

A Comparison of QTc Abnormalities in Cirrhotics with Non-Cirrhotic

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Author's Contribution

^{1,3,4} Conception of study

^{2,5} Experimentation/Study conduction

^{5,6} Analysis/Interpretation/Discussion

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Abstract

Objective: To compare the frequency of prolonged QTc interval in cirrhotics with non-cirrhotics having chronic liver disease.

Study design: Cohort study.

Place and Duration of Study: Department of Gastroenterology AK CMH/Sheikh Khalifa Bin Zayed Al Nahyan Hospital Rawalakot Azad Kashmir. Six months; (27-03-2019 to 26-09-2019).

Material and Methods: One hundred patients with liver cirrhosis (group I) and 100 non-cirrhotic patients ((group II) had 12 lead ECGs. QT interval was calculated. And the patients were evaluated for the presence of prolonged QT interval. Statistical significant determined by chi-square test ($p < 0.05$ was taken as significant).

Results: The mean QTc duration in Group I was 0.536 ± 0.012 seconds and group II was 0.431 ± 0.015 seconds ($p < 0.05$). Prolonged QTc interval was present among 36(36%) patients in Group I and 6 (6%) patients in Group II. ($p < 0.05$).

Conclusion: Our study findings revealed that cirrhotic patients have more chances of developing the QTc abnormalities as compared to the patients without the presence of cirrhotic liver.

Keywords: Cirrhosis; cardiomyopathy; prolonged QTc interval.

Introduction

Liver cirrhosis (LC) is a late stage of progressive hepatic fibrosis is characterized by distortion of the architecture and formation of regenerative nodules and different degrees of liver function impairment; these patients are prone to a variety of complications reducing life expectancy markedly.¹

The World Health Organization (WHO) indicates that 10% of the world's population has chronic liver disease. 2 Liver cirrhosis is an epidemic in Pakistan due to the very high prevalence of Hepatitis B and C in our community. Hepatitis C is the leading cause of Cirrhosis in Pakistan.³

Approximately 10 million peoples have been infected with Hepatitis C infection in Pakistan.⁴ It is estimated that 3% of the world's population has been infected with Hepatitis C infection. The prevalence of hepatitis C in Pakistan is 4-6%.⁵

In the evolution of many chronic liver diseases, cirrhosis is a stage that is considered to be irreversible. The most common complications of cirrhosis are gastrointestinal hemorrhage, ascites, encephalopathy, bacterial infections, renal failure, hepatocellular carcinoma, and hepatic failure. Certain reversible components of cirrhosis have been indicated where significant histological improvement has occurred with regression of cirrhosis but complete resolution with a return to normal architecture seems unlikely.⁶ The underlying immunological response has usually been acting for months or years where inflammation and tissue repairing are in progress simultaneously which leads in the end to fibrosis and cirrhosis.⁷

The main causes of cirrhosis are alcoholic liver disease (ALD), hepatitis B (HBV), hepatitis C (HCV), non-alcoholic steatohepatitis (NASH), haemochromatosis, auto-immune hepatitis (AIH), primary biliary cirrhosis (PBC), and primary sclerosing cholangitis (PSC).⁸ The natural history of cirrhosis can be divided into a preclinical and a subsequent clinical phase. The preclinical phase is usually prolonged over several years; once clinical events occur, such as ascites, encephalopathy, variceal bleeding, or the development of hepatocellular carcinoma the remaining course of the disease is much shorter and usually fatal.⁹

Liver cirrhosis is associated with different cardiovascular abnormalities called cirrhotic cardiomyopathy which is defined as the constellation of one or more of the following changes:

1. normal or augmented systolic function at rest but blunted contractile responsiveness to stress,

2. altered diastolic relaxation,
3. structural abnormalities in the cardiac chambers, and
4. electrophysiological changes such as prolonged QT.¹⁰⁻¹²

The QT interval is a measure of ventricular electrical recovery after excitation.¹³ Acquired QTc prolongation has been described in association with cardiac diseases, electrolyte abnormalities (such as hypocalcemia, hypomagnesemia, and hypokalemia), and many commonly used drugs. Prolonged QTc may provide the substrate for ventricular arrhythmias.^{14,15,16} Cirrhotic cardiomyopathy may play a role in the pathogenesis of the hepatorenal syndrome.^{17,18} It is a new entity and very little work has been done in Pakistan. Exact data is lacking in our population and my study will help in the early detection of cardiac abnormalities, which will help better management and also the risk of sudden cardiac death in cirrhotic patients.

Materials and Methods

This cohort study was conducted at the Department of Gastroenterology AK CMH/Sheikh Khalifa Bin Zayed Al Nahyan Hospital Rawalakot Azad Kashmir for six months after the approval from the hospital ethical committee (27/03/19 to 26/09/19). A sample size of 200 cases (100 in each group) was calculated with 80% power of the test, 1% level of significance, and taking an expected percentage of QTc abnormality in both groups i.e. 37% in patients with cirrhosis versus 5.9% in non-cirrhotics having chronic liver disease. The non-probability purposive sampling technique was used to gather the sample. Patient from 18 to 70 years of age from both genders who had cirrhosis of liver proved (by ultrasound by Radiology department of AK CMH/Sheikh Khalifa Bin Zayed Al Nahyan Hospital Rawalakot Azad Kashmir), were placed in Group I, and patient having HCV positive (by pathology department of AK CMH/Sheikh Khalifa Bin Zayed Al Nahyan Hospital Rawalakot Azad Kashmir) but had not developed cirrhosis (by ultrasound by Radiology department of AK CMH/Sheikh Khalifa Bin Zayed Al Nahyan Hospital Rawalakot Azad Kashmir) were placed in Group II. Patients with HTN, IHD and taking cardio-selective drugs such as B-Blockers, Ca channel blockers, anti-arrhythmic and cardiac glycosides (assessed on patient history) and those with conduction defect on ECG or those with valvular heart disease and heart failure on Echocardiography were

excluded from the study Hyperkalemic patients were also not included in the study.

100 patients with cirrhosis of the liver (Group-I) and 100 non-cirrhotic patients (Group-II) were enrolled from the Department of Gastroenterology AK CMH/Sheikh Khalifa Bin Zayed Al Nahyan Hospital Rawalakot Azad Kashmir. After informed consent, patients' demographic details like name, age, the sex were recorded. Every patient had three ECGs by the same ECG machine (Nihon Kohden Cardioline), which was used for taking mean QTc interval for each patient, and all the ECGs were interpreted by the same observer following standard criteria to avoid observer bias for detection of prolonged QTc interval. Data was entered on the specifically designed study proforma. Data was entered and analyzed by using the Statistical Package for Social Sciences version 23.0. The qualitative data like gender and prolonged QTc were presented as frequency distribution and quantitative data like age (in years) were presented as mean \pm SD. Comparison of prolonged QTc interval in Cirrhotics and non-Cirrhotics was done by Chi-square test. P-value ≤ 0.05 was considered statistically significant.

Results

Two hundred patients were included in this study. Each group had 100 patients. The mean age of the patients in Group I was 40.22 ± 10.66 years [range 19 – 68]. There were 7 (7%) patients of the age range of 18 – 30 years, 13 (13%) patients of the age range of 31 – 40 years, 39 (39%) patients of the age range of 41– 50 years, 32 (32 %) patients of the age range of 51 – 60 years and 9 (9%) patients of the age range of 61 – 70 years. The mean age of the patients in Group II was 37.81 ± 10.58 years [range 20 – 69]. There were 11 (11%) patients of the age range of 20 – 30 years, 24 (24%) patients of the age range of 31 – 40 years, 29 (29%) patients of the age range of 41– 50 years, 24 (24%) patients of the age range of 51 – 60 years and 12 (12%) patients of the age range of 61 – 70 years. There were 55 (55%) female patients in Group I and 34 (34%) in Group II. Similarly, there were 55 (55%) male patients in Group I and 67 (67%) patients in Group II. The mean QTc duration in Group I was $0.536 + 0.012$ seconds and Group II was $0.431 + 0.015$ seconds. The results were statistically significant (p-value < 0.05) (Table 1). Prolonged QTc interval was present among 36 (36%) patients in Group I and 6 (6%) patients in Group II. QTc interval was not prolonged among 64 (64%) patients in Group I and in 94 (94%) patients in

Group II. The results were statistically significant (p < 0.05) (Table 2).

Table 1: Distribution of patients based on QTc duration (Student t-test)

QTc Duration (seconds)	Group I Mean + SD	Group II Mean + SD
	0.536 + 0.012	0.431 + 0.015
p-value	0.001**	

Table 2: Distribution of patients by prolonged QTc (Chi-square test)

Prolonged QTc Interval	Group I		Group II		p-value*
	No.	%	No.	%	
Yes	36	36	8	6	0.000*
No	64	64	92	94	*
Total	100	100	100	100	

Discussion

Cardiovascular changes among cirrhotic patients are not infrequent which is not diagnosed routinely because of relative unawareness regarding this entity. It has many features including prolongation of QTc, increased HR, decreased myocardial contraction force, and diastolic dysfunction. Prolonged QTc interval was a common finding in our study, which was present more frequently, i.e. 36% among cirrhotic patients as compared to 6% in non-cirrhotic patients (p < 0.05).

Previously, a study was carried out by Ahmad U, et al. 69 including 100 patients. The mean age in both groups was 38.2 years and 37.4 years. Like our study, male patients dominated the female population. The mean \pm SD of QTc on Group-I was 0.472 ± 0.012 sec and that in Group-II was 0.434 ± 0.014 sec. Like our study, they also observed prolongation of the QTc interval. The criterion for prolonged QTc interval was ≥ 0.440 sec.

Zuberi BF, et al.¹⁸ also conducted a study to compare the cardiovascular changes among cirrhotic with non-cirrhotic patients. The mean \pm SD of QTc among cirrhotic patients was 0.438 ± 0.015 sec and that in non-cirrhotic was 0.432 ± 0.010 sec (p < 0.05). The frequency of prolonged QTc interval (i.e. > 0.44 sec) was seen among 19.2% of patients in cirrhotic patients, while it was 5.1% among non-cirrhotic patients. The results were statistically significant (p=0.014). These observations were also similar to that of the study i.e. higher frequency of prolonged QTc interval was observed among cirrhotic patients as compared to

non-cirrhotics. Tarique S, et al.⁷⁰ studied 117 patients with liver cirrhosis and determined that 52.1% of patients had prolonged QTc intervals with a mean of 0.425 ± 0.053 seconds.

Trevisani F, et al.⁷¹ reviewed the clinical records of 70 consecutive cirrhotic and 40 non-cirrhotic patients with acute gastrointestinal bleeding. They observed a lengthened QTc at the time of bleeding, 453.4 ± 4.3 ms in cirrhotics; contrariwise while QTc did not change in non-cirrhotic patients. The studies have shown that the QTc interval may be prolonged among the cirrhotic population. However, there remains a question about its clinical significance. Prolongation of QTc duration can also be used as a non-invasive and rapid diagnostic marker of cirrhotic cardiomyopathy as was proved in the study conducted by Zubairi BF, et al.¹⁸ Prolongation of QTc interval is useful for assessment of the severity of chronic liver disease by Aarikan C, et al.²² However, this has been negated by Tarique S, et al.²⁰ Zamirian M, et al.²³ showed that prolonged QTc interval improves with the liver transplantation suggesting that liver cirrhosis has independently unfavorable, but reversible electrophysiological effects.

This study had some limitations. This was a single-center study with limited population size. This was not a double-blind study. However, we did randomization of the patients to make the results relatively more generalizable.

Conclusion

In conclusion, this study concluded that the prolongation of the QTc interval is seen among cirrhotic patients as compared to non-cirrhotic patients. So, it is recommended that every patient diagnosed with liver cirrhosis should have a routine 12 lead ECG for the screening of QT interval abnormalities.

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