Journal of Rawalpindi Medical College (JRMC); 2016;20(2):79-81

Original Article

Frequency of Corrected QT Interval in Patients With Cirrhosis

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Abstract

Background:. To assess the frequency of QTc prolongation in patients with liver cirrhosis and to observe its association with the severity of cirrhosis.

Methods: This cross-sectional observational study included 189 diagnosed cases of liver cirrhosis who were consecutively recruited and categorized according to Child-Pugh class, to rate the severity. QTc interval prolongation was observed, and its association with Child-Pugh class scores (severity of Liver Cirrhosis) was assessed using Chi-square test keeping p-value less than 0.05 as statistically significant.

Results: The mean age of the participants was 51.25 ±14.34, and gender distribution showed that96 (51%) were male and 93 (49%) were female. Q-Tc interval was normal in 99 (52%) patients and was prolonged in 90 (48%) patients. The QT-c interval prolongation was significantly associated with severity of liver cirrhosis. (p-value =0.000)

Conclusion: QTc interval was prolonged in almost half of the patients and the frequency of prolonged QTc was directly proportional to the severity of the hepatic cirrhosis according to Child-Pugh criteria.

Key Words: Liver Cirrhosis, Long QT syndrome, Cardiomyopathies.

Introduction

Cirrhotic cardiomyopathy is one relatively common cardiovascular complication arising secondary to liver cirrhosis. The prolongation of QTc interval has been found in various studies to be linked directly to the severity of liver cirrhosis. Liver cirrhosis refers to scarring of the liver which results in abnormal liver function as a consequence of chronic liver injury.[1,2] It is a major cause of mortality and morbidity worldwide.[3] It is also a common cause of mortality amongst Pakistani population and frequent cause of admission in our hospitals.[4] Cirrhosis is a leading cause of illness and death in the United States.[5]Cirrhosis of the liver is a consequence of long-term liver injury of many types. The most common cause being viral hepatitis as compared to West where alcohol is more common.[6,7]

Majority of patients (90%) with chronic liver disease have evidence of Hepatitis B Virus, Hepatitis C Virus or co-infection. Disease is reported more severe in patients with co-infection and cirrhosis is recorded in 74% of patients.[8,9] HCV is now more common as compared to HBV in our country, and a high frequency of HCV seropositive individuals of both genders among patients referred for chronic liver disease.[10]

Portal hypertension, ascites and variceal haemorrhage are common complications in cirrhotic patients. Esophagogastric varices have the greatest clinical impact, with a risk of mortality of 17–42% per bleeding episode. Ascites, important complication of advanced cirrhosis and severe portal hypertension, is sometimes refractory to treatment and is complicated by spontaneous bacterial peritonitis and hepatorenal syndrome.[11,12] Hepatic encephalopathy is another complication, with a mortality of about 30%.[13]

The effects of cirrhosis on cardiovascular and circulatory system are not well studied.[14] The use of new investigative modalities has shown several lines of evidence of impaired cardiac contractility and performance in patients with cirrhosis and has led to the introduction of the new clinical entity, cirrhotic cardiomyopathy. Cirrhotic cardiomyopathy is a new clinical entity, which is diagnosed infrequently because of relative unawareness regarding this entity. It has many features including prolongation of QTc interval, increased heart rate, decreased myocardial contraction force and diastolic dysfunction.[15]A prolonged QTc duration in chronic liver disease could potentially lead to ventricular arrhythmias and sudden cardiac death.[16-18]

Patients and Methods

This was a descriptive cross-sectional study which was conducted at the Gastroenterology Department of Pakistan Institute of Medical Sciences from December to^{h} June 2010.A total of 189 diagnosed cases of cirrhosis i.e Ultrasound proven cirrhosis with shrunken liver less than 9 cm, portal vein diameter more than 12 mm and splenomegaly of more than 12cm, were enrolled in the study. The patients with

congestive cardiac failure, primary biliary cirrhosis, ischemic heart disease, hypertension, valvular heart diseases, heart block, cardiomyopathy and recent use of drugs affecting QT interval less than 72 hours, were excluded. Blood samples were taken for bilirubin, albumin and prothrombin time . All patients underwent ultrasound.Electrocardiography was done by using standardized 12 lead ECG modules with speed of 25mm/s and voltage of 1mV, and QT interval was measured and QTc was calculated. Chi-square test was applied to associate severity of cirrhosis(Child-Pugh class) with prolonged QTc interval, keeping p value less than 0.05 statistically significant.

Results

Out of 189, 96 (51%) were male and 93 (49%) were female. Most of the cirrhotic patients belonged to age group from 45 to 65 years of age (Range 18-90).Mean age was 51.25 ±14.34 . Majority belonged to Child-Pugh class C (57%)(Table 1). QTc interval was prolonged in 90 (48%) patients (Table 2). Chi-square test revealed a significant association between severity of liver cirrhosis and prolongation of Q-tc interval with p-value =0.00 (<0.05) (Table 3 &4)

Table 1: Distribution of Child-Pugh Class in Study Population

Child-Pugh Class	No(%)
Class A	22(11)
Class B	60(32%)
Class C	108 (57%)

Table 2: QTc Interval in patients with cirrhosis

QTc interval	No(%)
Normal	99(52)
Prolonged	90(48)

Table 3: Association between severity of cirrhosis and QT interval prolongation (Child-Turcot-Pugh QTc Interval Cross tabulation)

Child-Turcot-Pugh class	QTc Interval		Total
	Normal	Prolonged	
Class A	16	5	21
Class B	40	20	60
Class C	43	65	108

Table 4: Association between severity of cirrhosis and QTc interval prolongation

Chi-Square	DF	*p-Value
16.52	2	0.00

*p- Value less than 0.05 considered statistically significant

Discussion

In our study almost half of the patients had prolonged Q-Tc interval. This prolonged Q-Tc interval was found in all classes of the Child-Turcot-Pugh from A to C. But frequency of prolonged Q-Tc interval was much less in patients belonging to child class A, where only 6% of the patients had prolonged interval. On the other hand in patients belonging to child class B, 22% of the patients had prolonged QTc interval and in the patients who were most serious, i.e. in class C, 72% of the patients had abnormally prolonged Q-Tc interval. In present study frequency of prolonged QTcinterval was found less prevalent in Child class A patients. Its frequency had slightly increased in Child class B and in class C which is the worst class of Child's criteria, the frequency of prolonged QTc interval had reached to 72%. The frequency of the prolonged or abnormal QTc interval is directly proportional to the severity of the liver cirrhotic disease according to the Child – Turcot-Pugh class and this association was statistically significant i.e p value =0.00 (< 0.05).

In another trial conducted in Italy by Genovesi S et al, it was found that QTc interval was progressively prolonged from Child class A to Child Class C with significant P value. [19] There was a positive correlation between prolonged QTc interval and hepatic vein pressure gradient and it was found that frequency of prolonged QTc is increased with the increase in Child class and also with increase in hepatic vein pressure gradients. It might be due to the presence of severe portal hypertension that was associated with decreased heart rate variability.Cirrhotic patients with a more severe disease, especially of alcoholic etiology, who have greater HVPG (hepatic vein pressure gradients) and lower calcium plasma levels, have an altered ventricular repolarization and a reduced vagal activity to the heart, which may predispose to life-threatening arrhythmias.Study of Bashir A et al, found that frequency of QTc prolongation was 4.5% in Child PughGrade A, 23.2% in Child Pugh Grade B, and 32.0% in Child Pugh Grade C. Association of Child Pugh Scoring with QTc prolongation was determined and found to be statistically significant (p < 0.05).[20] The results presented by Zuberi et al. in their study, in which they showed the frequency of QTc prolongation to be 19.2%. [21] This is much in contrast with our study as the current study findings revealed the frequency of QTc prolongation to be 48%. But a wide range of values are available across a number of International studies.

It was found to be 46.2% in a study by Bernardi et al, 46.93% in a study by Li et al. Bal et al demonstrated a QTc prolongation frequency of 56%in their study. [23,24]

Kosar et al determined the frequency of QTc prolongation to be 32% in their study population. [25] This discrepancy may be explained by the presence of other compounding factors such as electrolyte disturbances, concomitant cardiac problems, or use of QTc prolonging drugs, which were excluded in our study but might have been included in other studies. Moreover, the variable spread of severity of cirrhosis as shown by Child Pugh Score or any other model in all these studies would also have played a role in this wide range of results.

A direct relationship between the stage of cirrhosis and the development of cirrhotic cardiomyopathy has been consistently observed in various studies. More advanced the cirrhosis, the greater the chances of developing cirrhotic cardiomyopathy and the associated symptoms, as evident from the current study finding suggesting a statistically significant association between severity of Cirrhosis and QTc prolongation.

Conclusion

1.Q-Tc interval was prolonged in almost half of the patients and the frequency of prolonged Q-Tc was directly proportional to the severity of the hepatic cirrhosis according to Child-Pugh criteria.

2. The healthcare providers must be mindful of this serious complication and must carefully evaluate such patients, and manage them as necessary.

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