 0.282 and it is not significant (Table 4). This implies that abnormality of ESV is not a significant feature of cirrhotic cardiomyopathy.

29 cases had ejection fraction above 60. 1 patient had EF below 60. 25 patients with cirrhotic cardiomyopathy had EF above 60. 1 case with diastolic dysfunction had EF below 60. 4 patients with EF above 60 did not have diastolic dysfunction. The 'p' value of this association between EF and diastolic dysfunction is 0.689 and it is not significant (Table 5). This implies that abnormality of EF is not a significant feature of cirrhotic cardiomyopathy.

24 of the 30 cases had ascites. Of the 26 cases that had cirrhotic cardiomyopathy 24 cases had ascites. All the cases that had ascites showed features of cirrhotic cardiomyopathy. 2 cases without ascites also showed features of cirrhotic cardiomyopathy. 4 of the 30 cases did not show features of cirrhotic cardiomyopathy. All these 4 cases did not have ascites. The 'p' value of the association of ascites and cirrhotic cardiomyopathy is 0.0002 and it is significant (Table 6). This implies presence of ascites is a significant finding in cases who have cirrhotic cardiomyopathy.

DISCUSSION

In our study, various etiology of cirrhosis are HBV infection (12/30), HCV infection (1/30), PBC (1/30), NAFLD (10/30) and cryptogenic (6/30).We found that cirrhotic cardiomyopathy (26/30) is independent to the etiology and our results corresponds to the study done by Torregrosa M et al[19] and Lunzer et al[20].

In our study, females (18/22) and males(8/8) showed features of cirrhotic cardiomyopathy. Study reveals that sex distribution has no significance in cirrhotic cardiomyopathy and similar results found in study done by Liu et al[10].

In our study 33.3% of the cases were below 40 years and 66.7% of them are above 40 years. It was statistically significant and reveals cirrhotic cardiomyopathy is more prevalent in older individuals. Rabie et al[21] also found that similar correlation of elder age and diastolic dysfunction.

In our study, all the cases who presented with ascites had features of cirrhotic cardiomyopathy. This shows that presence of ascites correlates significantly with the presence of cirrhotic cardiomyopathy ('p'=0.0002). Wong et al[22] have found that diastolic dysfunction is a significant factor in the development of heart failure and may play a part in the pathogenesis of sodium fluid retention in cirrhosis and thus related to ascites. Lee et al[10] found that once cirrhosis is advanced to development of ascites, some degree of diastolic dysfunction is always present.

In our study 61.5% of the cases with cirrhotic cardiomyopathy had Class A cirrhosis and 38.5% had Class B cirrhosis. The severity of cirrhosis as based on CTP does not correlate with the presence of cirrhotic cardiomyopathy ('p'= 0.128). Bernardi et al[23] and Rabie et al[21] found positive correlation of cardiac dysfunction with Child Turcotte Pugh score. But in our study no such correlation was found.

Of the 22 females included in the study, 50% had QTc interval above 440 msec. Of the 8 males 62.5% had prolonged QTc interval. These findings show that sex is not a factor in influencing the prolongation of QTc interval in cirrhotics ('p'= 0.543). Bader Faiyaz Zuberi et al[24] found that QTc were significantly higher in cirrhotic patients as compared with non-cirrhotic controls. Lehman[25] found that prolonged QTc interval was seen more in female cirrhotics. But our study did not show any such correlation.

In our study 46.2% of the cases with E/A ratio below 1 had EDV above 90 and 53.8% of the cases with E/A ratio below 1 had EDV below 90. These findings indicate that end diastolic volume is not significant indicator of diastolic dysfunction ('p' = 0.885). Studies by Alexander Jacob et al[26] and Kelbaek et al[27]also shows similar findings. Rectar et al[28] found that the size of the left ventricle was normal in cirrhotics. However Laffi et al[29] found that left ventricular end diastolic volume is increased in cirrhotic patients.

In our study 7.7% of the cases with E/A ratio below 1 had ESV above 38. 25% of the cases with E/A ratio above 1 also had ESV above 38. These findings indicate that end systolic volume is not significant indicator of diastolic dysfunction ('p' = 0.282). Alexander Jacob et al and Kelbek et al also has similar findings. However, Laffi et al study found that left ventricular end systolic volume is increased in cirrhotic patients.

All the cases that had E/A ratio above 1 also had EF above 60. These findings indicate that ejection fraction is not significant indicator of diastolic dysfunction ('p' = 0.689). Alexander Jacob et al also shows

similar findings. As cardiac reserve is borderline in patients with cirrhosis, cardiovascular status should be carefully monitored in patients undergoing liver transplantation or portosystemic shunting procedures.

CONCLUSION

Non alcoholic Cirrhotic patients also have evidence of cirrhotic cardiomyopathy in the form of diastolic dysfunction and prolonged QTc interval. The severity of cirrhosis does not correlate with the presence of diastolic dysfunction. Prolongation of QTc interval is influenced by the sex of the cirrhotic individuals. Ventricular end diastolic volume, end systolic volume and ejection fraction are not significantly affected in cirrhotic individuals. Cirrhotic cardiomyopathy in these patients is independent of the etiology of cirrhosis and Ascites is a significant feature of all cases with diastolic dysfunction.

Tables

1. Association between Cirrhotic Cardiomyopathy and CTP class.

	Class A CTP score	Class B CTP score	Total
Cirrhotic cardiomyopathy Present	16 (61.5%)	10 (38.5%)	26 (86.7%)
Cirrhotic cardiomyopathy Absent	4 (100%)		4 (13.3%)
			P value = 0.128

2. Association between QTc interval and sex.

Sex	QTc above 440 msec	QTc below 440 msec	Total
Female	11 (50%)	11 (50%)	22 (73.3%)
Male	5 (62.5%)	3 (37.5%)	8 (26.7%)
Total	16 (53.3%)	14 (46.7%)	30 (100%)
			P value = 0.543

3. Association between Diastolic dysfunction and end diastolic volume.

	EDV > 90	EDV < 90	Total
Diastolic dysfunction present	12 (46.2%)	14 (53.8%)	26 (86.7%)
Diastolic dysfunction absent	2 (50%)	2 (50%)	4 (13.3%)
			P value = 0.885

4. Association between Diastolic dysfunction and end systolic volume.

	ESV > 38	ESV < 38	Total
Diastolic dysfunction present	2 (7.7%)	24 (92.3%)	26 (86.7%)
Diastolic dysfunction absent	1 (25%)	3 (75%)	4 (100%)
			P value = 0.282

5. Association between Diastolic dysfunction and Ejection fraction

	EF > 60	EF < 60	Total
Diastolic dysfunction present	25 (96.2%)	1 (3.8%)	26 (86.7%)
Diastolic dysfunction absent	4 (100%)		4 (13.3%)
			P value = 0.689

6. Association between Cirrhotic cardiomyopathy and Ascites.

	Ascites Present	Ascites absent	Total
Cirrhotic cardiomyopathy Present	24 (92.3%)	2 (7.7%)	26 (86.7%)
Cirrhotic cardiomyopathy Absent		4 (100%)	4 (13.3%)
			P value = 0.0002

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