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CARDIOVASCULAR DYSFUNCTION IN CIRRHOSIS AND ITS RELATION TO SEVERITY OF CIRRHOSIS.

General Medicine

Dr Waseem Ahmed MD Medicine, Currently pursuing DM Endocrinology, SKIMS, Soura, Srinagar.

Dr. Aakriti Mahajan MD Medicine, Senior Resident, Department of General Medicine, GMC Jammu.

Dr. Aabhasha Parotra* MD Medicine, Senior Resident, Department of General Medicine, Govt. Medical College, Jammu *Corresponding Author

Dr Adnan Lone Pursuing MD Medicine, SKIMS soura, Srinagar.

ABSTRACT

Liver cirrhosis is associated with a wide range of cardio vascular abnormalities. Cardiac dysfunction in patients with cirrhosis, contributes significantly to mortality and morbidity. Circulatory abnormalities are predominantly due to liver derived toxic factors causing arterial dilation and hyper dynamic circulation. The present prospective, observational cross-sectional study was conducted in the Department of Medicine, Government Medical College, Jammu for a period of one year, w.e.f 1st November 2020 to 31st October 2021 with the aim to analyse the cardiovascular dysfunction in cirrhosis and to determine its relation to severity of cirrhosis. A total of 100 patients were included in the study. Detailed clinical evaluation including history was recorded and required investigations and tests was done. Descriptive data was expressed as range and mean standard deviation with the help of SPSS software version 24. In the present study, there was a male predominance (81%) over females (19%). The male female ratio was 4.26:1. Most of the subjects belonged to the 41-60 years age group (n=48, 48%) followed by >60years age group (41%) and minimum subjects (11%) belonged to the 18-40 years age group. It was seen that 69% had alcohol as an aetiology, followed by hepatitis C (16%), HBV (10%), and Wilson disease (5%). The study concluded that Indian patients with cirrhosis do have diastolic dysfunction.

KEYWORDS

Cardiac dysfunction, Cardiovascular health, Liver cirrhosis, Hypertension and Comorbidity

INTRODUCTION

Liver cirrhosis is characterised by the presence of fibrosis and regeneration of nodules in liver whose consequences are development of portal hypertension and liver failure.[1] It is associated with a wide range of cardio vascular abnormalities.[2] Cardiac dysfunction in patients with cirrhosis, contributes significantly to mortality and morbidity.

The cardiovascular abnormalities were initially thought to be a manifestation of latent alcoholic cardiomyopathy. But in the mid-1980s, studies in non-alcoholic patients and in experimental animal models showed a similar pattern of blunted cardiac contractile responsiveness.[3] Thus these cardiovascular changes are now termed 'cirrhotic cardiomyopathy'.[4] The term "cirrhotic cardiomyopathy" describes impaired contractile responsiveness to stress diastolic dysfunction and electrophysiological abnormalities in patients with cirrhosis without known cardiac disease.[5]

Cirrhotic cardiomyopathy has been attributed to a cirrhotic proinflammatory state leading to increased cardiomyocyte apoptosis and shift in myosin heavy chain isoform from a subtype to the weaker b isoform. Circulatory abnormalities are predominantly due to liver derived toxic factors causing arterial dilation and hyper dynamic circulation.[6]

It is a syndrome characterised by systolic dysfunction (blunted increase in stress induced cardiac output with resting LVEF<55%), impaired diastolic relaxation (early (E) to late (A) ratio <1.0, prolonged deceleration time (>200ms)), prolonged isovolumetric relaxation time (>80ms), and electrophysiological disturbance such as prolonged QTc interval.[7]

It was observed that the liver transplantation results in clinical improvement and may cure cardiomyopathy. However, post transplantation prognosis depends on pre transplantation identification and management of cirrhosis with cardiomyopathy.[8]

Cardiac dysfunction in cirrhotics can pose significant morbidity and mortality in presence of stressful events like infections, TIPS and liver transplantation. Due to its diagnostic difficulties, increases awareness is important in preventing the complications of cirrhotic cardiomyopathy. Understanding the pathophysiological process of systolic dysfunction, diastolic dysfunction and electrophysiological abnormalities is crucial for further development of more accurate diagnostic tools and specific treatment. So present trial was undertaken to study cardiac dysfunction in liver cirrhosis and its relation to its severity.

AIMS AND OBJECTIVES

1. To study the cardiac changes in patients with chronic liver disease using echocardiography by evaluating LV systolic dysfunction, diastolic dysfunction, pulmonary artery pressures and hypertension.
2. To assess the correlation of cardiovascular dysfunction with the severity of liver cirrhosis.

MATERIAL AND METHODS

The present prospective, observational cross-sectional study was conducted in the Department of Medicine, Government Medical College, Jammu for a period of one year, w.e.f 1st November 2020 to 31st October 2021 after taking the approval from The Institutional Research Committee and The Ethical committee.

Inclusion criteria:

1. >18 years of age.
2. Patients diagnosed with chronic liver disease either newly diagnosed or follow up cases on the basis of characteristic clinical history and examination, liver biomarkers and USG abdomen and upper gastrointestinal endoscopy evidence of portal hypertension.

Exclusion criteria:

1. Patients suffering from other disease which are likely to affect LV function, such as; Clinical evidence of myocardial ischemia and effort angina, long standing diabetics and hypertensives, valvular heart diseases & ischemic heart disease

A total of 100 patients were included in the study after obtaining the informed consent. Diagnosis of cirrhosis of liver was done on basis of clinical examination, biochemical testing, serological and ultrasound imaging and upper GI endoscopy evidence of portal hypertension and esophageal varices. Detailed clinical evaluation including history about risk factors for chronic liver disease, history of hepatitis, alcohol consumption, diabetes mellitus, use of illicit drugs, transfusions, family history of liver disease, travel and presence of autoimmune disease was recorded. Investigations like complete blood count, liver function tests, renal function tests, coagulogram, ascitic fluid analysis, electrocardiography, upper GI endoscopy, chest X-Ray, 2D echocardiography was performed.

Descriptive data was expressed as range and mean standard deviation. SPSS software version 24 was used to analyse the data. Difference between two groups was determined using student t-test as well as chi square test and the level of significance was set at $p < 0.05$.

OBSERVATIONS & RESULTS

In the present study, of the total 100 subjects included in study, there was a male predominance (n=81, 81%) over females (n=19, 19%). The male female ratio was 4.26:1. Most of the subjects belonged to the 41-60 years age group (n=48, 48%) followed by >60years age group (n=41, 41%) and minimum subjects (n=11, 11%) belonged to the 18-40 years age group.

Figure 1, shows the results of aetiology of cirrhosis. It was seen that 69% had alcohol as an aetiology, followed by hepatitis C (16%), HBV (10%), and Wilson disease (5%).

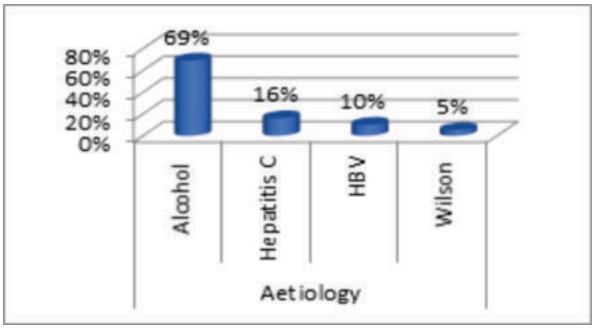

Figure 1. Aetiology of cirrhosis

It was seen that maximum subjects had a complaint of Ascites (87%), followed by pedal oedema (67%), disorientation (62%), constipation (58%), abdominal pain (51%), bleeding (46%), fever (44%), confusion (23%) and vomiting (22%). Among few patients the complaint of diarrhea (11%) and coma was observed (2%) as presented in figure 2.

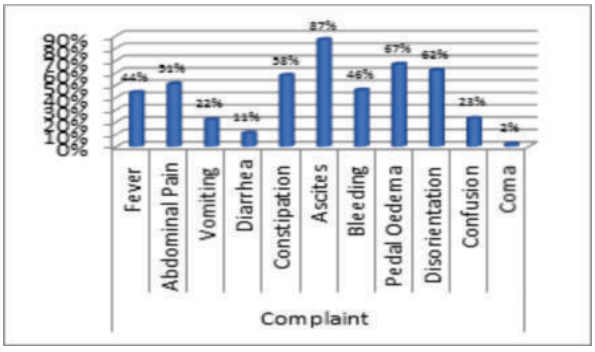

Figure 2. Presenting complaints

Figure 3 shows that maximum patients (49%) belong to Class B, 33% subjects were in Class A and only 18% subjects were in Class C.

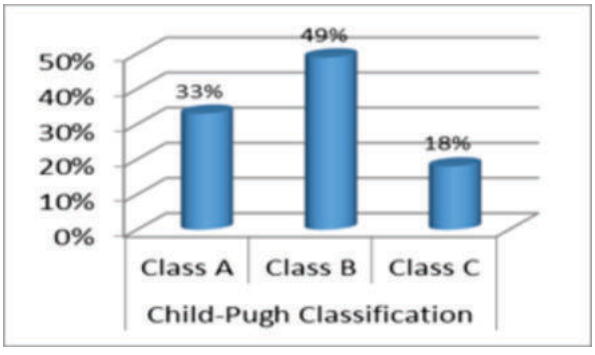

Figure 3. Child -Pugh Classification

Table 1 reported that mean ±SD of RBS (mg/dl) was 92.51±10.83, SGOT (IU/L was 74.16±31.28, SGPT (IU/L) was 37.62± 16.91, ALP (IU/L) was 187.24±76.58, INR was 1.77±0.38, Urea (mg/dl) was 11.13±2.19 and Creatinine (mg/dl) was 1.19±0.22.

Table 1 Laboratory investigations

Investigations	Mean	SD
RBS (mg/dl)	92.51	10.83
SGOT (IU/L)	74.16	31.28
SGPT (IU/L)	37.62	16.91
ALP (IU/L)	187.24	76.58
INR	1.77	0.38
Urea (mg/dl)	11.13	2.19
Creatinine (mg/dl)	1.19	0.22

Table 2. depicted the mean Echocardiographic data among study subjects, LVEDD (mm) was 50.2±4.9, LVESD (mm 30.5±5.4, LVEDV (ml) 113.6±32.5, IVS (mm) 9.1±1.4, PWDT (mm) 8.59±1.2, LAESV (ml/m2) 32.4±7.7, E/A ratio 1±0.4, DT (ms) 217.29±35.82, IVRT (ms) 73.8±16.1, EF (%) 60.87±4.4 and E lateral (cm/s) 11.39±2.6.

Table 2 Echocardiography

Variables	Mean	SD
LVEDD (mm)	50.2	4.9
LVESD (mm)	30.5	5.4
LVEDV (ml)	113.6	32.5
IVS (mm)	9.1	1.4
PWDT (mm)	8.59	1.2
LAESV (ml/m2)	32.4	7.7
E/A ratio	1	0.4
DT (ms)	217.29	35.82
IVRT (ms)	73.8	16.1
EF (%)	60.87	4.4
E lateral (cm/s)	11.39	2.6

In present study Echocardiographic data among the study subjects according to severity of cirrhosis was recorded. In Child Pugh A mean was LVEDD (mm) 51.7±4.2, LVESD (mm) 31.4±4.97, LVEDV (ml) 108.5±30.3, IVS (mm) 9±1.1, PWDT (mm) 8.47±1.8, LAESV (ml/m2) 33.81±7.2, E/A ratio 1.2±0.3, DT (ms) 223.38±34.81, IVRT (ms) 71.3±14.4, EF (%) 61.64±3.93 and E lateral (cm/s) 10.32±2.2. In Child Pugh B mean was LVEDD (mm) 49.4±4.1, LVESD (mm) 29.7±4.99, LVEDV (ml) 116.32±34.19, IVS (mm) 9.2±1.2, PWDT (mm) 8.71±0.99, LAESV (ml/m2) 31.69±8.4, E/A ratio 0.96±0.1, DT (ms) 229.13±36.07, IVRT (ms) 75.79±17.42, EF (%) 60.41±4.86 and E lateral (cm/s) 11.36±2.4. In Child Pugh C mean was LVEDD (mm) 48.2±4.4, LVESD (mm) 29.3±5.2, LVEDV (ml) 115.11±32.38, IVS (mm) 9.1±1.1, PWDT (mm) 8.82±1.4, LAESV (ml/m2) 31.55±8.3, E/A ratio 0.89±0.1, DT (ms) 229.34±35.18, IVRT (ms) 75.70±17.27, EF (%) 60.19±4.74 and E lateral (cm/s) 11.26±2.7. The mean E/A ratio was compared of Child Pugh A, Child Pugh B and Child Pugh C and it showed a statistically significant difference (p=0.043) as shown in table 3.

Table 3 Echocardiographic data among the study subjects according to severity of cirrhosis

Variables	Child Pugh A		Child Pugh B		Child Pugh C		p value
	Mean	SD	Mean	SD	Mean	SD	
LVEDD (mm)	51.7	4.2	49.4	4.1	48.2	4.4	0.13
LVESD (mm)	31.4	4.97	29.7	4.99	29.3	5.2	0.24
LVEDV (ml)	108.5	30.3	116.32	34.19	115.11	32.38	0.37
IVS (mm)	9	1.1	9.2	1.2	9.1	1.1	0.74
PWDT (mm)	8.47	1.8	8.71	0.99	8.82	1.4	0.42
LAESV (ml/m2)	33.81	7.2	31.69	8.4	31.55	8.3	0.27
E/A ratio	1.2	0.3	0.96	0.1	0.89	0.1	0.043*
DT (ms)	223.38	34.81	229.13	36.07	229.34	35.18	0.72
IVRT (ms)	71.3	14.4	75.79	17.42	75.70	17.27	0.21
EF (%)	61.64	3.93	60.41	4.86	60.19	4.74	0.35
E lateral (cm/s)	10.32	2.2	11.36	2.4	11.26	2.7	0.11

Diastolic dysfunction among the study subjects was recorded. 29 subjects were within normal range. 27 subject had Grade 1 Diastolic

dysfunction, 41 had Grade 2 and 3 subjects were of Grade 3. There was no subject with grade 4 Diastolic dysfunction as shown in figure 4.

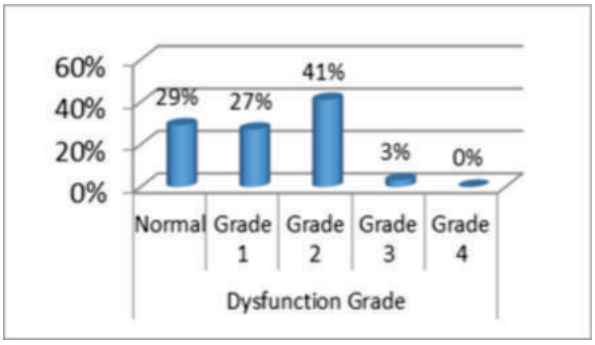

Figure 4. Diastolic dysfunction grades

Diastolic dysfunction among the study subjects according to severity of cirrhosis was recorded. 29 subjects were within normal range of them 27 were of Class A, 2 were of Class B. 27 subject had Grade 1 Diastolic dysfunction, of them 5 had Class A and 22 were of Class B. 41 had Grade 2 of them 1 was of Class A, 25 of Class B and 15 were of Class C. 3 subjects were of Grade 3 of them all 3 were of Class C. There was no subject with grade 4 Diastolic dysfunction. The p value was statistically significant (p= 0.005) as reported in table 4.

Table 4 Diastolic dysfunction among the study subjects according to severity of cirrhosis

Dysfunction Grade	N	Child-Pugh Classification			p value
		Class A	Class B	Class C	
Normal	29	27	2	0	0.005*
Grade 1	27	5	22	0	
Grade 2	41	1	25	15	
Grade 3	3	0	0	3	
Grade 4	0	0	0	0	

DISCUSSION

In the present study there was a male predominance and the male female ratio was 4.26:1. It may be because males are more prone to have habit of alcohol consumption compared to females, which is one of the major causes of liver cirrhosis. The most of the subjects belonged to the 41-60 years age group (n=48, 48%) followed by >60years age group (n=41, 41%) and minimum subjects (n=11, 11%) belonged to the 18-40 years age group. The result of present trial was in accordance to result of Chandey M et al., (2020), who found that cirrhosis was more common in males (91.1%) as compared to females (8.89%) and the maximum number of patients were in the age group of 41-60 years constituting 56.7% of the patients followed by age group of 18-40 years constituting 22.2% of the patients.[9]

It was seen that 69% had alcohol as an aetiology, followed by hepatitis C (16%), HBV (10%), and Wilson disease (5%). In a study done by Meena RK et al., (2019), similar findings were seen where 90.7% had alcohol as an aetiology, followed by hepatitis C (4%), HBV (4%), and Wilson disease (1.3%).[10]

It was seen that maximum subjects had a complaint of Ascites (87%), followed by pedal oedema (67%), disorientation (62%), constipation (58%), abdominal pain (51%), bleeding (46%), fever(44%), confusion (23%) and vomiting (22%). Among few patients the complaint of diarrhea (11%) and coma was observed (2%). These findings were similar in study done by Meena RK et al., (2019). According to study of Chandey M et al., (2020), most common clinical symptom with which patients presented was abdominal distention patients (37.78%), yellowish discoloration of eyes/urine (33.33%), malena (21.11%), abdominal pain (13.33%), fever (7.78%). Ascites (80.0%), pallor (66.67%), splenomegaly (54.44%), icterus and pedal edema (44.44% respectively) and hepatomegaly (17.78%).[10,9]

According to Child-Pugh classification, maximum patients (n=49) belong to Class B, 33 subjects were in Class A and only 18 subjects were in Class C. according to study done by Salari A et al., (2013), when subjects were classified according to Child-Pugh classification, Child A had 22 (22%) subjects, Child B had 38 (38%) and in Child C had 40 (40%) subjects.[11]

Liver and renal function tests results of subjects showed that mean ±SD of RBS (mg/dl) was 92.51±10.83, SGOT (IU/L was 74.16±31.28, SGPT (IU/L) was 37.62± 16.91, ALP (IU/L) was 187.24±76.58, INR was 1.77±0.38, Urea (mg/dl) was 11.13±2.19 and Creatinine (mg/dl) was 1.19±0.22. According to study done by Somani PO et al., (2014), mean ±SD of RBS (mg/dl) was85.7±4.6, SGOT (IU/L was 76.3±47.3, SGPT (IU/L) was 38.3±17.6, ALP (IU/L) was 193.3±81.2, INR was 1.8±0.4, Urea (mg/dl) was 11.3±2.7 and Creatinine (mg/dl) was 0.9±0.1.[12]

The mean Echocardiographic data among study subjects was LVEDD (mm) 50.2±4.9, LVESD (mm) 30.5±5.4, LVEDV(ml) 113.6±32.5, IVS (mm) 9.1±1.4, PWDT (mm) 8.59±1.2, LAESV (ml/m2) 32.4±7.7, E/A ratio 1±0.4, DT (ms) 217.29±35.82, IVRT (ms) 73.8±16.1, EF (%) 60.87±4.4 and E lateral (cm/s) 11.39±2.6. According to findings of Merli M et al., (2013) mean LVEDD (mm) 50.4±5.8, LVESD (mm) 30.4±6, LVEDV (ml) 114.2±34, PWDT (mm) 8.9±1.3, LAESV (ml/m2) 32.7±8.3, E/A ratio 1±0.3, DT (ms) 219.8±38.7, IVRT (ms) 74.7±17.4, EF (%) 61.2±4.8 and E lateral (cm/s) 11.6±2.9.[13]

In present study Echocardiographic data among the study subjects according to severity of cirrhosis was recorded. In Child Pugh A mean was LVEDD (mm) 51.7±4.2, LVESD (mm) 31.4±4.97, LVEDV (ml) 108.5±30.3, IVS (mm) 9±1.1, PWDT (mm) 8.47±1.8, LAESV (ml/m2) 33.81±7.2, E/A ratio 1.2±0.3, DT (ms) 223.38±34.81, IVRT (ms) 71.3±14.4, EF (%) 61.64±3.93 and E lateral (cm/s) 10.32±2.2. In Child Pugh B mean was LVEDD (mm) 49.4±4.1, LVESD (mm) 29.7±4.99, LVEDV (ml) 116.32±34.19, IVS (mm) 9.2±1.2, PWDT (mm) 8.71±0.99, LAESV (ml/m2) 31.69±8.4, E/A ratio 0.96±0.1, DT (ms) 229.13±36.07, IVRT (ms) 75.79±17.42, EF (%) 60.41±4.86 and E lateral (cm/s) 11.36±2.4. In Child Pugh C mean was LVEDD (mm) 48.2±4.4, LVESD (mm) 29.3±5.2, LVEDV (ml) 115.11±32.38, IVS (mm) 9.1±1.1, PWDT (mm) 8.82±1.4, LAESV (ml/m2) 31.55±8.3, E/A ratio 0.89±0.1, DT (ms) 229.34±35.18, IVRT (ms) 75.70±17.27, EF (%) 60.19±4.74 and E lateral (cm/s) 11.26±2.7. The mean E/A ratio was compared of Child Pugh A, Child Pugh B and Child Pugh C and it showed a statistically significant difference (p=0.043). The result of present study was in accordance to result of Merli M et al., (2013).[13]

Diastolic dysfunction among the study subjects according to severity of cirrhosis was recorded. 29 subjects were within normal range of them 27 were of Class A, 2 were of Class B. 27 subject had Grade 1 Diastolic dysfunction, of them 5 had Class A and 22 were of Class B. 41 had Grade 2 of them 1 was of Class A, 25 of Class B and 15 were of Class C. 3 subjects were of Grade 3 of them all 3 were of Class C. The p value was statistically significant (p= 0.005). So, it can be said that Diastolic dysfunction appeared to deteriorate as the severity of cirrhosis increased from Child A to Child C. According to study of Chandey M et al., (2020). In Child-Pugh class A 2(33%) patients had grade 1 diastolic dysfunction, in child Pugh class B 23(59%) patients had grade 1 diastolic dysfunction, whereas in child Pugh class C 3(7%) patients had grade 1 diastolic dysfunction, 33(73%) patients had grade 2 diastolic dysfunction and 1(2%) patients had grade 3 diastolic dysfunction with p value of 0.040 which is significant.[9]

CONCLUSION

The present study concluded that Indian patients with cirrhosis do have diastolic dysfunction. In the absence of other risk factors for cardiac disease, this dysfunction could be attributed only to cirrhotic cardiomyopathy. According to the relation between Child-Pugh score and diastolic dysfunction, we recommend cardiac assessment, especially echocardiographic evaluation in all Child B and Child C (decompensated) cirrhotic patients. Diastolic dysfunction, which is a major criterion of cirrhotic cardiomyopathy as measured by E/A ratio was proportional to the severity of liver cirrhosis.

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