CAN HEART RATE AND QTc DURATION BE USED AS A MARKER OF CIRRHOTIC CARDIOMYOPATHY? A CASE CONTROL STUDY

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ABSTRACT

Objective: *To assess the value of QTc prolongation and heart rate variation as a marker of cirrhotic cardiomyopathy and severity of liver disease.*

Methodology: *This comparative study was conducted on selected patients with cirrhosis of liver, fulfilling inclusion criteria and were enrolled as group 1. An equal number of non cirrhotic patients were enrolled and included in group 2. QTc and heart rate were calculated and compared between the two groups. Analysis of QTc prolongation and increase in heart rate with regard to severity of liver disease was also made.*

Results*: Fifty confirmed cases of cirrhosis of liver were included in group 1 with equal number of age and sex matched non-cirrhotic patients included in group 2 as controls. The mean ±SEM of QTc in group1 and group 2 were 0.4707±0.0065 and 0.3893±0.00542 seconds respectively. The mean ±SEM of heart rate was 90.50±2.839 beats/min and 82.85±2.207 beats/min in group 1 and 2 respectively. The mean of QTc and heart rate in group 1 was significantly higher as compared to group 2 (p=.001 and p=.0179 respectively). The mean of QTc and heart rate in subgroup 1A, 1B and 1C was not statistically significant.*

Conclusions: *Patients with cirrhosis have a higher mean QTc and heart rate as compared to non cirrhotic adults. Both tests may be useful markers of Cirrhotic Cardiomyopathy.*

Key words*: Cirrhotic cardiomyopathy, QTc, Heart rate.*

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INTRODUCTION

Cirrhosis of liver is the consequence of hepatic fibrosis mostly caused by chronic infection with hepatitis B and C viruses and is common in Pakistan[1-3]. The prevalence of cirrhosis is still high despite improved public awareness and measures to control transmission of viruses causing chronic infections. Its major manifestations include ascites, upper GI bleed, hepatic encephalopathy and a variety of effects on other organ systems. The effects of cirrhosis on cardiovascular system are still considered an understudied aspect of this entity. Cirrhosis causes homodynamic alteration in cardiovascular system including increased heart rate, increased cardiac output and decreased arterial pressure[4,5]. Attenuated ventricular response in cirrhotic patients to physiological or pharmacological stress has led to the introduction of a new clinical entity i.e. cirrhotic cardiomyopathy (CCM)[6]. Changes in heart rate and prolongation of QTc are part of this new syndrome which could lead to ventricular arrhythmias and sudden cardiac death[7,8]. Cirrhotic cardiomyopathy is usually latent but additional stress in the form of infection, bleeding, surgery and insertion of transjugular intrahepatic portosystemic shunts (TIPPS) can unmask the disease[9,10]. Data on this important complication of cirrhosis is scanty from South East Asia and especially Pakistan. Liver transplantation programme is being launched in the near future in our country and hepatologists are bound to face the cardiovascular complications of cirrhosis especially after liver transplantation.

The purpose of this study was to compare the cha nges in QTc duration and heart rate in

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patients with cirrhosis of liver with non- cirrhotic controls.

METHODOLOGY

This comparative study was conducted at medical wards of the Fauji Foundation hospital Rawalpindi from January 2009 to August 2009.Fifty confirmed patients with cirrhosis of liver were enrolled in the study using convenience sampling. Equal numbers of age and sex matched patients without liver disease were recruited as controls. Sample size was estimated for recording of difference in the two groups and also keeping in view the expected frequency of QTc abnormalities reported at 5.9%[11] in general population and that in cirrhosis at 37%[12]. Written consent was taken from all patients on separate proformas.Cirrhotic patients fulfilling inclusion criteria were included in group 1 while equal number of patients without cirrhosis were included in group 2.Group 1 was further subdivided according to the severity using Child pugh[13, 14] scoring into 1A, 1B and 1C to see difference in QTc and heart rate variation. Cirrhosis was confirmed with the help of laboratory data and ultrasonography. Endoscopy was also performed in all group 1C patients thereby confirming portal hypertension and cirrhosis of liver. Patients with known ischemic heart disease, systemic hypertension,valvular heart disease,hyperkalemia ,conduction defects and those on drugs like beta blockers, cardiac glycosides, calcium channel blockers and anti arrhythmic drugs were excluded from the study. Detailed scrutiny of the medical record was carried out and all the clinical details were recorded on a separate proforma.Three ECGs of each patient were done and record saved. Subsequently QTc was calculated for each individual ECG and a mean value was taken for the analysis. QTc was calculated with the help of following formula: $QTc=QT(sec)/\sqrt{RR'}$[15, 16] Heart rate was measured from ECG by applying this formula: HR=1500/R-R All the patients in cirrhotic group were investigated which included LFTs, complete blood count, serum albumin, PT, renal function tests, electrolytes, and blood glucose. Mean values of QTc and heart rate of two groups were compared by't test'. 95% confidence interval and p values were calculated and documented. Significance of p value was set at <.05. SPSS was used for statistical analysis.

RESULTS

A total number of study patients were fifty with equal numbers in the control group. The mean age of patients in group 1 was 54.86±10.59 years. Female patients in this group were 34(68%) as compared male patients 16 (32%).

Mean age of patients in the control group was 50±17.90 years with 32(64%) females and 18(36%) males (Table 1). The mean value (Mean±SEM) of QTc for group 1(cirrhotic) was 0.4707±0.0065 seconds while the value of QTc (Mean±SEM) for group 2(controls) was 0.3893±0.00542 seconds (p=.001) (Figure 1).

The mean value (Mean±SEM) of heart rate for group 1(cirrhotic) was 90.50±2.839 beats/min while the value of heart rate (Mean±SEM) for group 2(controls) was 82.85±2.207 beats/min (p=.0179) (Figure 2).

Further analysis in group 1 was carried out to see the relationship of severity of liver disease and QTc and heart rate variations. Group 1A, 1B and 1C comprised of 8, 23 and 19 patients respectively. Results of the subanalysis clearly shows significant difference between sub group1A and 1B, but there was hardly any difference between subgroup 1B an1C regarding heart rate and QTc duration (Table 2).

The scatter plot of heart rate against Child Pugh score in cirrhotic patients was linear but nearly a straight line (Figure 3). The Pearson's correlation coefficient for heart rate and Child Pugh score was 0.100 with 95% confidence interval of -1.968 to 4.063 which was statistically not significant (p=0.488).

The scatter plot of QTc interval against Child Pugh score in cirrhotic patients was also linear but almost a straight line (Figure 5).

Table 1: Demographic features of groups

		Group 2	Group 1	1A	1B	1C
Gender		50	50	8	23	19
	Male	18	16	3	5	8
	Female	32	34	5	18	11
Age(mean years)		50	54.86	52.25	53.21	57.95

Figure 1: QTc Control Vs QTc Cirrhosis

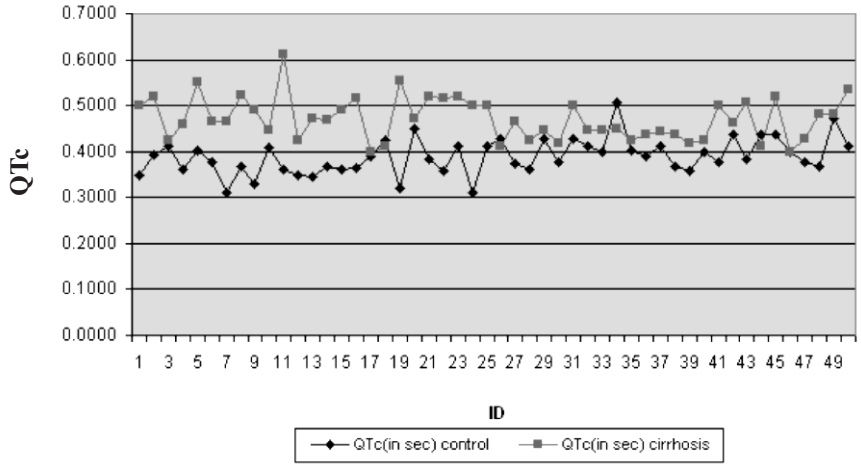


Figure 2: Heart Rate Control Vs Heart Rate Cirrhosis

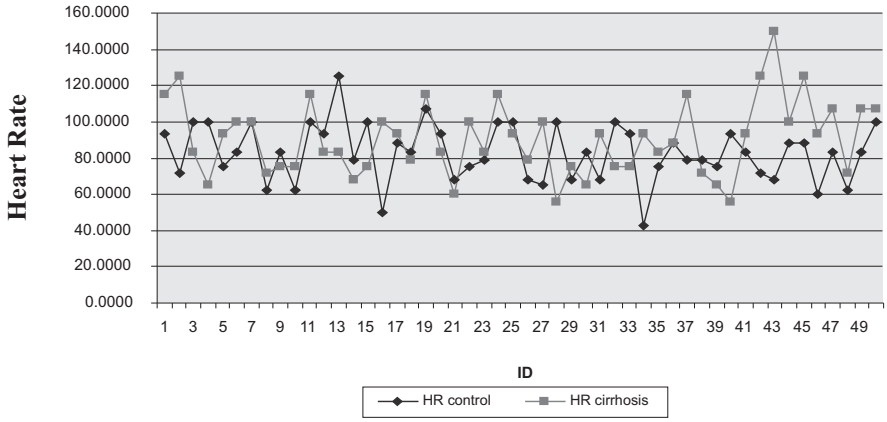


Table 2

	1A	1B	1C
Mean Heart Rate	78.432	92.506	93.150
Mean QTc	0.456	0.473	0.473

Figure 3: Scatterplot of heart rate against child Pugh score in Cirrhotic patients

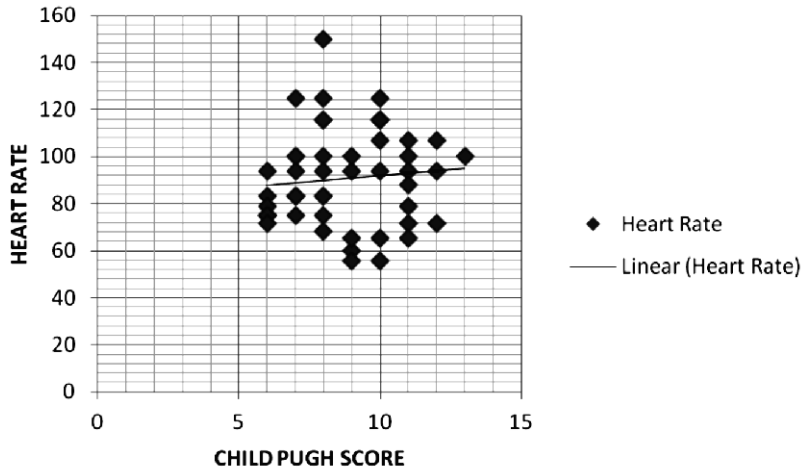


Figure 4: Linear Logistic Regression Analysis plot of Heart rate score against child Pugh score in Cirrhotic patients

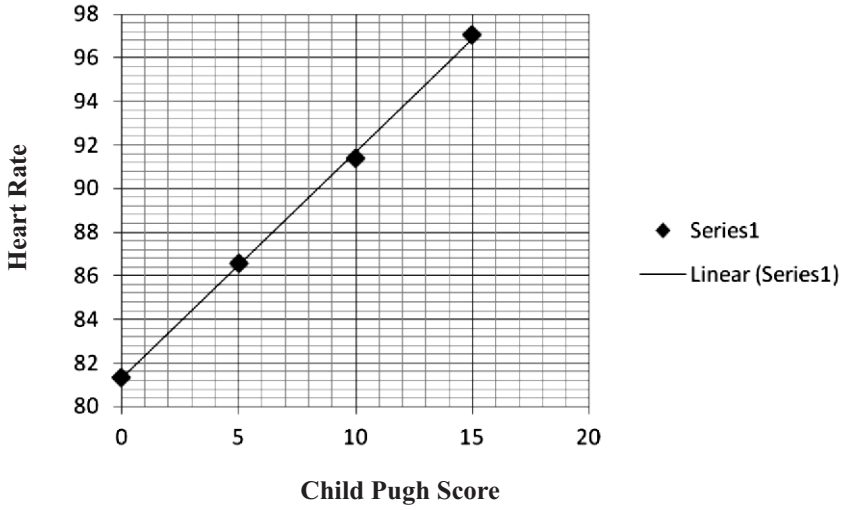
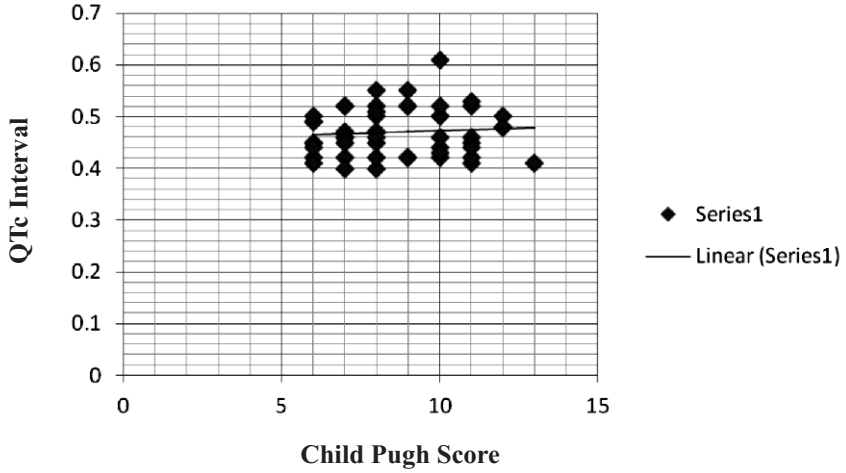


Figure 5: Scatterplot of QTc Interval against Child Pugh score in Cirrhotic patients



DISCUSSION

Cardiac contractility is compromised in cirrhotic patients and manifests clinically under stressful situations. In the current study value of QTc and heart rate variability was evaluated and compared with controls. Female gender was dominant in the study population because Fauji Foundation Hospital which is a tertiary care facility for the families of ex-servicemen mostly caters female patients and their children as their counterparts are not entitled here. Patients with early disease represented by Child's class 'A' were small in number as they are mostly asymptomatic and do not seek medical attention. Child C patients had fairly good representation in our study as they are usually symptomatic and also seek medical attention and admission to the hospital. But majority of patients had liver disease with intermediate severity as represented by predominance of child's class B. The findings of this study show that prolongation of QTc and increased heart rate can be attributed to the cardiac changes in cirrhosis of liver. However, when subgroup analysis was carried out, QTc elongation and heart rate changes did not maintain their positive correlation vis-à-vis severity of liver disease. Difference was observed between subgroup 1A and 1B but no difference between group1B and 1C was noted. The results of the present study corroborate the findings of Zuberi et

al's[17] findings that QTc duration and heart rate are significantly increased in cirrhotics. Another study from Italy by Genovesi S et al[18] also observed progressive prolongation of QTc and increasing heart rate variability with severity of liver disease according to child Pugh scoring. The present study has found no linear relationship between severity of liver disease using Child-Pugh scoring with QTc and heart rate variations. This aspect of our study could be different from others owing to the composition of the sample with predominance of female patients. Another possible explanation is that QTc and heart rate changes may depend on factors not incorporated in Child-pugh scoring system for severity of liver disease. A recent study by Tarique S and Sarwar S, however did not reveal any significant relationship between QTc duration and heart rate variability with severity of liver disease although they used MELD scoring system to grade severity of liver disease [19]. There are studies in the literature which showed that cardiac changes parallel the severity of cirrhosis[20] while other did not find any correlation, so this issue is yet unsettled[21]. Furthermore subtle trends of correlation between severity of liver disease vis-à-vis QTc and heart rate might not come to light unless larger sample size and entire spectrum of the disease is analyzed. Further studies dedicated to specifically look at this aspect of the disease are required to accurately delineate the extent of correlation between severity of hepatic dysfunction and cardiac changes in cirrhotics. However it is important to note that normal QTc, heart rate and even normal echocardiography do not rule out the presence of cardiac dysfunction in cirrhotics[22]. These parameters detect only the 'tip of the iceberg' of cardiac complications in cirrhosis.

CONCLUSION

In the absence of other cardiac risk factors QTc prolongation and increase in heart rate can be attributed to cirrhotic cardiomyopathy. QTc and heart rate changes do not correlate with the severity of liver disease.

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CONTRIBUTORS

SMA conceived the idea and planned the study. YA, SM, NY& MSA did the data collection and analyzed the study. All the authors contributed significantly to the research that resulted in the submitted manuscript.