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Comparison of Heart Rate and QTc Interval in Patients of Cirrhosis of Liver with Non Cirrhotic Controls

Khadim Hussain[1], Dolat Singh[2] ,Sadia Nizamani[3]

[1,2] Senior Registrar, Medicine department Indus Medical College Tando Muhammad Khan
[3] Assistant Professor Medicine, Medicine department Indus Medical College Tando Muhammad Khan

Author`s Contribution

[1,3]Drafting the work or revising it critically for important intellectual content
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Address of Correspondent
Dr. Khadim Hussain
Senior registrar, Medicine department Indus Medical College Tando Muhammad Khan
hussain_khadim786@yahoo.com

ABSTRACT

Objective: To determine the heart rate and QTc interval in cirrhotic patients by taking non cirrhotic as control.

Methodology: The present cross-sectional study was conducted at the department of general Medicine in Civil Hospital Karachi from May 2015 to October 2015. All the cirrhotic patients were taken age study group and an equal number of non-cirrhotic patients other reasons without any cardiac disease was taken as control Group. All patients underwent the testing ECG. Values for HR and QTc were computed from lead II. Data was entered in the self-made proforma.

Results: A total of 174 subjects were enrolled in this study; 87 cirrhotic patients 87 non-cirrhotic patients. Average heart rate was statistically higher in cirrhosis patients (i.e. 83.45 beats /min) than non-cirrhotic patients (i.e 74.23 beats/min), p-value 0.0005. Average QTc value was significantly high in study group (0.434) than control group (0.407), p-value 0.003.

Conclusion: Heart rate and QTc were frequently prolonged in cirrhotic patients as compared to non-cirrhotic controls.

Key Words: Cirrhosis, Heart rate, prolonged QTc interval.

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Introduction

Cirrhosis is a late phase of progressive liver fibrosis marked by hepatic structure distortion and regenerative nodules formation. In its advanced phase, it is usually considered irreversible.[1] In Pakistan, hepatic cirrhosis is most frequent, induced by hepatitis B and hepatitis C virus.[2,3] As a consequence of cirrhosis several well-known complications such as ascites, varices, and portal hypertension can take place. Besides this, many fresh complications,including sleep-apnoea and hepato-pulmonary syndromes, are being reported.[4] With its associated complications, liver cirrhosis results in elevated mortality and morbidity.[5] In individuals with cirrhosis, several findings have also shown an elevated incidence of prolonged QT interval.[6,7] In 1953 reported that prolonged QT intervals and atypical cardiovascular reflexes in subjects with cirrhosis. The electrocardiographic QT interval represents ventricular repolarization as well as its prolongation is a substrate for acquired and congenital ventricular arrhythmias.[8] In cirrhotic individuals secondary to ventricular arrhythmias, prolonged QTc intervals could possibly lead to unexpected cardiac failure.[9] The application of fresh research modalities has revealed many evidences of compromised cardiac contractility and efficiency in cirrhosis individuals and has resulted in the implementation of "Cirrhotic Cardiomyopathy". If no other cardiac-associated disease is present, cirrhotic cardiomyopathy is characterized as functional and structural cardiac deformities that occur in cirrhotic patients. Its primary clinical characteristics include diastolic and systolic dysfunctions and modifications in electrophysiology. Cirrhotic cardiomyopathy is usually clinically deep rooted and revealed when a person is

subjected to significant emotional stress or even after certain interventions, resulting in a subtle cardiac dysfunction.[10] Subsequently, caution is needed in the event of stressful interventions such as heavy paracentesis without sufficient expansion of plasma volume, transjugular intrahepatic Porto systemic shunt insertion, surgery and peritoneovenous shunting.[11] The plasma membrane's fluidity and its ion channel's function have been shown to be effected in cirrhosis. In terms of prolonged QT interval, this could lead to conduction abnormalities. In health and several disease states, such as chronic hepatic disease, a prolonged QT intervals have been reported.[12,13] QT prolongation is frequently correlated with potentially fatal torsade de pointes arrhythmias that evolve due to amplification of the ventricular myocardium's inherent electrical heterogeneities. These heterogeneities occur due to variations in the repolarization of the three prevailing cell types that comprise the ventricular myocardium, resulting in repolarization dispersion and trans mural voltage gradients that is accountable for the electrocardiographic T wave inscription.[14] In individuals with hereditary and acquired types of long-QT syndrome, following myocardial infarction, as well as in healthy people, an extended QT interval is correlated with a greater risk of cardiac mortality and unexpected death. An association was proposed in patients with hepatic dysfunction between general mortality and extended QT interval.[15]It has been proposed that a high severity of hepatic disease is correlated with the QT interval prolongation in cirrhotic subjects. Though, with reference to etiology, gender and corresponding therapies, the studied populations of patients are heterogeneous.[16,17] Because in cirrhosis patients the incidence of extended QTc interval is quite high, thus EKG is necessary before prescribing medications approved to prolong the QTc interval.[18] Cirrhosis liver is common condition in Pakistan.In a recent study stated that the mechanisms underlying prolonged QTc interval among hepatic disease patients is still unclear.[19]As there are insufficient studies regarding heart rate and QTc disorder in cirrhosis from our area, therefore this study has been conducted to compare the QTc interval and heart rate in non-cirrhotic and cirrhotic subjects at tertiary care Hospital.

Methodology

This study was conducted at medical department, Civil Hospital Karachi, from May 2015 to October 2015. All the cirrhotic patients were considered as study group and an equal number of non-cirrhotic patients admitted in ward for other reasons without any cardiac disease were taken as control Group. Patients with variceal hemorrhage, hepatocellular carcinoma, valvular and ischemic cardiac disease, uncontrolled hypertension, cardiac failure, hyperkalemia, conduction defects and subjects taking anti arrhythmic, calcium channel blockers, cardiac glycosides and beta blockers were excluded. Clinical examination was done and routine laboratory investigations were done. All patients underwent the resting ECG. HR &QTc values were computed from lead II. Heart rate of > 100 was considered as increased and QTc interval of > 0.44 seconds was considered as prolonged. CBC, LFT, Serum Protein AG ratio, X-Ray Chest, Ultrasound Abdomen, Ascitic Fluid DR, PT and INR was done in all patients. Well-versed consent was received from every patient and all controls.

Results

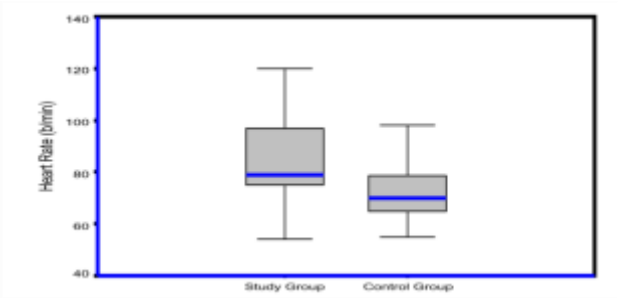
The overall average age of the patients was 47.24 ± 12.86 years and no significant difference of average age was observed between groups (46.97±13.27 vs. 47.52±12.51; p=0.78); similarly average HB, bilirubin, serum albumin, pro thrombin time and INR were also not significant between groups. Out of 174 patients, 88(50.6%) were males and 86(49.4%) were females. Table No. 1.

Table 1: Comparison of Characteristics Between Groups n=174

Variables	Study group n=87	Control group n=87	P-Values
Age (Years) (mean±sd)	46.97±13.27	47.52±12.51	0.783
HB (mean±sd)	12.01±1.22	12.83±1.18	0.221
Total Bilirubin(mean±sd)	2.49±2.38	2.68±1.39	0.892
Serum Albumin(mean±sd)	2.84±0.49	1.94±0.59	0.186
Pro thrombin Time (mean±sd)	11.08±6.70	10.09±4.8	0.655
INR(mean±sd)	1.85±0.51	1.86±0.41	0.976
Male (n. of pt (%))	47(54%)	41(47.1%)	
Female (n. of pt (%))	40(46%)	46(52.9%)	0.365
Total (n. of pt (%))	87(100.0%)	87(100.0%)	

Mean heart rate was significantly high in cirrhotic patients (study group) than non-cirrhotic patients (control

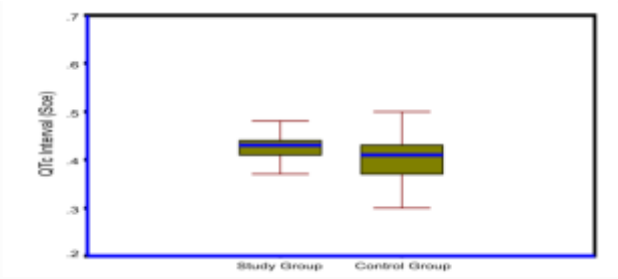
group) as 83.86±14.26 and 74.85±13.10 respectively p=0.0005. Similarly, average QTc value is presented in figure 2. Average QTc were also significantly high in study group than control group as 0.45±0.05 and 0.40±0.05 respectively p=0.003. Fig. No. 1 and 2



Hear Rate	Study Group	Control Group	p-Value
Mean ± SD	83.86±14.26	74.85±13.10	0.0005
Median (IQR)	79(22)	13(14)	

Figure 1: Comparison of Heart Rate between Cirrhotic (Study Group) and Non Cirrhotic (Control Group)

Comparison of frequency of increased heart rate above 100 /min were not significant between cirrhotic and non-cirrhotic patients (23% vs. 12.6%; p=0.075), while frequency of prolonged QTc>0.44 was significantly high in case than control (21.8% vs. 9.2%; p=0.021) as shown in table II.



QTc Interval	Study Group	Control Group	p-Value
Mean ± SD	0.47±0.05	0.40±0.05	0.003
Median (IQR)	0.43(0.03)	0.41(0.06)	

Figure 2: Comparison of QTc Interval between Cirrhotic (Study Group) and Non Cirrhotic (Control Group)

Table II: Comparison of Heart Rate NadQTc Interval with Respect to Cutoff Between Groups n=174

Heart Rate (b/min) Cutoff	Study Group n=87	Control Group N=87	Total n=174	P-Value
≤ 100	67(77%)	76(87.4%)	143(82.2%)	0.075
>100	20(23%)	11(12.6%)	31(17.8%)	
QTc Interval (Sec)				
≤ 0.44	68(78.2%)	79(90.8%)	143(84.5%)	0.021
> 0.44	19(21.8%)*	08(9.2%)	31(15.5%)	

Discussion

Cirrhosis, the end result of liver damage resulting in nodular regeneration across the liver and fibrosis, is a severe and permanent disease and among the world's major causes of death.[20] Cirrhotic cardiovascular complication includes cardiac failure as well as central, peripheral circulation, and splanchnic abnormalities, as well as hemodynamic alterations induced by deregulation of humor and nerves.[11] Cirrhotic cardiomyopathy has been recently recognized as a disorder of cirrhosis comprised of systolic failure under stress, diastolic failure associated with modified diastolic stress relief, and electrophysiological anomalies if there is no any recognized heart diseases.[21] Electrophysiological abnormalities involve uncoupling electromechanical, chronotropic incompetence, and prolonged QT intervals. In cirrhosis, prolongation of QT interval happens commonly, regardless of the disease's etiology.[21] In chronic hepatic disease, extended QT duration may result in unexpected cardiac mortality and ventricular arrhythmias.[6] The current study documents that average QTc were significantly high in cirrhotic group as compared to non-cirrhotic control group (0.47 vs 0.40; P=0.003). Significant prolongation of QTc (> 0.44 sec) in cirrhotic patients were seen as compared to non-cirrhotic control (21.8% vs 9.2%; P= 0.021). This is comparable to most of previous studies. Day et at[13] in UK were one of the first to report a prolonged QTc in patients with alcoholic liver disease, the mean QTc was 0.45 seconds in cirrhosis as compared to 0.43 seconds in control (P=0.016). Another study done by Jasdeep Singh et al[18] showed prolonged QTc in cirrhotic (40 %) irrespective of etiology. He also observed that this prolongation was further frequent in subjects with alcoholic cirrhosis 60%

than non-alcoholic cirrhosis 35% (P<0.001). In more recent studies QTc prolongation has been observed in 19.2%, 46.93%, 33%[6,17,22] respectively in cirrhotic patients as compared to non-cirrhotic control. Our study also correlated QTc interval prolongation with child Pugh's score. Other studies also showed that QTc prolongation correlate with severity of hepatic disease as evaluated by child Pugh's score.[12] In our study average heart rate in cirrhotic patients was significantly high (group 1) than non-cirrhotic patients i.e. 83.86 vs. 74.85; P=0.0005. However comparison of frequency of increase heart rate above 100/min were not significant between cirrhotic and non-cirrhotic patients (23% vs. 12.6%; P=0.075). These results also comparable with previous studies.[6,8] A much longer study with patient follow up is required to show any effect of prolonged QT interval on survival. Nonetheless, prolonged QTc interval is a marker of life threatening arrhythmias. Therefore ECG will be prescribed to all patients with cirrhosis to timely diagnosed prolonged QTc interval and to escape an otherwise impending death. QTc interval improvement has been reported with improvement in beta-blockers, hepatic functions, and liver transplantations.[7]

Conclusion

The results showed importance of measuring QTc interval prolongation and Heart rate increase in cirrhotic patients. As, not much work has been done on HR and QTc interval in cirrhosis at local level, so these results emphasize the need for identification of risk factor of QTc prolongation and minimizing the occurrence of arrhythmias.

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