Original Article
DOI: https://doi.org/10.70749/ijbr.v3i4.2475

INDUS JOURNAL OF BIOSCIENCE RESEARCH
https://ijbr.com.pk
ISSN: 2960-2793/ 2960-2807

Frequency of Prolonged QTc Interval in Patients with Cirrhotic Liver Disease in Medical Unit-4 DHQ Hospital Faisalabad

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ARTICLE INFO

Keywords: Cirrhosis, QTc Prolongation, Electrocardiography, Child–Pugh Class, Liver Disease Severity.

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Declaration
Authors' Contribution
All authors equally contributed to the study and approved the final manuscript

Conflict of Interest: No conflict of interest.

Funding: No funding received by the authors.

Article History
Received: 10-01-2025 Revised: 28-03-2025
Accepted: 14-04-2025 Published: 30-04-2025

ABSTRACT

Background: Cirrhotic liver disease is linked to a number of abnormalities in the cardiovascular system such as prolongation of the corrected QT (QTc) interval, which may predispose patients to life-threatening arrhythmia. QTc prolongation has been recognized as a part of cirrhotic cardiomyopathy increasingly and is believed to get worse with the progression of liver disease. Early identification is necessary to reduce morbidity and mortality. **Objective:** To calculate the frequency of prolonged QTc interval in patients with cirrhotic liver disease, and to evaluate the association between prolonged QTc and demographic and clinical variables. **Methodology:** This descriptive cross sectional study was carried out from the Department of Medicine, DHQ Hospital Faisalabad during the period of 6 months. A total of 145 clinically diagnosed cirrhotic patients aged between 18-60 years old were recruited using non-probability consecutive sampling technique. Patients with cardiac diseases, hypertension, chronic renal failure, COPD or pregnancy were excluded. After informed consent, clinical assessment, laboratory tests, ultrasound of abdomen and standard 12-lead ECG were carried out in detail. QTc was calculated by Bazett ka formula. Data were analyzed in SPSS 25. Mean +- SD were reported for quantitative variables while frequencies and percentages were used for qualitative data. **Results:** The mean age of the participants was 40.53 +- 12.74 years and 54.5% were males. Prolonged QTc interval was found in 21.4% of patients. QTc prolongation was significantly linked to female gender ($p = 0.005$), upper age groups ($p = 0.003$), higher Child-Pugh class ($p < 0.001$) and higher severity of the disease ($p < 0.001$). **Conclusion:** QTc prolongation is a common electrophysiologic abnormality in cirrhotic patients and is related to higher liver disease severity. Routine ECG screening is advised because it allows early identification and management of small subgroups of high-risk individuals.

INTRODUCTION

Chronic liver diseases resulting in liver cirrhosis are one of the major health concerns worldwide(1, 2). Liver cirrhosis is a disease that progressively disrupts the normal architecture of the liver and can be caused by some conditions. Up to 90% of liver parenchyma undergoes destruction before liver failure becomes clinically evident. Cirrhosis is a very common ailment in Pakistan(3), mostly caused by viral hepatitis B and C. The prevalence of this disease is still very high despite adequate measures to control the viral infections. Liver cirrhosis results in many complications, out of which ascites, esophageal varices, and portal hypertension are well known (4).

The consequences of liver cirrhosis on the cardiovascular and circulatory system are not well studied. The use of modern investigative modalities has revealed several lines of evidence of abnormal cardiac contractility and impaired heart functioning. These pathologies have led to the introduction of a new clinical term, cirrhotic cardiomyopathy. It has many features, including prolongation of the QTc interval, increased heart rate, decreased myocardial contraction force, and diastolic dysfunction(5).

Cirrhotic cardiomyopathy is characterized by increased cardiac output, decreased response to physiologic and pharmacologic stimuli, systolic and diastolic dysfunction, and electrophysiologic abnormalities in the absence of any known cardiac disease. A prolonged QT interval on electrocardiography (ECG) is the hallmark of cirrhotic cardiomyopathy(6). QT duration prolongation occurs in 30–50% of patients with liver cirrhosis. QT interval varies widely with age, gender, and heart rate (Min Ou). The QT interval represents ventricular depolarization and repolarization. Prolonged QT interval results in malignant ventricular tachyarrhythmias. This has a high impact on the patient's activity, work, quality of

life, life expectancy, and the economic burden it constitutes(7).

Several studies have shown that patients with liver cirrhosis have prolonged QT intervals. A prolonged QTc interval in patients with chronic liver disease could potentially lead to ventricular arrhythmias and can result in sudden cardiac death(8). Prolonged QTc interval in patients with chronic liver disease showed higher mortality rates than those with a normal QTc interval. There was a 7-fold increased risk of mortality in patients with chronic liver disease who had prolonged QTc(9).

Qadir et al conducted a study to determine the frequency of prolonged QTc interval in patients with chronic disease. This study included 239 patients having chronic liver disease. The QTc interval ranged from 384ms to 476ms, the mean of which is 421.8±25.2ms. Using a cut-off value of 440ms for prolonged QTc, the frequency of prolonged QTc was found to be 23.8% in all the patients, regardless of age and gender(10).

QTc interval is prolonged in almost half of the patients and the frequency of prolonged QTc is directly proportional to the severity of the hepatic cirrhosis according to Child-Pugh criteria. [9] This study will be used in early screening of all patients with chronic liver disease for QTc prolongation during their hospital stay or at presentation, which predicts malignant arrhythmias. So in the future, patients with cirrhosis can be investigated for prolonged QTc, and the proper diagnosis and treatment can reduce the morbidity and mortality associated with this problem.

METHODOLOGY

This descriptive cross sectional study was carried out in the department of medicine, DHQ Hospital, Faisalabad over a 6 months period of time after approval of synopsis. A total of 145 patients were used to develop this study using non-probability consecutive sampling, which was based on a sample size calculated for WHS using the WHO calculator, by taking a previously reported QTc prolongation frequency of 23.8% and the margin of error of 7% at a 95% confidence level. Both male and female patients between the age group of 18-60 years years old, clinically diagnosed with liver cirrhosis according to the operational criteria were included in the study. Patients under the ages of <18 or >60 years and patients with pre-existing cardiac conditions such as valvular heart disease, ischemic heart disease, heart failure, hypertension, chronic renal failure, chronic obstructive pulmonary disease, and pregnancy, were excluded, to avoid any confounding factors.

After having ethical approval from the Institutional Review Committee and CPSP, eligible patients admitted to the medical ward or presenting in the out-patient department, were approached and informed consent was obtained. Participants were provided with information regarding the study objectives, confidentiality and absence of associated risk. Detailed History and detailed clinical examination were carried out followed by laboratory investigations (complete blood counts, renal function tests, liver function tests and prothrombin time and serum albumin, electrolytes, and viral markers anti-HCV and HBsAg using Enzyme immunoassays). Radiological assessment using ultrasonography and chest X-ray of abdomen was also performed. A conventional 12-lead ECG was obtained on each patient. The measures of the QT and R-R intervals were taken and the corrected QT interval (QTc) was calculated using Bazett's formula (QTc = QT/ square root of RR). All the findings were recorded on a pre-designed proforma.

Data were analyzed with the help of the statistical software, version 25, of the International Statistical Institute (SPSS). Quantitative variables, e.g., age, were reported as mean +- standard deviation and qualitative variables, e.g., gender and QTc status (normal or prolonged), were reported as frequencies and percentages. Potential effect modifiers, such as age, gender, duration and severity of disease assessed with Child-Pugh classification, were controlled for using stratification calculation. Following stratification, the association of these modifiers and QTc prolongation was determined using the chi-square test. P-value <= 0.05 was considered statistically significant.

RESULTS

A total of 145 patients were diagnosed with cirrhotic liver disease and included in this study. The mean age of the participants was 40.53+-12.74 years. Of these, 79 (54.5%) were males and 66 (45.5%) were females. The average time of liver disease was 14.67 +- 13.75 months. According to the Child-Pugh classification, the majority of patients were in Class B, which consisted of 65%, followed by Class A (24.1%) and Class C (15.9%). Disease severity also showed a similar distribution with moderate disease being the most prevalent (58.6%), followed by mild (25.5%) and severe disease (15.9%). The details are summarized in Table 1.

Regarding the primary outcome, the cases of prolonged QTc interval were 21.4% (31 patients) and 78.6% (114 patients) with a normal QTc interval (Table 2).

Stratified analysis showed statistically significant links with QTc prolongation for many variables. QTc prolongation was more frequent in females (67.7%) than in male (32.3%) with significant p-value of 0.005. QTc prolongation was also seen with increasing age, which was not seen in patients between the age of 18-30 years and highest in patients who were 46-60 years old (87.1%) and showed a significant association (p = 0.003).

A strong link was also found to severity of liver disease. No patient with a mild disease had QTc prolongation. 41.9% of patients with a severe disease had QTc prolongation (p < 0.001). Similarly, QTc prolongation was also progressively found with increasing severity of Child-Pugh class: QTc prolongation in none in Class A, 58.1% in Class B, and 41.9% in Class C (p < 0.001). These results are presented in Table 3.

Table 1

Demographic Features of Patients (n = 145)

Variable	n (%) or Mean ± SD
Age (years)	40.53 ± 12.74
Gender	
Male	79 (54.5%)
Female	66 (45.5%)
Duration of Disease (months)	14.67 ± 13.75
Child-Pugh Class	
A	35 (24.1%)

B	87 (65%)
C	23 (15.9%)
Severity of Disease	
Mild	37 (25.5%)
Moderate	85 (58.6%)
Severe	23 (15.9%)

This table outlines the baseline characteristics of 145 patients who were enrolled in the study. It involves the average age, distribution of genders, time of the disease along with Child-Pugh classifications and severity of cirrhosis. The data indicates that most of the patients were in Child-Pugh Class B and were moderately sick.

Table 2

Frequency of QTc Prolongation

	Frequency	Percent
Normal	114	78.6
Prolonged	31	21.4
Total	145	100.0

Table 2 summarizes the chief outcome variable of the study. Out of 145 patients, 31 (21.4%) patients had prolonged QTc interval, and 114 (78.6%) patients had a normal QTc interval. This table shows the general prevalence of QTc prolongation in cirrhotic patients.

Figure 1

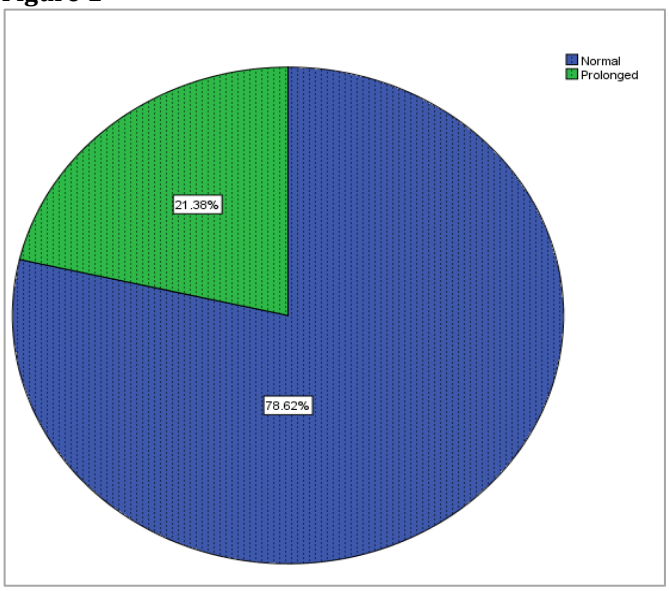

Table 3

QTc Prolongation by Gender, Child Pugh Class and Severity of Disease

Variable		Normal n (%)	Prolonged n (%)	p-value
Gender	Male	69 (60.5%)	10 (32.3%)	0.005
	Female	45 (39.5%)	21 (67.7%)	
Age Groups	18-30 years	20 (17.5%)	0 (0.0%)	0.003
	31-45 years	18 (15.8%)	4 (12.9%)	
	46- 60 years	76 (66.7%)	27 (87.1%)	
Child Pugh Class	Class A	35(30.7%)	0 (0.0%)	0.000
	Class B	69 (60.5%)	18 (58.1%)	
	Class C	10 (8.8%)	13 (41.9%)	
Disease Severity	Mild	37 (32.5%)	0 (0.0%)	0.000
	Moderate	67 (58.8)	18(58.1%)	
	Severe	10 (8.8%)	13(41.9%)	
Total		114 (100.0%)	31 (100.0%)	

This table cross compares the QTc status in various demographic and clinical variables. It displays the count and percentage of normal versus prolonged QTc in each of the subgroups and p-values to establish statistical significance. QTc prolongation was significantly linked to gender, age, severity of the disease and Child-Pugh class. The prevalence was highest among females, the older age groups, and patients with advanced liver disease.

DISCUSSION

We found a 21.4% frequency of QTc prolongation in this cross-sectional study of 145 liver cirrhosis patients. Moreover, QTc prolongation was significantly correlated with female gender, old age and more advanced liver disease (higher disease severity and poor Child-Pugh score classes). These results offer not only new data from our population but also differ in some ways from other regional and international reports highlighting the variability in QTc prolongation among cirrhotic patients.

Few previous studies have reported increased prevalence of QTc prolongation in cirrhosis. For example, a cross-sectional study from Gujrat on 150 cirrhotic patients reported the frequency of QTc prolongation to be 29.3% (11). Another study noted prevalence around 35% among 380 cirrhotic patients in Karachi(12). Some older but widely cited literature reported prevalence ranging from ~45% to ~53% (or greater) in chronic liver disease / cirrhosis cohorts. A recent meta-analysis also concluded that QTc is significantly prolonged in cirrhotic patients compared with non-cirrhotic controls, and that prolongation correlates strongly with disease severity (higher Child–Pugh class or model-for-end-stage-liver-disease score), regardless of sex, age, or etiology(13).

The lower frequency (21.4%) in our cohort could be due to several factors. First, variation in cutoff values used to define "prolonged QTc" may play a role; different studies have used slightly different thresholds (e.g.,> 440 ms, or sex-specific cutoffs). For instance, in the study from the tertiary care hospital in Karachi, the mean QTc was 0.44 ± 0.067 sec with 35% having prolonged QTc(12). Second, demographic, etiological, or biochemical differences among populations may influence the electrophysiological impact of cirrhosis. Third, exclusion of patients with cardiac comorbidities and other confounders may have resulted in a "healthier" cirrhotic cohort in our study, thereby reducing the observed QTc prolongation frequency.

Our finding that QTc prolongation was associated with female gender and older age is congruent with some studies but not all. In our cohort, more females had QT prolongation compared to males; similarly, a 2021 cross-sectional study found that among its cirrhotic patients, females had a higher prevalence of QTc prolongation (p = 0.047). However, the recent meta-analysis did **not** find a significant association with sex or age overall(13). This discrepancy may arise from the relatively small sample sizes, demographic differences, or differing statistical power in subgroups. It also suggests that while cirrhosis-related QTc prolongation is common, the influence of age or sex may be population-specific or modulated by other factors (e.g., comorbidities, medications, biochemical derangements).

Importantly, our data reinforce the association between QTc prolongation and severity of liver disease (both in terms of clinical severity and Child–Pugh

classification). This parallels findings from several prior investigations. In the original landmark study by Bernardi et al, QTc was prolonged in 46.8% of cirrhotic patients and the prolongation correlated significantly with Child–Pugh score, serum albumin, bilirubin, bile salts, and plasma norepinephrine levels. (14, 15). A more recent large observational study involving 300 cirrhotic patients reported 64.7% had prolonged QTc; QTc was significantly associated with complications of cirrhosis (portal hypertension, ascites, splenomegaly), elevated liver enzymes and Child–Pugh class(14). Another cohort from decompensated chronic liver disease reported QTc prolongation in ~30% of patients, with significant association with age, bilirubin, and disease class(16).

The clinical and prognostic relevance of QTc prolongation in cirrhosis has been suggested. The earlier Bernardi et al. study found that patients with QTc > 440 ms had significantly lower survival over follow-up compared to those with normal QTc(15). Also, in a scenario of acute stress (e.g. gastrointestinal bleeding), QTc may further prolong transiently, and longer QTc at the time of bleeding was associated with higher short-term mortality(17). Conversely, data from post-transplantation settings suggest that QTc prolongation in cirrhosis may be reversible: in a study of patients undergoing Liver transplantation (LT), mean QTc significantly reduced by six months post-LT in 73% of patients, though early post-operative QTc was transiently increased(18). This reversibility supports the concept that QTc prolongation in cirrhosis reflects functional (rather than fixed structural) cardiac/electrophysiological alterations possibly mediated via metabolic, autonomic or hormonal disturbances inherent to liver failure(19).

Given these observations, our study, despite a lower absolute prevalence, supports the notion that QTc prolongation is a frequent and clinically relevant phenomenon in cirrhosis, especially as disease severity advances. It underscores the importance of routine ECG screening in cirrhotic patients, as recommended by earlier authors(12). Our study lacks a control (non-cirrhotic) group, which restricts comparison to general population baseline QTc values. Also, we used only a single ECG per patient; serial ECGs could better capture transient QTc changes (e.g., with electrolyte fluctuations or acute stress). Moreover, we did not evaluate biochemical parameters (electrolytes, bile salts, neurohormonal markers) that could help explore pathophysiological mechanisms.

Our findings add to existing evidence that QTc prolongation is linked to cirrhosis and its severity, and highlight variability across populations. Given the potential prognostic significance (arrhythmias, sudden death, mortality), we recommend periodic ECG monitoring in cirrhotic patients, especially those with advanced disease, and further prospective studies to evaluate outcomes.

CONCLUSION

In this study, QTc prolongation was identified in 21.4% of patients with liver cirrhosis, with a strong association observed between prolonged QTc interval and advanced age, female gender, higher Child–Pugh class, and greater disease severity. These findings highlight that electrophysiological abnormalities become more pronounced as cirrhosis progresses. Given the potential risk of malignant arrhythmias and increased mortality linked to prolonged QTc, routine ECG monitoring should be incorporated into the clinical evaluation of cirrhotic patients, particularly those with advanced disease. Early detection and timely management may help reduce cardiac complications and improve overall outcomes in this high-risk population.

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