Evaluation of cardiac functions of cirrhotic children using serum brain natriuretic peptide and tissue Doppler imaging

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ABSTRACT

Background : **Cirrhotic cardiomyopathy (CCM) is described as the presence of cardiac dysfunction in cirrhotic patients. In children with chronic liver disease, CCM has been very rarely investigated.**

The Aim of the Study : **Is to evaluate the cardiac function of cirrhotic children to identify those with CCM.**

Patients and Methods : **Fifty-two cirrhotic patients and 53 age and sex matched controls were assessed using serum brain-type natriuretic peptide (BNP), conventional echocardiography, and tissue Doppler imaging.**

Results : **Patients' mean ages were 7.66 ± 4.16 years (vs. 6.88 ± 3.04 years for the controls). The study included 27 males and 25 females (28 and 25 respectively for the controls). Patients had larger left atrium and right ventricle (RV) (*P* value 0.05) and increased LV posterior wall thickness than controls (*P* value 0.04). They had higher late atrial diastolic filling velocity (A) of tricuspid valve (TV) inflow (0.59 ± 0.17 vs. 0.5 ± 0.1 m/s, *P* < 0.001) and lower ratios between the early diastolic filling velocity (E) and A wave velocity (E/A) of both mitral valve and TV inflow (1.7 ± 0.35 vs. 1.87 ± 0.34 and 1.3 ± 0.3 vs. 1.5 ± 0.3, *P* < 0.005 and 0.0008, respectively). Patients had significantly longer isovolumic relaxation time of LV (45.5 ± 11.1 vs. 40.5 ± 7.7 ms *P* 0.008), higher late diastolic peak myocardial velocity (A′) (11.8 ± 3.6 vs. 9.5 ± 2.7 ms, *P* 0.0003) and systolic velocity (S′) of the RV (14.5 ± 2.7 vs. 13.2 ± 2.9, *P* 0.01) and significantly higher myocardial performance index of both LV and RV (*P* 0.001 and 0.01). BNP levels were significantly higher in cases than controls (5.25 ng/l vs. 3.75 ng/l, *P* < 0.04) and was correlated with the E wave velocity of the TV (*r* 0.004) and the E/E′ ratio of the RV (*r* 0.001). None of the clinical or laboratory data were correlated with the BNP level.**

Conclusion : **Cirrhotic children have cardiac dysfunction mainly in the form of diastolic dysfunction. There is a need that CCM be more accurately described in children.**

Keywords : Brain-type natriuretic peptide, cirrhotic cardiomyopathy, liver cirrhosis, tissue Doppler imaging

INTRODUCTION

Cirrhosis is associated with an increased risk for the development of cardiovascular diseases. Decreased

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systemic vascular resistance, increased cardiac output, and abnormal myocardial contractile function are the characteristic features and likely to appear as consequences of cirrhosis. The functional and structural changes of the myocardium have been referred as cirrhotic cardiomyopathy (CCM), a slow progression of myocardial dysfunction associated with cirrhosis.[1] It is defined as cardiac dysfunction in patients with cirrhosis characterized by impaired contractile responsiveness to stress and/or altered diastolic relaxation with electrophysiological abnormalities in the absence of other known cardiac disease. Diagnostic criteria included: Systolic dysfunction (blunted increase in cardiac output with exercise, volume challenge or pharmacological stimuli and resting ejection fraction [EF] <55%), diastolic dysfunction (E/A ratio <1.0, prolonged deceleration time (Dt) >200 ms, prolonged isovolumetric relaxation time, >80 ms), and other supportive criteria (electrophysiological abnormalities, abnormal chronotropic response, electromechanical uncoupling or dyssynchrony, prolonged Q-T interval, enlarged left atrium (LA), increased myocardial mass, increased brain-type natriuretic peptide (BNP) and pro-BNP, and increased troponin I).[2]

Not all of the above are necessary to make a diagnosis.[3] Although this cardiac dysfunction due to hepatic disease is not yet finally classified and its mechanisms are not fully understood, early detection of this condition is perhaps important.[4] This cardiac dysfunction may affect the prognosis of the patients and aggravate the course during invasive procedures such as surgery, insertion of a transjugular intrahepatic portosystemic shunt, and liver transplantation.[5]

BNP has been recently used in the differential diagnosis and follow-up of patients with heart failure. It is a neurohormone released by the ventricular myocytes and plays a key role in volume homeostasis.[6]

Plasma BNP level is a sensitive indicator of ventricular dysfunction both in symptomatic and asymptomatic patients and its plasma concentration increases with volume and pressure overload in patients with heart failure.[7]

Several studies have shown increased plasma levels of BNP in some patients with cirrhosis, and these findings may suggest cardiac dysfunction.[8] In addition to the left ventricular (LV) systolic dysfunction, plasma BNP levels have been suggested to be significantly associated with diastolic stage (including newer echocardiographic parameters as tissue Doppler imaging (TDI) and color M-mode propagation velocity) and right ventricle (RV) functions as well.[9]

We sought to determine whether children with cirrhosis and without heart failure have compromised myocardial function detectable in the resting stage. Thus, the objective of our study was to evaluate the serum level of BNP and its relationship with clinical, laboratory, echocardiographic, and TDI functions in cirrhotic children in an attempt to diagnose pediatric CCM.

PATIENTS AND METHODS

The design was a case control observational study, including 52 consecutive ambulatory and hospitalized patients with cirrhosis concomitantly with 53 controls matched for age and sex. These controls were volunteers, friends, or neighbors of the patients or workers or nurses in the hospital.

They were matched prospectively for age, gender, and BMI. Full physical examination including cardiac examination and blood pressure measurement, as well as echocardiography was performed before recruiting them to ensure that they do not have an underlying cardiac problem. The diagnosis of cirrhosis was established through a combination of biochemical, clinical, liver biopsy, and ultrasonographic findings. Patients with congenital and other acquired heart diseases were excluded from the study. Informed consent was obtained from all included patients and controls. The study was approved by the Institutional Ethical Committee.

Clinical evaluation

On the day of the study, heart rate and blood pressure were measured. Patients provided a detailed clinical history and had a thorough clinical examination and blood tests (including hematologic and biochemical profile). Patients were classified as with compensated or decompensated cirrhosis based on the absence or presence of ascites, esophageal varices and hepatic encephalopathy. Therapies administered in the last weeks were recorded. All the controls were subjected to detailed history taking and full clinical examination with thorough cardiac examination.

Echocardiography

Echocardiography was performed for all cases and controls in the supine, left lateral position using General Electric (GE, Vivid-5) system with probe 3 or 5 MHz (multi-frequency transducer) according to the age of patient, having tissue velocity imaging capabilities. The electrocardiography cable was connected to the ultrasound machine to define and to time the cardiac cycle events. The examination was performed by a pediatric cardiologist who had expert in echocardiography and TDI in accordance with the recommendations of the American Society of Echocardiography.[10] The echocardiographer was not blind to patients versus controls. The examination consisted of M-mode, two-dimensional, pulsed-wave, and color Doppler blood flow velocity measurements of the heart valves. LV fractional shortening (FS) and EF were calculated.

Trans-mitral and trans-tricuspid flows were obtained with pulsed wave Doppler at the leaflet tips; early diastolic inflow velocity (E), velocity during active atrial contraction(A), E to A wave (E/A) ratio, and Dt were measured.

TDI was obtained from the four chambers apical view, and tissue velocities were calculated. Using pulsed tissue velocity indices, the sample volumes were placed in the lateral sides of the mitral and tricuspid annuluses and the base of the interventricular septum. The peak systolic and early and late diastolic velocities (E' and A', respectively) at these points were measured, and the E/E' ratio was calculated. The isovolumic relaxation time (IVRT) and isovolumic contraction time (IVCT) were both measured for both LV and RV lateral walls.

Calculation of global myocardial performance index (MPI index) was performed by pulsed tissue velocity imaging. For tissue Doppler, all interval measurements were performed within one cardiac cycle. The MPI index was calculated a′–b′/b′ where a′ is the time interval from the end of A' wave to the onset of E' wave and b′ the time from the onset to the end of the S' wave.

To reduce the effect of respiration on tissue velocities and as breath holding was not applicable in young children, three cardiac cycles were, recorded, and the average velocity was calculated. To reduce intraobserver variability three different measurements for each tissue Doppler index was done and the average was taken.

Laboratory investigations

Routine laboratory for the cases included: Complete blood count, prothrombin time, and prothrombin concentration (PT and PC) and the International Normalized Ratio (INR), biochemical liver function tests: Alanine aminotransferase, aspartate aminotransferase (AST), alkaline phosphatase (ALP), total and direct bilirubin, and serum albumin.

Measurement of brain natriuretic peptide level

Blood sample was withdrawn from each patient and collected in a plain tube, left to clot for 10-20 min. at room temperature before centrifugation for 10 min at the speed of 2000-3000 rounds/min. The serum was separated stored at –20°C till the time of assay for serum BNP. BNP measurement was performed using quantitative enzyme linked immunosorbent assay using kit supplied by WKEA Med Supplies Corp (China).

Statistical methods

The SPSS 15.0 for windows (SPSS Inc., Chicago, IL, USA) was used for data management and analysis and the Microsoft power point for charts. Parametric quantitative data were presented as a mean ± standard deviation. For comparison of *t* three groups' means, one-way analysis of variance was used followed by *post hoc* test. Nonparametric quantitative data were expressed as median (range), Kruskall–Wallis and Mann–Whitney tests were used for comparison of medians. Correlation between quantitative variables was done applying Pearson ranked correlation test (for parametric data) and Spearmen ranked correlation test (for non-parametric data). Qualitative data was expressed as frequency and percentage. The diagnostic performance of serum BNP was evaluated using the receiver operating characteristics (ROC) curve, in which sensitivity was plotted on the Y-axis and 100-specificity on the X-axis. *P* value was considered significant at 0.05.

RESULTS

The baseline characteristics of the included patients are shown in Table 1.

The cases and controls were age and sex matched. Patient's mean ages were 7.66 ± 4.16 years (vs. 6.88 ± 3.04 years for the controls, *P* 0.3). The study included 27 males and 25 females versus 28 males and 25 females for the controls. The *P* value between the mean age of cases and controls was 0.3 while between the numbers of male patients was 0.4, and the number of female patients was 0.3.

The patients had significantly dilated LA, RV, and pulmonary artery (PA) diameters and increased LV posterior wall thickness than controls. They also had significantly lower E/A (of both mitral and tricuspid inflow) and higher A wave of the tricuspid inflow as shown in Table 2.

TDI showed that patients had significantly longer IVRT (*P* value 0.008) and shorter IVCT of the LV (*P* value 0.03). They also had higher late diastolic peak myocardial velocity (A') and systolic velocity (S') of the RV (*P* value of 0.0003 and 0.01, respectively) and shorter IVCT of the RV (*P* value 0.02). The patients also had

Table 1: Baseline characteristics of patients included in the study (original)

Categorical variables	Frequency	Percentage
Sex		
Males	27	51.9
Females	25	48.1
Underlying liver pathology		
Chronic hepatitis	10	19.2
Extrahepatic biliary atresia	6	11.5
Autoimmune hepatitis	5	9.5
Wilson's disease	1	1.9
α-1 antitrypsin deficiency	1	1.9
Cryptogenic cirrhosis	29	55.8
Disease state		
Compensated	34	65.4
Decompensated	18	34.6
Continuous variables	Mean±SD	
Age (years)	7.66±4.16	

SD: Standard deviation

higher septal A' velocity (*P* value 0.0001), lower septal E' velocity (*P* value 0.04) and higher septal S' velocity (*P* value 0.001) than controls. MPI index of both LV and RV was significantly higher in cases than controls (*P* value 0.0001 and 0.0001) denoting global cardiac dysfunction. Table 3 shows the comparison between cases and controls regarding the tissue Doppler indices.

Patients had a significantly higher level of BNP as shown in Figure 1. The median level of BNP in patients was 5.25 ng/L (range 1-168) versus 3.75 ng/L (0-110) in controls (*P* value 0.04). Figure 2 showed the ROC curve for BNP cut-off among cases and controls.

There was no significant correlation between BNP level and the clinical and laboratory findings of our patients, as shown in Table 4, and there was no significant correlation also between BNP level and etiology of liver cirrhosis. BNP levels were significantly correlated with the E wave velocity of the TV inflow as shown in Table 5 and with E/É wave of TV as shown in Table 6.

The patients with decompensated liver cirrhosis had significantly lower systolic blood pressure and higher heart rate (*P* value 0.02 and 0.03, respectively). Patients with decompensated liver disease had significantly larger RV diameter, increased IVS thickness, and shorter Dt of the tricuspid inflow as shown in Table 7. TDI results showed no significant difference between both groups of patients [Table 8]. There was no significant difference between the median levels of the BNP in both groups (*P* value 0.4).

DISCUSSION

Most patients with stable liver disease have subtle myocardial impairment that is not or less apparent on routine examination. However, with progression of the liver disease or under physiological or pharmacological strain, the cardiac failure becomes manifest.[11] During the last years several studies have focused their attention on the presence of specific cardiac abnormalities in cirrhotic patients.

In this cross-sectional study, we evaluated the cardiac functions of 52 cirrhotic children using both conventional echocardiography and TDI in addition to serum BNP level. We found that our patients had significantly larger LA, RV, and PA diameters and increased LVPW as reported by other investigators' studies.[10,12] The

Table 2: Comparison between echo findings (M-mode dimensions and Doppler indices between patients and controls)

Parameter	Patients (*n* = 52) Mean ± SD	Controls (*n* = 53)	*P*
AO (mm)	20.1 (4.6)	18.8 (3.4)	0.13
LA (mm)	24.8 (4.9)	22.79 (3.3)	0.01*
RV (mm)	14 (3.6)	12.5 (2.6)	0.02*
PA (mm)	17.7 (4.4)	16.2 (3.4)	0.04*
LVPW (mm)	5.8 (1.4)	5.4 (1.1)	0.04*
IVS (mm)	6.1 (1.3)	5.6 (1.1)	0.14
LVEDD (mm)	36.4 (6.6)	34.8 (4.5)	0.15
LVESD (mm)	22 (4.8)	20.6 (3.6)	0.09
EF percentage	71.3 (7.2)	71 (8.6)	0.85
FS percentage	41.2 (6.5)	41.7 (7.7)	0.71
MV			
E (m/s)	1.1 (0.19)	1.1 (0.15)	0.26
A (m/s)	0.65 (0.14)	0.61 (0.26)	0.35
E/A	1.7 (0.35)	1.87 (0.34)	0.005**
DT (ms)	127.2 (51.66)	138.7 (25.7)	0.16
TV			
E (m/s)	0.75 (0.17)	0.73 (0.13)	0.09
A (m/s)	0.59 (0.17)	0.5 (0.1)	0.001*
E/A	1.3 (0.3)	1.5 (0.3)	0.0008**
DT (ms)	148.3 (69.5)	146.7 (49.8)	0.89

AO: Aorta, LA: Left atrium, PA: Pulmonary artery, RV: Right ventricle, IVS: Interventricular septum, LVPW: Left ventricular posterior wall, LVEDD: Left ventricle end diastolic diameter, LVEDS: Left ventricle end systolic diameter, EF: Ejection fraction, FS: Fractional shortening, MV: Mitral valve, E: E wave velocity, A: A wave velocity, E/A: E/A ratio, Dt: Deceleration time, TV: Tricuspid valve, SD: Standard deviation, *P* value considered significant if <0.05

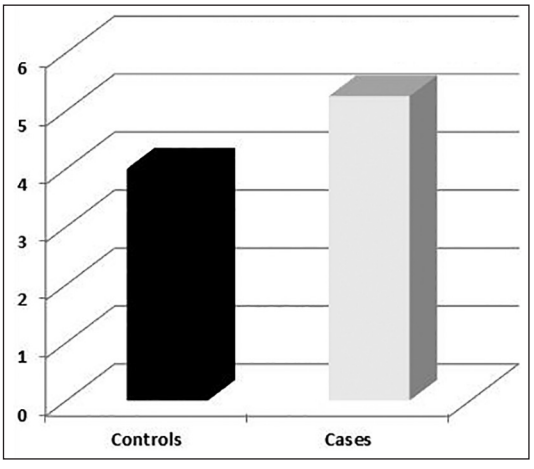

Figure 1: Comparison between patients and controls regarding the brain-type natriuretic peptide level

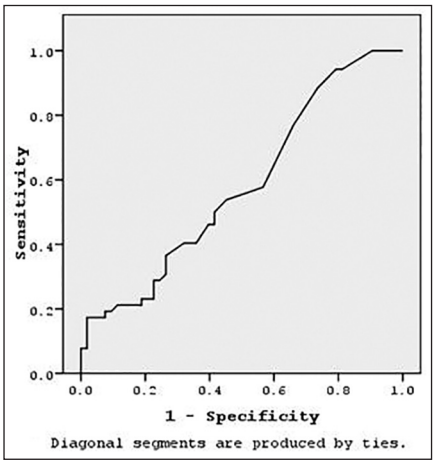

Figure 2: Receiver operating characteristics curve for brain-type natriuretic peptide cut-off among patients and controls. At a cut-off value of brain-type natriuretic peptide of 4.25 ng/l; sensitivity was 53.8%, and specificity was 45.3%

Table 3: Comparison between tissue Doppler indices for patients and controls

Parameter	Mean ± SD		*P*
	Patients (*n* = 52)	Controls (*n* = 53)	
LV			
Á (cm/s)	7.7 (2.3)	6.9 (1.9)	0.08
É (cm/s)	16.94 (3.98)	18.19 (3.31)	0.16
Ś (cm/s)	9.4 (2.4)	8.9 (2.3)	0.26
E/É	6.68 (2.14)	6.01 (1.39)	0.07
IVRT (ms)	45.5 (11.1)	40.5 (7.7)	0.008**
IVCT (ms)	41.7 (8.7)	45.9 (10.8)	0.03**
MPI index	0.36 (0.09)	0.3 (0.04)	0.001
RV			
Á (cm/s)	11.8 (3.6)	9.5 (2.7)	0.0003**
É (cm/s)	17.67 (3.9)	17.65 (3.5)	0.76
Ś (cm/s)	14.5 (2.7)	13.2 (2.9)	0.01*
E/É	4.53 (1.7)	4.28 (1.25)	0.29
IVRT (ms)	40.4 (9.6)	37.4 (7.9)	0.08
IVCT (ms)	42.2 (9.4)	46.8 (10.2)	0.02*
MPI index	0.32 (0.06)	0.3 (0.034)	0.01*
Septum			
Á (cm/s)	7.38 (2.1)	5.9 (1.3)	0.0001*
É (cm/s)	13.4 (2.5)	14.4 (2.6)	0.04*
Ś (cm/s)	8.7 (2.5)	7.4 (1.3)	0.001**

LV: Left ventricle, RV: Right ventricle, IVRT: Isovolumetric relaxation time, IVCT: Isovolumetric contraction time, MPI: Myocardial performance index, Ś: Systolic myocardial velocity, É and Á: Early and late diastolic myocardial velocities, SD: Standard deviation, *P* value considered significant if <0.05

Table 4: Correlation between BNP values and the clinical and laboratory data of patients

Parameter	*r*	*P*
Age (months)	−0.024	0.9
Liver (cm)	0.106	0.5
Spleen (cm)	0.050	0.7
BP (systolic)	0.082	0.5
BP (diastolic)	0.084	0.5
HR (beat/min)	0.084	0.5
ALT (U/L)	−0.140	0.3
AST (U/L)	−0.260	0.06
GGT (U/L)	−0.147	0.3
ALB (g/dl)	0.023	0.9
ALP (U/L)	−0.238	0.09
PT (s)	−0.134	0.3
PC (%)	0101	0.5
INR	−0.005	0.9

BP: Blood pressure, HR: Heart rate, ALT: Alanine transferase, AST: Aspartate transferase, GGT: Gamma glutamine tranferase, ALB: Albumin, ALP: Alkaline phosphatase, PT: Prothrombin time, PC: Prothrombin concentration, INR: International Normalized Ratio, BNP: Brain-type natriuretic peptide

Table 5: Correlation between BNP values and echo parameters (M-mode dimensions and Doppler indices) of patients

Parameter	*r*	*P*
AO (mm)	−0.036	0.8
LA (mm)	−0.072	0.6
RV (mm)	−0.074	0.6
PA (mm)	−0.032	0.8
IVS (mm)	−0.082	0.5
PW (mm)	−0.141	0.3
EDD (mm)	0.150	0.3
ESD (mm)	0.127	0.4
EF percentage	−0.062	0.6
FS percentage	−0.120	0.4
MV		
E (m/s)	−0.075	0.6
A (m/s)	0.583	0.3
E/A	0.144	0.1
DT (ms)	0.213	0.2
TV		
E (m/s)	0.398	0.004*
A (m/s)	0.046	0.8
E/A	0.169	0.2
DT (ms)	−0.124	0.4

P value considered significant if <0.05

Table 6: Correlation between BNP values and tissue Doppler parameters of cases

Parameter	*r*	*P*
LV		
É (m/s)	−0.124	0.4
Á (m/s)	0.114	0.4
Ś (m/s)	−0.021	0.9
E/É	−0.036	0.8
IVRT (ms)	0.024	0.9
IVCT (ms)	−0.037	0.8
MPI index	−0.086	0.5
RV		
É (m/s)	−0.084	0.5
Á (m/s)	−0.248	0.08
Ś (m/s)	0.108	0.4
E/É	0.525	0.001*
IVRT (ms)	−0.056	0.6
IVCT (ms)	−0.086	0.5
Tie index	−0.147	0.6
Septum		
É (m/s)	−0.061	0.7
Á (m/s)	0.130	0.4
Ś (m/s)	−0.074	0.6

LV: Left ventricle, RV: Right ventricle, IVRT: Isovolumetric relaxation time, IVCT: Isovolumetric contraction time, MPI: Myocardial performance index, Ś: Systolic myocardial velocity, É and Á: Early and late diastolic myocardial velocities, BNP: Brain-type natriuretic peptide, *P* value considered significant if <0.05

systolic functions of our patients were not affected when assessed by FS and EF which were within normal limits. Systolic peak velocity of the LV measured by TDI was not reduced which could be attributed to the hyperdynamic status accompanying cirrhosis. The E/A ratio of both mitral and TVs inflow were significantly lower in cases than controls and the IVRT was significantly longer. The underlying mechanism of diastolic dysfunction in cirrhosis is likely due to the increased myocardial wall stiffness caused by myocardial hypertrophy, fibrosis and subendothelial edema, and subsequently resulting in high filling pressures of the left ventricle and atrium.[11] Combining TDI with Doppler indices by using parameters as E/E' allows refining the criteria required to detect patients with diastolic dysfunction especially for those with hyperdynamic state accompanying liver cirrhosis.

The MPI which reflects both the global; systolic and diastolic, function of the heart[13] was significantly higher in cases than controls denoting global cardiac dysfunction.

Table 7: Comparison between compensated and decompensated patients regarding the M-mode and Doppler indices

Parameter	Mean ± SD		*P*
	Compensated (*n* = 34)	Decompensated (*n* = 18)	
AO (mm)	20.5 (4.8)	19.3 (4.1)	0.38
LA (mm)	24.7 (4.11)	25.2 (6.4)	0.8
RV (mm)	14.7 (3.8)	12.8 (2.9)	0.05*
PA (mm)	18.1 (4.5)	16.9 (4.2)	0.37
PW (mm)	6.3 (1.4)	5.9 (1.2)	0.29
IVS (mm)	6.1 (1.4)	5.3 (1.1)	0.04*
EDD (mm)	36.1 (6.4)	36.9 (7.2)	0.65
ESD (mm)	21.8 (4.9)	22.5 (4.6)	0.6
EF percentage	71.5 (8.3)	70.9 (4.7)	0.8
FS percentage	42 (74)	39.6 (3.98)	0.2
LV			
E (m/s)	1.09 (0.2)	1.01 (0.13)	0.1
A (m/s)	0.64 (0.13)	0.66 (0.2)	0.6
E/A	1.7 (0.36)	1.6 (0.33)	0.2
DT (ms)	138.1 (45.9)	104.1 (57.1)	0.02*
RV			
E (m/s)	0.75 (0.18)	0.76 (0.2)	0.89
A (m/s)	0.54 (0.14)	0.64 (0.22)	0.2
E/A	1.4 (0.28)	1.3 (0.32)	0.2
DT (ms)	156.3 (60.9)	131.3 (84.6)	0.2

AO: Aorta, LA: Left atrium, PA: Pulmonary artery, RV: Right ventricle, IVS: Interventricular septum, LVPW: Left ventricular posterior wall, EF: Ejection fraction, FS: Fractional shortening, MV: Mitral valve, E: E wave velocity, A: A wave velocity, E/A: E/A ratio, Dt: Deceleration time, TV: Tricuspid valve, SD: Standard deviation, PW: Pulsed wave, EDD: End diastolic dimension, ESD: End systolic dimensions, *P* value considered significant if <0.05

Table 8: Comparison between the compensated and decompensated patients regarding the tissue Doppler indices (original)

Parameter	Compensated (*n* = 34) mean ± SD	Decompensated (*n* = 18) mean ± SD	*P*-value
LV			
Á (m/sec)	7.7(2.02)	7.7(2.8)	0.9
É (m/sec)	17.1(3.96)	16.6(4.1)	0.7
Ś (m/sec)	9.5(2.5)	9.3(2.4)	0.8
E/É	0.067(0.02)	0.07(0.02)	0.7
IVRT (msec)	45.9(11.2)	44.8(10.96)	0.7
IVCT (msec)	40.5(8.6)	43.9(8.6)	0.2
Tie index	0.35(0.1)	0.37(0.09)	0.6
RV			
Á (m/sec)	11.97(3.4)	11.5(4.1)	0.7
É (m/sec)	18(4.1)	17.05(3.4)	0.4
Ś (m/sec)	14.5(2.5)	14.6(3.2)	0.89
E/É	0.04(0.01)	0.04(0.02)	0.4
IVRT (msec)	40.2(9.1)	40.8(10.7)	0.8
IVCT (msec)	42.4(9.5)	41.9(9.4)	0.8
Tie index	0.32(0.05)	0.3(0.07)	0.5
Septum			
Á (m/sec)	7.3(1.5)	7.5(2.9)	0.8
É (m/sec)	13.5(2.6)	13.1(2.3)	0.57
Ś (m/sec)	8.6(2.2)	9(3)	0.5

LV: left ventricle, RV: right ventricle, IVRT: Isovolumetric relaxation time, IVCT: Isovolumetric contraction time, MPI: myocardial performance index, Ś: systolic myocardial velocity, É & Á: early and late diastolic myocardial velocities

Decompensated patients in our study had dilated RV and more IVS thickness than compensated patients which can be attributed to the prolonged volume overload. They also had statistically longer DT which implies evidence of LV diastolic dysfunction in this group of patients. TDI showed no significant difference between compensated and decompensated cirrhotic patients; a finding that was also reported by other investigators.[13,14]

The BNP level was significantly higher in cirrhotic patients than controls and this was also reported by others[8,12,15,16] but the state of liver disease whether compensated or not did not affect its level. Other investigators reported association between the level of BNP and pro-BNP and the severity of lever disease.[8,15,16]

In this study, serum BNP level was correlated with E wave velocity of TV inflow and E/A ratio of RV. Other studies had demonstrated correlations with different parameters as PW thickness,[8,10,12] DT, and EDD,[12] as well as IVS.[8] To the best of our knowledge, no studies had correlated between BNP and TDI in pediatric patients with liver cirrhosis.

There is difficulty in applying the current diagnostic criteria for diagnosing CCM in the pediatric age group. There is not enough data regarding how much of these criteria are required for diagnosis. Systolic functions are usually preserved till very late in the course, so it cannot be counted on for early diagnosis. Our patients may have had better cardiac reserves that might mask the manifestations of CCM more than the in adults, especially those with cardiovascular risk factors. Not enough data about the normal range of BNP in children. These factors made the application of the diagnostic criteria not so much convenient for use in children.

Limitations of the study included

Lack of data concerning long-term follow-up and progression of the patient condition. Our patients were at different stages of diuresis and intravascular volume status which was another limitation of our study. Another limitation was the inability to perform blinded echocardiographic examination to patients versus controls.

CONCLUSION

Cirrhotic children might have cardiac dysfunction in the absence of other known cardiac disease; that might be labeled as genuine "cirrhotic cardiomyopathy." Currently, there is no single diagnostic tool that can help to identify patients with CCM. The use of TDI offers a better tool for early detection of both diastolic and global cardiac dysfunction. BNP is a useful marker of cardiac dysfunction yet it could not be correlated with specific clinical or laboratory findings and still further studies are required to correlate it with echocardiographic findings. There is a need that the entity CCM be more accurately described particularly in children.

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Conflicts of interest

There are no conflicts of interest.

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