ORIGINAL RESEARCH

Evaluation of electrocardiographic changes in patients with cirrhosis and their correlation with severity of disease

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ABSTRACT

Background: Cirrhotic cardiomyo pathy (CCM) is a distinct heart condition closely associated with liver damage. It involves impaired ventricular function, prolonged ventricular depolarization, and an inadequate response to stress. The study aimed to examine the prevalence of electrocardiographic (ECG) changes in cirrhotic patients and explore their potential correlation with liver disease severity, as evaluated by Child Turcotte Pugh (CTP) class and model for end-stage liver disease (MELD) scores.

Methods: This cross-sectional study was conducted on 50 patients of liver cirrhosis (compensated and decompensated), who attended emergency/outpatient services of Guru Nanak Dev Hospital, Amritsar. Electrocardiography findings were assessed using a 12 lead ECG. Compar isons between groups was performed using student t test for continuous variables and chi square and ANOVA test for categorical variables. Pearson's coefficient of correlation (r value) is used to assess the correlation between two variables.

Results: Seventy two percent patients had sinus tachycardia, 74% had QTc prolongation, 34% had low voltage QRS. Only 2 patients had normal ECG while all others had some ECG changes. The heart rate and QTc interval, increased progressively with increasing CTP class (P<0.001) and low voltage QRS and increased QTc correlated positively with increasing MELD scores (P<0.05).

Conclusion: Our results show that QTc prolongation and low voltage QRS are significantly related to liver cirrhosis severity as assessed by its relation with CTP and MELD score and that these ECG changes are present in higher frequency in patients having complications of decompensated liver cirrhosis like ascites and hepatic encephalopathy.

Keywords: Cirrhosis, Electrocardiography, Cirrhotic cardiomyopathy.

INTRODUCTION

Cirrhotic cardiomyopathy (CCM) was first defined in 1953, as a separate entity in the spectrum of heart conditions, strictly related to liver damage.[1] Since then, clinical and experimental trials have defined CCM as chronic cardiac dysfunction associated with liver cirrhosis, in patients without heart disease, irrespective of the etiology of cirrhosis.[2] From a physio-pathological perspective, CCM is characterized by a hyperdynamic state, with both diastolic and systolic ventricular dysfunction, prolonged ventricular depolarization and an inappropriate chronotropic response to stress.[2-4]Several toxins have been implicated in cardiac dysfunction in cirrhosis. The prevalence of CCM is difficult to determine, mainly because the condition remains asymptomatic for a long time in the evolution of cirrhosis.[5] On the other hand, signs and symptoms of heart failure may resemble those of decompensated cirrhosis, making a differential diagnosis very difficult.[6] The current proposed criteria include assessment of systolic dysfunction (a left ventricle ejection fraction of less than 50%) and several signs of diastolic dysfunction (low septal e' velocity, high E/e' ratio, high indexed volume of left atrium and high velocity of tricuspid regurgitation), while ECG modifications, MRI aspects and biomarkers are considered to add supportive information for the diagnosis .Electrocardiography (ECG) is the first indicator of CCM. The most commonly encountered

ECG pattern in CCM is a prolonged QT interval.[3] This occurs in more than half of cirrhotic patients and may lead to ventricular arrhythmias and sudden death.[7] Possible explanatory mechanisms for prolonged QT interval include dysfunction of membrane potassium channels and a hyper-reactivity of the sympathetic–adrenergic discharges, causing down-regulation of beta-adrenergic receptors.[8] Low-voltage ECG is also frequent in cirrhotic patients and has been associated with a higher mortality risk in patients without prior cardiovascular diseases.[9] Newer ECG markers for arrhythmogenesis include the T-peak to T-end interval (Tpe) and the T p e/QT ratio.[10]This study was conducted to investigate the frequency of electrocardiographic changes in cirrhotic patients and to further investigate whether these changes (QT-prolongation and or low-voltage QRS pattern) have any correlation to the severity of liver disease as assessed by Child Turcotte Pugh (CTP) class and model for end-stage liver disease (MELD) scores.

METHODS

This was a cross-sectional study conducted at the Guru Nanak Dev Hospital, Amritsar. A total of 50 patients of liver cirrhosis were enrolled in this study. The patients were explained in their vernacular language about the procedures to be adopted in the study and there written informed consent was taken. The study was carried out after seeking permission from Institutional Ethics Committee. Patients who had features suggestive of cirrhosis on ultrasonography (coarse echotexture and nodularity in liver, ascites, splenomegaly, features suggestive of portal hypertension), or patients who presented with complications of cirrhosis (hepatic encephalopathy or variceal bleeding) were included in the study. Patients with COVID-19 infection, hepatocellular carcinoma, cardiovascular disease, type 1 or 2 diabetes mellitus, electrolyte abnormalities, and renal failure not attributable to cirrhosis were excluded from the study. A detailed history, clinical examination and laboratory investigation was performed. Electrocardiography findings were assessed using a 12-lead electrocardiograph. CTP score and MELD score was calculated. Patients with cirrhosis and without ascites, varices and encephalopathy were considered as compensated cirrhosis and patients with cirrhosis and ascites, variceal bleed and encephalopathy were considered as decompensated cirrhosis. The data was analysed using SPSS software (windows version 21.0). Comparisons between groups was performed using student t test and ANOVA test for continuous variables and chi square for categorical variables. Pearsons coefficient of correlation (r value) is used to assess the correlation between two variables.

RESULTS

Table 1 shows baseline characteristics of the patients enrolled in the study. Mean age of the patients included in the study was 53.7 (10.9) years. Most of the patients were male (80%, n = 40). Alcoholic liver disease alone was the most common etiology of cirrhosis (52%, n = 26). Overall, 78% (n = 39) patients had a history of chronic alcohol intake.

Table 1: Baseline Characteristics of the patients enrolled for the study

Characteristic	Value
Age (years) Mean [SD]	53.7 (11.9)
Sex	
Male	80 (40)
Female	20 (10)
Substance Abuse	
Alcohol	78 (39)
Recreational drug abuse (intravenous or oral)	34 (17)
Smoking	22 (11)
Underlying Etiology	
Alcoholic Liver Disease	52 (26)
Hepatitis B	8 (4)
Hepatitis C	14 (7)
Alcohol use with Hepatitis B	8 (4)
Alcohol use with Hepatitis C	18 (9)
Child Pugh Class	
Class A	16 (8)
Class B	48 (24)
Class C	36 (18)
ECG changes	
Sinus Tachycardia (HR>100)	72 (36)
Prolonged QTc interval (>440 ms)	74 (37)
Low Voltage QRS*	34 (17)
Data presented as n(%), unless otherwise specified. *average amplitude of QRS complex in limb leads < 5mm and in chest leads<10mm SD, Standard Deviation; ECG, Electrocardiograph; HR, Heart Rate.	

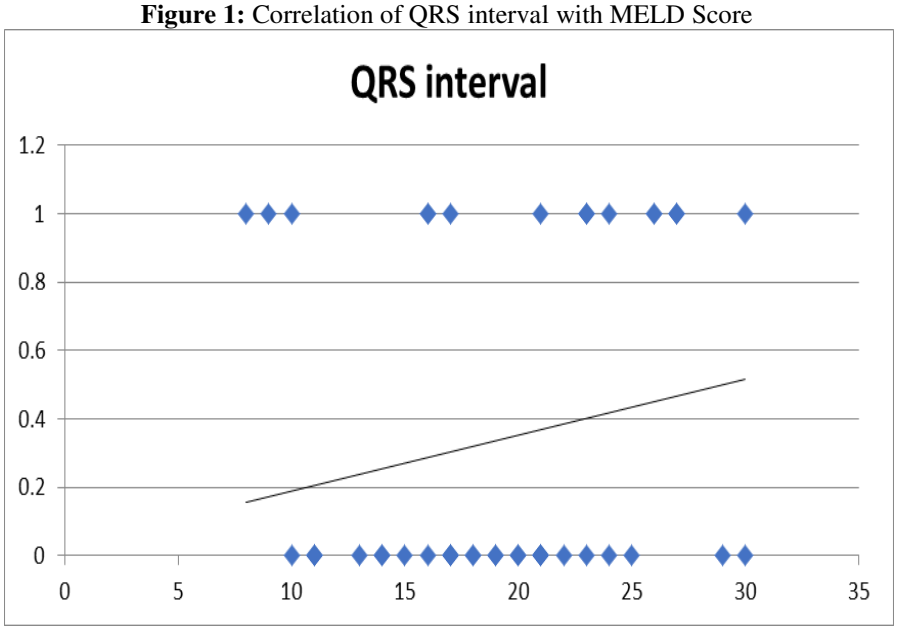
Table 2: Comparison of ECG changes according to CTP Class

Variables		CTP Class			P-Value
		A (n=8)	B (n=24)	C (n=18)	
QRS Voltage (mm)	Normal	8 (100)	17 (70.8)	9 (50)	<0.001
	Low	0	7 (29.1)	9 (50)	
PR interval (ms)	Normal	8 (100)	24 (100)	18 (100)	1.00
QRS interval (ms)	Normal	8 (100)	24 (100)	16 (88.9)	0.045
	Broad	0	0	2 (11.1)	
Heart Rate (bpm) Mean [SD]		98.53 (21.3)	102.80 (17.7)	105.76 (15.7)	<0.05
QTc interval (ms) Mean [SD]		474.8 (38.5)	475.26 (42.4)	479 (41.1)	<0.05
Data presented as n (%), unless otherwise specified. CTP, Child Turcotte Pugh; bpm, beats per minute; SD, Standard Deviation; mm, millimetres; ms, milliseconds.					

Table 3: Comparison of ECG changes according to MELD Score

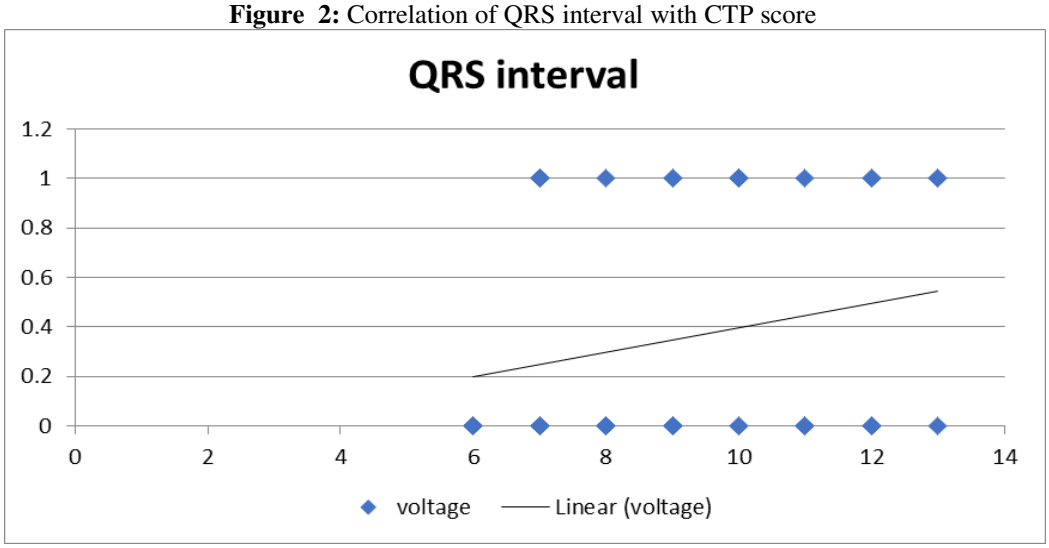
Variables		MELD (low)* (n=26)	MELD (high)* (n=24)	P-Value
Heart rate (bpm) Mean [SD]		104.04 (15.92)	107.41 (14.22)	0.046
QRS Voltage (mm)	Normal	21 (80.76)	12 (50)	0.024
	Low	5	12 (50)	
PR Interval (ms)	Normal	26 (100)	24 (100)	1.00
QRS interval (ms)	Normal	26 (100)	22 (91.66)	0.098
	Broad	0	2	
QTc Interval (ms) Mean [SD]		358.31 (32.68)	493.63 (43.28)	< 0.001
Data presented as n (%), unless otherwise specified. * Low MELD score was defined as MELD score < 18 and high MELD score was defined as MELD score ≥ 18. MELD, model for end-stage liver disease; bpm, beats per minute; SD, Standard Deviation; mm, millimetres; ms, milliseconds.				

Figure 1: Correlation of QRS interval with MELD Score



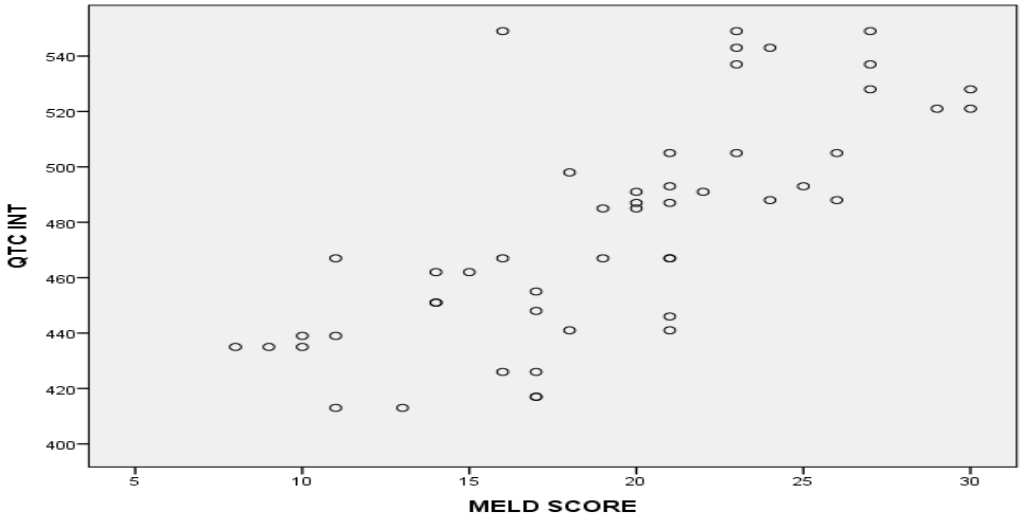
Abbreviations: MELD – model for end-stage liver disease.

Figure 2: Correlation of QRS interval with CTP score



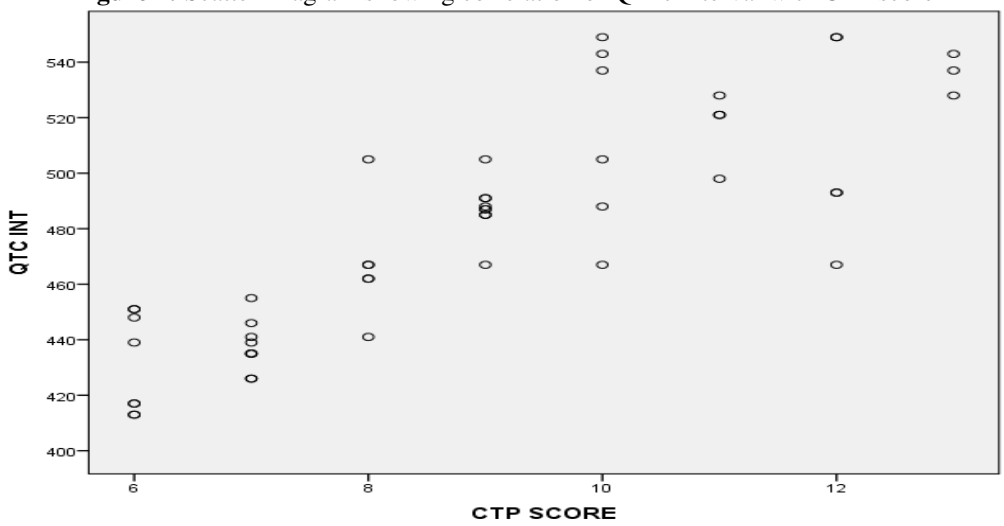
Abbreviations: CTP score – Child Turcotte Pugh score

Figure 3: Scatter Diagram showing correlation of QTc interval with MELD score



Abbreviations: MELD score – model end-stage liver disease score.

Figure 4: Scatter Diagram showing correlation of Q T c interval with CTP score



Abbreviations: CTP score – Child Turcotte Pugh score

A majority of the patients were in CTP class B (48%, n = 24). Prolonged QTc interval (> 440 ms) and sinus tachycardia were the most common baseline ECG changes (found in 74% (n = 37) and 72% (n = 36) patients, respectively). There was a statistically significant increase in number of patients with low QRS amplitudes and broad QRS complex, from CTP Class A to C ($p<0.001$ and $p=0.045$ respectively). Also, there was a statistically significant increase in heart rate and QTc interval from CTP class A to C ($p<0.05$ for both) (Table 2). Similar results were found when these patients were divided into two classes according to their MELD scores. Low MELD score was defined as MELD score < 18 and high MELD score was defined as MELD score $\geq$ 18. There was a statistically significant increase in number of patients with low QRS amplitudes in patients with high MELD Score ($p=0.024$). Also, there was a statistically significant increase in heart rate and QTc with high MELD Score ($p=0.046$ and $p<0.001$ respectively) (Table 3). Both the QRS interval and QTc interval showed a positive correlation with increasing MELD scores ($r = 0.465$ and 0.738; $p=0.001$ and <0.001, respectively) and with increasing CTP scores ($r = 0.304$ and 0.846; $p=0.032$ and <0.01, respectively) (Figures 1 to 4). In our study, we found that significantly more patients with ascites and hepatic encephalopathy had a higher QTc interval as compared to those without these complications ($p=0.001$ and 0.012, respectively).

DISCUSSION

ECG abnormalities that were frequently encountered in patients with liver cirrhosis were sinus tachycardia, QTc prolongation, low voltage QRS complex and broad QRS complex. Prolongation of the QTc-interval and low-voltage of QRS complex were thought to reflect cardiac dysfunction secondary to cirrhosis. In the study done by Moaref et al.,[11] a direct correlation was described between the QTc prolongation and the ventricular loading in patients with severe cirrhosis. Our study demonstrates that QTc-prolongation can be found in early, well-compensated cirrhosis as well as late stages of the disease. With regard to the etiology, alcohol was the leading cause of cirrhosis followed by HCV and HBV.In the present study, it was found that, higher the CTP score and MELD score (denote the severity of cirrhosis), more is the frequency of patients with sinus tachycardia, low QRS voltage, broad QRS and QTc-prolongation. Also, there was significant difference in QTc-interval, heart rate and QRS interval (which tend to increase) and QRS voltage (which tends to decrease) with increase in CTP score and MELD score. The results are consistent with the results found in numerous earlier studies by Genovesi et al.,[1] [2]Pourafkari et al,[13]Toma L et al,[14] and Bernardi M et al.,[15] QTc prolongation is an ECG abnormality strongly associated with torsades de points and can lead to significant cardiovascular mortality (Campbell RW et al.).[7] ECG abnormalities in patients lined-up for liver transplant can have deleterious effect on the post-transplant survival. Pre-transplant ECG abnormalities are associated with 14 times more risk of cardiac events after the liver transplant.[16]Therefore, it becomes important to be aware of these abnormalities in patients planned for liver transplant. These abnormalities are also shown to be at least partially reversible in some patients after liver transplant.[17]So, patients with these abnormalities may benefit more from liver transplant in terms of cardiovascular mortality, as compared to those without these abnormal lities. In our study, we found that significantly more patients with ascites and hepatic encephalopathy had a higher QTc interval and ascites ($p=0.001$ and 0.012, respectively). This may denote an increased prevalence of these complications with increasing severity of the liver disease. The study is not without limitations. The first limitation is the small sample size. The results of this study need to be established in larger studies. Secondly, this is a cross-sectional study. Clear association of ECG abnormalities with poor prognosis in patients with liver cirrhosis can only be established by long term prospective survival studies. Thirdly, since majority of the patients enrolled in the study were CTP class B or C, the results of this study may be more relevant to the patients with severe cirrhosis and not relevant much to the patients with lesser severity of cirrhosis. Nevertheless, despite all these limitations, our study has shown a highly significant association of ECG abnormalities like QTc prolongation, sinus tachycardia, low QRS voltage and broad QRS complex with progressively increasing severity of cirrhosis, which is in concurrence with the data from earlier studies.

CONCLUSION

ECG abnormalities like QTc prolongation, sinus tachycardia, low QRS voltage and broad QRS complex are increased amongst patients with cirrhosis patients and these abnormalities correlate with severity of cirrhosis. The presence of these abnormalities may be a harbinger of underlying CCM, which has been shown to adversely impact the mortality in earlier studies. Thus, ECG can be used as a simple parameter that can help in assessing the severity of cirrhosis and the impact of these changes on mortality outcomes of liver transplant. This becomes especially relevant in resource-poor settings where access to other investigations may not be immediately available.

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