Prolongation of QTc Duration and Increased Heart Rate in Patients with Cirrhosis of Liver
Umair Ahmed, Aamir Shaukat, Asim Shaukat, Hooria Aamir

INTRODUCTION
Cirrhosis of liver is very common in Pakistan. Hepatitis C is the commonest underlying cause in patients presenting with cirrhosis of liver followed by Hepatitis B virus. Both the viruses account for about three-fourth of all the patients presenting with cirrhosis of liver. According to World Health Organization (WHO), about 3% of world’s population is infected with Hepatitis C virus infection (HCV), with 3-4 million new cases arising every year. Many complications can occur as a result of cirrhosis, in which ascites, portal hypertension and varices are most common. Many new complications are being recognized which include hepatopulmonary and sleep-apnoea syndromes. Abnormalities in cardiac electro physiology are well documented in patients with liver cirrhosis. 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. Although it was first described in 1953, but was forgotten and not much work was done on it. Changes in Heart Rate (HR) and QTc duration are part of this new syndrome. A prolonged QTc duration in chronic liver disease could potentially lead to ventricular arrhythmias and sudden cardiac death. In one of the studies conducted in this regard, The mean QTc and HR values were significantly more in patients with cirrhosis of liver as compared to non-cirrhotic controls. The aim of this study was to compare the HR and QTc duration in patients of cirrhosis with non-cirrhotic controls.

PATIENTS AND METHODS
It was a cross-sectional study conducted in Medical Unit I Allied Hospital Faisalabad from 1st March 2011 to 30th August 2011. 50 patients of cirrhosis of liver were included in the study and 50 controls were also included. Using convenience sampling, confirmed patients of cirrhosis were inducted after taking informed consent. All the selected patients were allocated to Group-I. 50 normal individuals were taken as control and were allocated to Group-II. Patients...
with ischemic and valvular heart disease, conduction
defects, cardiac failure, hypertension, hyperkalemia and patients taking blockers, calcium channel blockers, antiarrhythmic and cardiac glycosides were excluded. Clinical details were recorded of all the selected individuals on a proforma. Three 12 lead ECG recordings were taken of each patient, 5 minutes apart, and HR and QTc were calculated for each ECG and then mean of the three were calculated and used for the analysis. QTc values were calculated for all patients by the formula: QTc = QT/√R-R.9Heart rate were calculated on ECG by formula HR=1500/R-R10 A mean value of QTc > 0.44 seconds was taken as prolonged, while the HR > 100 was taken as increased. Blood sample were taken for complete blood counts, urea, creatinine, electrolytes, LFTs, albumin, and prothrombin time. SPSS version 10.0 was used for statistical analysis. Means of HR and QTc were compared by independent samples‘t-test’ between the two groups. 95% confidence intervals and p-values were calculated with significance level set at 0.05.

RESULTS
Fifty confirmed patients of cirrhosis of liver were inducted in Group-I with same number of non-cirrhotic individuals were included in Group-II. The mean age in Group-I was 38.2 years and that in Group-II was 37.4 years (Table I). In Group I 22 patients were male and 28 were female. In Group II 18 were male and 32 were female (Table 2). Figure 1,2 show the QTc interval and heart rate in both groups respectively. The mean ± SD of QTc on Group-I was 0.472 ± 0.012 sec and that in Group-II was 0.434 ± 0.014 sec (Table 3) and that for HR in Group-I and II were 79.26 ± 10.08 and 74.24 ± 7.58 beats/min (Table 4) respectively. Comparing the mean QTc values of the two groups proved to be statistically significant with p = 0.0001.(Table 5) Similar comparison testing for HR also proved to be significant with p= 0.0001. (Table 5) Means of both HR and QTc were significantly higher in Group-I as compared with Group-II.

Table-1
Age Of participants

<table>
<thead>
<tr>
<th>Groups of Patients</th>
<th>Age</th>
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</thead>
<tbody>
<tr>
<td>Group I</td>
<td>38.2</td>
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<tr>
<td>Group II</td>
<td>37.4</td>
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</tbody>
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Table-2
Gender of participants

<table>
<thead>
<tr>
<th>Groups</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group I</td>
<td>22</td>
<td>28</td>
</tr>
<tr>
<td>Group II</td>
<td>18</td>
<td>32</td>
</tr>
</tbody>
</table>
Table-4
Mean Heart Rate

<table>
<thead>
<tr>
<th>Group</th>
<th>Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group I</td>
<td>79.26 ±10.08</td>
</tr>
<tr>
<td>Group II</td>
<td>74.24 ± 7.58</td>
</tr>
</tbody>
</table>

Table-5
Independent Samples Test

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<tr>
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<th>t</th>
<th>Sig. (2-tailed)</th>
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</thead>
<tbody>
<tr>
<td>QT interval</td>
<td>25.418</td>
<td>.000</td>
</tr>
<tr>
<td>heart rate</td>
<td>4.515</td>
<td>.000</td>
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</tbody>
</table>

DISCUSSION
Cirrhotic cardiomyopathy is diagnosed infrequently because of relative unawareness regarding this entity. It has many features including prolongation of QTc, increased HR, decreased myocardial contraction force and diastolic dysfunction. Several electrophysiological mechanisms like reduced beta-adrenoeceptor density, postreceptor signal defects, abnormal excitation-contraction coupling have been suggested as the cause of molecular abnormalities for the conductance and impaired cardiac contractility. Beta-receptor density and sensitivity is reduced in cirrhosis, along with altered G protein and calcium channel functions. This results in both impaired chronotropic responses and electromechanical uncoupling; The coupling between the cardiac output and arterial compliance is an important factor affecting the left ventricular stress and work done by it. The increased interval correlates with a higher incidence of sudden cardiac death. The pathogenesis of increased QT interval is unclear. The structural changes in cardiomyocyte membrane with increased cholesterol content with resultant membrane fluidity compromises the calcium and potassium pumps. In cirrhotics increased plasma levels of estrogens has also been implicated for the increased incidence of QT interval prolongation. This interval is increased in 30 to 60% of patients and level of increase relates to degree of hepatic dysfunction. On the other hand, a too compliant arterial system will hamper prompt and timely delivery of blood to different parts of the body and also delay flow in important vascular beds. These effects will be more prominent in the patients with excessive cardiac output, stroke volume and vascular beds of varying vascular resistance as in cirrhotic cardiomyopathy. Prolongation of QTc duration and increased Heart rate can be used as a non-invasive and rapid diagnostic marker of cirrhotic cardiomyopathy as was proved in the study conducted in 2007. Prolongation of QTc interval has been shown to be useful for assessment of severity of chronic liver disease. QTc duration can be reduced by prompt usage of beta-blockers, preventing life threatening arrythmias so early diagnosis is important. In our study, we found significant increase in mean values of QTc duration and HR between the two groups.

CONCLUSION
Prolongation of QTc duration and increased Heart rate can be used an important bedside marker of cirrhotic cardiomyopathy in patients with cirrhosis of liver. However larger cross-sectional studies are needed to chalk out guidelines for diagnosis of cirrhotic cardiomyopathy and cutoff values of QTc duration.

REFERENCES

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