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Original Article

Prevalance of Prolonged Qt Interval In Patients with Chronic Liver Disease

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ABSTRACT

The incidence of QT prolongation in CLD patients is greater than 45% compared to approximately 5% in the general population. Multiple researches have revealed that end-stage liver disease is related with a variety of changes in electrophysiological parameters; especially in our population, a higher incidence of QT interval prolongation is observed. Prolonged QT intervals in chronic liver disease patients are related with augmented mortality and morbidity. **Objective:** To determine the frequency of QT prolongation in patients with chronic liver disease. **Methods:** A cross-sectional and descriptive study. 96 total patients aged 20-85 years of both sexes with chronic liver disease (CLD) were included. Patients with a history of coronary artery disease and the use of any anti-arrhythmic medication were excluded from the study. The 12-lead ECG was performed and interpreted by an electrophysiologist with over five years of experience. The Bazett-based QT interval (QTc) was automatically obtained using a computerized electrocardiograph to avoid inter-observer variability. **Results:** 20 to 60 years was the patients age in this study, with 39.44 ± 9.91 years of mean age. The maximum patients, 86 (89.58%), were 20-40 years of age. Among the 96 patients, 17 (17.71%) were female and 79 (82.17%) were male, with a M: F ratio of 1.3: 1. While the incidence of QT prolongation was found in 47 (48.96%) patients, 49 (51.04%) patients did not have QT prolongation. **Conclusions:** In this study it was found that the frequency of QT prolongation is quite high in patients with chronic liver disease.

INTRODUCTION

Cirrhosis of the liver, which continues to be a serious health problem in both developed and developing countries, is a disease that causes end stage liver disease and portal hypertension with characteristic clinical signs and histologically progression of regenerative nodules enclosed by fibrous bands in response to CLD [1-2]. The 12th important cause of mortality worldwide is liver cirrhosis, with over 27,000 deaths and over 421,000 hospitalizations annually [3-4]. While alcoholic liver disease and chronic hepatitis C virus infection are the communal reasons of cirrhosis in developed countries, chronic hepatitis B virus infection is the major source in under developed countries [5]. For the past several years, cardiac dysfunction related with cirrhosis caused by direct alcohol effect on heart [6]. Though, Abelmann and Kowalski in 1953 demonstrated the presence of a circulatory disturbance characteristic of CLD [7]. Subsequently then, few researches have constantly exhibited these results. Subsequent, clinical and experimental studies have introduced the notion that cirrhotic cardiomyopathy (CCM) is a medical condition separate from alcoholic heart disease [8-9]. Given that the liver receives 25% of cardiac output, an interaction of liver disease with circulatory and cardiac output can be anticipated. Cirrhosis of the liver results in circulatory hyperdynamic state that results in the cardiac dysfunction characteristic of CCM [10-11]. This clinical disorder sometimes comprises, hyperdynamic circulation,

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prolonged repolarization of the ventricles, a combination of diastolic and systolic dysfunction and the incapability of the sinus node to rise heart rate (HR) during exercise [12]. The incidence of QT prolongation in liver cirrhosis patients is greater than 45% compared to approximately 5% in the general population. Multiple researches have revealed that ESLD is related with a variety of changes in electrophysiological parameters; in particular, there is a higher incidence of prolongation of QT in our people. QT prolongation in CLD patients is related with augmented mortality and morbidity [13]. In a study by Ali et al, 48% of QT prolongation was reported and found to be directly proportional to the severity of cirrhosis [14]. The aim of the study was to determine the frequency of QT prolongation in patients with chronic liver disease.

METHODS

This cross-sectional descriptive study was conducted at JPMC Medical Unit III, Karachi, October 15, 2019 to April 14, 2020. 96 total patients with chronic liver disease (CLD) and 20 to 30 patients, 85 years of age, of both sexes were evaluated. included in the non-probabilistic sequential sampling technique. Inclusion criteria were patients of both sexes aged 20-85 years with chronic liver disease and patients who did not consent to the study, patients with coronary artery disease and patients taking medications. e.g. quinidine gluconate, procainamide hydrochloride and disopyramide phosphate etc. Before entering the study, all participants were explained the purpose and benefits of the study, and the principal investigator obtained oral consent from all patients for their participation in the study. Patient demographic characteristics such as age (year) and gender were recorded. The Child-Pugh Score was obtained according to the operational definition, and the severity of the disease was classified according to the operational definition. The 12-lead ECG was performed and interpreted by an electrophysiologist with over five years of experience. The Bazett-based QT interval (QTc) was automatically obtained using a computerized electrocardiograph to avoid inter-observer variability. Using Bazett's principle, the interval of QT was estimated from the start of the QRS complex to the end of the T wave and divided by the R-R interval square root in seconds. SPSS version 21.0 was used for analysis of data. The percentages and frequencies were calculated for categorical variables such as age group, gender, prolonged QT interval and disease severity. Effect modifiers such as age groups, gender, and disease severity were controlled by stratification. The Fisher's exact test and chi-square test was used post-stratification. Two-sided p value ≤ 0.05 taken as a criterion of statistical significance.

RESULTS

Among the 96 patients, 17 (17.71%) were female and 79 (82.17%) were male, with a M:F ratio of 1.3: 1 as shown in Figure I.

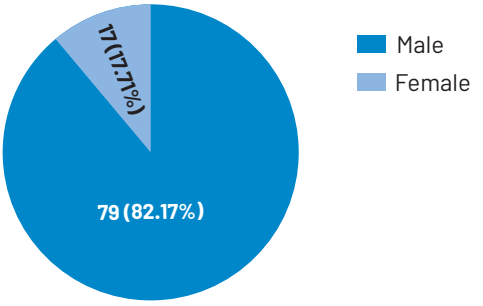

Figure 1: The patient's distribution conferring to gender (n=96)

Distribution of patients conferring to child pugh class and are shown in Figure 2. The males were 17.7% and females were 82.3%.

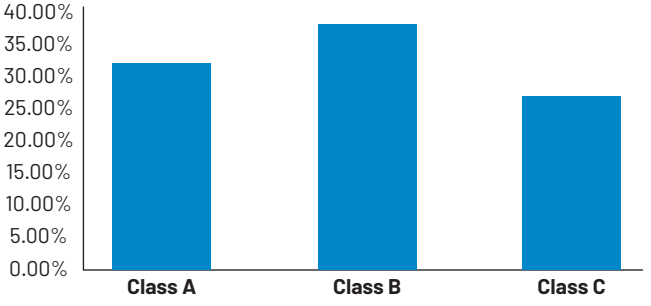

Figure 2: Distribution of patients according to Child Pugh Class (n=96)

32.29% of the patients were in the Class A, 39.58% in the class B and 28.13 were from Class C according to Child Pugh class. 20 to 60 years was the patients mean age in this study, with 39.44 ± 9.91 years of mean age. The maximum patients, 86 (89.58%), were 20-50 years of age as shown in Table 1.

Age (in years)	No. of Patients (%)
20-50	86 (89.58%)
51-85	10 (10.42%)
Total	96 (100.0%)

Table 1: shows the patients distribution with reference to age-groups (n=96)

Frequency of prolonged QT interval was found in 47 (48.96%) patients, whereas there was no prolonged QT interval in 49 (51.04%) patients as shown in Figure 3.

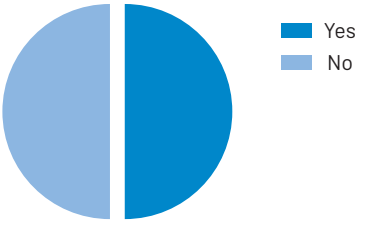

Figure 3: Frequency of prolonged QT interval in patients with

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chronic liver diseases (n=96)

The frequency of patients with prolonged QT interval was seen in 48.9% of patients with chronic liver disease. When Stratification of prolonged QT interval was done on age groups and no significant change was found among the various age groups as given in Table 2 while the prolonged QT interval stratification with respect to gender is given in Table 3 which also exhibited no significant change between females and males.

Age (years)	Prolonged QT interval		P-value
	Yes	No	
20-50	42	44	0.944
51-85	05	05	

Table 2: Stratification of prolonged QT interval with respect to age

With respect to age, 42 patients have prolonged QT interval in 20-50 years of age group and with respect to gender 42 males have prolonged QT interval as shown in Table 2 and 3.

Gender	Prolonged QT interval		P-value
	Yes	No	
Male	42	37	0.076
Female	05	12	

Table 3: Stratification of prolonged QT interval with respect to gender

Table 4 has shown the stratification of prolonged QT interval with respect to Child pugh class. The child Pugh Class shows that 15 patients in Class A, 20 in class B and 12 in class C have prolonged QT interval with respect to Child Pugh Class

Child Pugh Class	Prolonged QT interval		P-value
	Yes	No	
Class A	15	16	0.807
Class B	20	18	
Class C	12	15	

Table 4: Stratification of prolonged QT interval with respect to Child Pugh Class

DISCUSSION

Cirrhosis of the liver is a progressive pathological process considered by regeneration of nodules and fibrosis. The common causes of liver cirrhosis, including infection with hepatitis B and C viruses, autoimmune diseases, medications (including alcohol), non-alcoholic steatohepatitis and genetic diseases [15]. In addition to liver damage, patients with cirrhosis have pulmonary, renal, cardiac and hemodynamic dysfunctions that upsurge the mortality and morbidity. This study shows that chronic cardiac dysfunction is the characteristic feature in cirrhotic cardiomyopathy in patients with liver cirrhosis without prior any cardiac anomaly as shown by the results of Møller S et al [16]. It is well-defined by the presence of one of the subsequent variations: electrophysiological changes, increased or normal resting systolic function but poor stress response; structural abnormalities in the ventricles and diastolic dysfunction. These anomalies may be seen in up to 50% of subjects with cirrhosis in Ali M et al study as in our study [17]. Mostly, people with cardiomyopathy along with cirrhosis are symptomless, therefore follow-up testing is important to identify them [18-19]. An electrocardiogram (EKG) is a non-invasive, low-cost method that can support to recognize subjects with cirrhosis cardiomyopathy [20]. The most important cardiac abnormality, QT prolongation mostly associated with cirrhosis and can be simply detected by EC. A prolonged QT interval is associated with augmented mortality in chronic liver disease patients as exhibited by this study and the results of Tangerman A and Suurmond D exhibited the same results [21-22]. The mechanism accountable for the QT interval prolongation is unknown. Modifications at the molecular level have been suggested [23]. Other factors include electrolyte abnormalities, myocardial ischemia, and changes in the activity of the autonomic nerves, which, through various mechanisms, may affect heart rate and electromechanical abnormalities [24]. It has been suggested that the disturbances of gonadal hormone metabolism in advanced cirrhosis contribute to the prolongation of the QT interval in this condition. In the present study, we found that the QTc interval was significantly longer in women [25]. There are reports that women are more susceptible to torsade's de pointes than men, which correlates with the quantitative sex difference in the electrocardiographic manifestation of myocardial repolarization. This gender difference has been confirmed and applied to various ECG markers.

CONCLUSIONS

This study found that the frequency of QT prolongation in patients with chronic liver disease was quite high. Therefore, study commend considering QT prolongation and early detection and treatment in all chronic liver disease patients to reduce morbidity and mortality in the population.

Conflicts of Interest

The authors declare no conflict of interest.

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