

## ORIGINAL ARTICLE

## Assessment of Corrected QT Interval Prolongation in Liver Cirrhosis

AMIR SHAHZAD<sup>1</sup>, IRFAN YOUNUS<sup>2</sup>, MUHAMMAD ZAHID ALI<sup>3</sup>, ADNAN QADIR<sup>4</sup>, AMNA HAFEEZ<sup>5</sup><sup>1</sup>Senior Registrar, Aziz Bhatti Shaheed Teaching Hospital, Nawaz Sharif Medical College, Gujrat.<sup>2</sup>Assistant Professor of Gastroenterology, Nawaz Sharif Medical College, Gujrat.<sup>3</sup>Assistant Professor of Cardiology, Nawaz Sharif Medical College, Gujrat.<sup>4</sup>Assistant Professor of Gastroenterology, Islamic International Medical College, Rawalpindi.<sup>5</sup>Woman Medical Officer, Al-Rae Hospital, Wazir Abad.Correspondence to: Dr. Irfan Younus, Email: [irfanyounis7887@gmail.com](mailto:irfanyounis7887@gmail.com), Cell: +923347667887

## ABSTRACT

**Objective:** To find out the frequency of corrected QT interval (QTc) prolongation in patients with liver cirrhosis.**Study Design:** Cross-sectional study.**Place and Duration:** The department of medicine, "Aziz Bhatti Shaheed Teaching Hospital", Gujrat from April 2021 to October 2021.**Methodology:** A total of 150 patients of both genders aged 18-65 years having liver cirrhosis were included. Proper medical history and clinical examination were performed while electrocardiogram (ECG) was obtained to find out QT interval in all the patients. The frequency of QTc prolongation was recorded.**Results:** In a total of 150 patients, 66 (44.0%) were males and 84 (56.0%) females. The mean age was 48.67±16.67 years while the mean duration of cirrhosis was 4.71±1.18 years. Frequency of QTc prolongation was noted in 44 (29.3%) patients. Among ninety patients of liver cirrhosis with age more than 40 years, 31 (70.5%) had corrected QT interval prolongation (p=0.040). Among 84 female patients, there were 25 (56.8%) cases of corrected QT interval prolongation (p=0.047).**Practical Implications:** Potential cases of liver transplantation may be prioritized as per their risk of prolongation of QTc but further research is required in this regard.**Conclusion:** The frequency of QTc prolongation was quite high among patients of liver cirrhosis.**Keywords:** Cardiovascular disease, Electrocardiogram, liver cirrhosis, mortality, QT prolongation.

## INTRODUCTION

Liver cirrhosis is known to be one of the most significant causes of morbidity and mortality globally.<sup>1</sup> Chronic hepatitis, alcohol abuse and "non-alcoholic fatty liver disease (NAFLD)" are some of the major causes behind liver cirrhosis.<sup>2</sup> Important complications of cirrhosis include portal hypertension, upper gastrointestinal bleeding, hepatic encephalopathy and ascites. Complications of liver cirrhosis may further lead into multiple organ failure that commonly involve organs like heart, lungs, kidneys and immune system.<sup>3</sup>

Liver cirrhosis is also linked with a variety of cardiovascular disorders.<sup>4</sup> In liver cirrhosis, cardiomyopathy may exhibit in the form of increased cardiac output, systolic or diastolic dysfunction or electrophysiologic disorders like arrhythmias and electrocardiographic (ECG) abnormalities are noted among patients of liver cirrhosis.<sup>5</sup> A prolonged "corrected QT interval (QTc)" is described as the electrophysiologic hallmark representing cirrhotic cardiomyopathy.<sup>6</sup> Literature reports nearly half of the all cirrhotic cases to have cirrhotic cardiomyopathy.<sup>7</sup> Prolongation of QTc may predispose patients of liver cirrhosis to serious conditions like fatal polymorphic ventricular tachycardia known as "torsade de pointes". Torsade de pointes can further lead into ventricular fibrillation which can further inflict sudden cardiac death.<sup>8</sup> A study done by Tiran E et al in 2018 reported frequency of QTc prolongation among patients of liver cirrhosis as 60%.<sup>9</sup>

This study was aimed at finding out the frequency of QTc prolongation in patients with liver cirrhosis. The findings of this study were thought to assist clinicians to make appropriate prediction and treatment about the prognosis of these cases.

## METHODOLOGY

This cross-sectional research was performed at the department of medicine, "Aziz Bhatti Shaheed Teaching Hospital", Gujrat from 10<sup>th</sup> April 2021 to 10<sup>th</sup> October 2021. Approval from "Hospital Ethical Committee" was acquired. Informed as well as written consents were taken from all patients. A sample size of 145 cases taking anticipated frequency of QTc prolongation among patients of liver cirrhosis with 95% confidence level and 8% margin of error.

A total of 150 patients of both genders aged 18-65 years having liver cirrhosis were included. Patients with any bundle branch block as per ECG, previous history of ischemic/non-ischemic heart disease or previous history of using drugs that

could have prolonged the QT interval were excluded. Non-probability consecutive sampling technique was employed. At the time of enrollment, proper medical history was noted and clinical examination was performed. ECG were performed in all cases of liver cirrhosis and frequency of QTc prolongation was recorded. All study information was noted on a special proforma.

Data analysis was performed using "Statistical Package for Social Sciences (SPSS)" version 26.0. Categorical data were shown as frequency and percentages whereas numeric data were represented as mean and standard deviation (SD). Stratification was performed to control the effect modifiers like age, gender and duration of cirrhosis. For comparisons, chi-square test was utilized taking p<0.05 as significant.

## RESULTS

In a total of 150 patients, 66 (44.0%) were males and 84 (56.0%) females. The mean age was 48.67±16.67 years while the mean duration of cirrhosis was 4.71±1.18 years. Frequency of QTc prolongation was noted in 44 (29.3%) patients (table-1).

Table 1: Characteristics of Patients with Liver Cirrhosis (n=150)

Characteristics	Frequency (%) / Mean±SD	
Age	Mean ±SD	48.67 ±16.67
	<40 years	60 (40%)
	≥40 years	90 (60%)
Gender	Male	66 (44%)
	Female	84 (56%)
Duration of cirrhosis(years)	Mean ±SD	4.71±1.18
QT interval prolongation	Yes	44 (29.3%)
	No	106 (70.7%)

Table 2: Association of QT interval prolongation with age, gender and duration of disease.

Age, years	QT interval Prolongation		p-value
	Yes	No	
≤40	13 (29.5%)	39 (36.8%)	0.040
>40	31 (70.5%)	67 (63.2%)	
Gender			
Male	19 (43.2%)	47 (44.3%)	0.047
Female	25(56.8%)	59 (55.7%)	
Duration of disease (years)			
≤3	6 (18.75%)	26 (81.25%)	0.061
>3	38 (32.2%)	80 (67.7%)	

Among ninety patients of liver cirrhosis with age more than 40 years, 31 (70.5%) had corrected QT interval prolongation ( $p=0.040$ ). Among 84 female patients, there were 25 (56.8%) cases of corrected QT interval prolongation ( $p=0.047$ ). Association of QT interval prolongation with age, gender and duration of liver cirrhosis is represented in table-2.

## DISCUSSION

Cirrhosis is known to be the final stage of progressive fibrosis of liver and may influence other organs of the body like heart, lungs or kidneys but the exact mechanism behind this is not yet fully understood.<sup>10</sup> "Cirrhotic cardiomyopathy" was first described by 'Lee' to state the cardiac dysfunction among patients of liver cirrhosis.<sup>11</sup> In 2005, experts gathered at "The World Congress of Gastroenterology" and labeled cirrhotic cardiomyopathy as a form of the chronic cardiac dysfunction among patients having liver cirrhosis.<sup>12</sup> This mechanism was described as reduction in contractile response to stress and/or altered diastolic relaxation and/or electrophysiological dysfunction in the non-existence of other known cardiac diseases.<sup>13</sup> As electrophysiological abnormalities in such patients can be detected with the use of ECG, one of these findings are prolongation QTc. Prolongation of QTc represents prolongation of ventricular repolarization period which might further develop into fatal arrhythmias.<sup>14</sup>

Literature highlights that QT interval is known to be linked with portal hypertension, acute episodes of upper gastrointestinal bleeding, ascites as well as myocardial dysfunctioning.<sup>15</sup> Prolonged QTc interval might be improved following liver transplant or the utilization of "non-selective beta-blockers" but this need further verification.<sup>16</sup> Some other factors like serum electrolyte and diuretic treatment might also influence QT interval.

In another study,<sup>17</sup> the mean age in years was  $58.75 \pm 11.47$  while in our study, mean age was  $48.67 \pm 16.67$  years, the prevalence of QTc prolongation was 60% in that study while in our study 29.3% cases with liver cirrhosis had QTc prolongation. The higher frequency in that study may be due to difference in mean age of the patients. Large data have revealed association of prolongation of QTc with worse cardiovascular outcomes like mortality but further research is required to discover the extent of such association among patients of liver cirrhosis.<sup>18</sup> The perception remains that liver cirrhosis may influence prolongation of QTc that is further linked with the severity of the underlying liver disease. Researchers have shown that prolonged QTc can help in predicting relative risk regarding outcomes among patients of liver cirrhosis.<sup>19</sup> Potential cases of liver transplantation may be prioritized as per their risk of prolongation of QTc but further research is required in this regard.

## CONCLUSION

The frequency of corrected QT interval prolongation was quite high among patients of liver cirrhosis. Attention should be paid on close monitoring of the QT interval among patients of liver cirrhosis.

## REFERENCES

1. Cheemerla S, Balakrishnan M. Global epidemiology of chronic liver disease. *Clin Liver Dis (Hoboken)*. 2021;17(5):365-370. doi: 10.1002/cld.1061

2. Yoon JH, Jun CH, Kim JH, Yoon EL, Kim BS, Song JE, et al. Changing trends in liver cirrhosis etiology and severity in Korea: the increasing impact of alcohol. *J Korean Med Sci*. 2021;36(21):e145. doi: 10.3346/jkms.2021.36.e145
3. Møller S, Henriksen JH, Bendtsen F. Extrahepatic complications to cirrhosis and portal hypertension: Haemodynamic and homeostatic aspects. *World J Gastroenterol*. 2014;20(42):15499-15517.
4. El Hadi H, Di Vincenzo A, Vettor R, Rossato M. Relationship between Heart Disease and Liver Disease: A Two-Way Street. *Cells*. 2020;9(3):567. doi: 10.3390/cells9030567
5. Carvalho MVH, Kroll PC, Kroll RTM, Carvalho VN. Cirrhotic cardiomyopathy: the liver affects the heart. *Braz J Med Biol Res*. 2019;52(2):e7809. doi: 10.1590/1414-431X20187809
6. Committee for Proprietary Medicinal Products. London: Committee for Proprietary Medicinal Products; 1997. The assessment of the potential for QT interval prolongation by non-cardiovascular medicinal product
7. Goldenberg I, Moss AJ, Zareba W. QT interval: how to measure it and what is "normal" *J CardiovascElectrophysiol*. 2006;17:333-336.
8. Tsiompanidis E, Siakavellas SI, Tentolouris A, Eleftheriadou I, Chorepsima S, Manolakis A, et al. Liver cirrhosis-effect on QT interval and cardiac autonomic nervous system activity. *World J Gastrointest Pathophysiol*. 2018 Feb 15;9(1):28-36. doi: 10.4291/wjgp.v9.i1.28
9. Torean E, Donoiu I, Istrătoae O, Găman AE, Țieranu LM, Gheonea DI, et al. QT interval prolongation in patients with liver cirrhosis. *Cur Health Sci J*. 2018;44(3):274-27
10. Zhou WC, Zhang QB, Qiao L. Pathogenesis of liver cirrhosis. *World J Gastroenterol*. 2014 Jun 21;20(23):7312-24. doi: 10.3748/wjg.v20.i23.7312
11. Schiff ER, Sorrell MF, Maddrey EC, editors. *Schiff's Diseases of the Liver*. 9th Edition. Lippincott, Williams & Wilkins; Philadelphia: 2003.
12. Taggart NW, Haglund CM, Tester DJ, Ackerman MJ. Diagnostic miscues in congenital long-QT syndrome. *Circulation*. 2007;115:2613-20
13. Garg A, Lehmann MH. Prolonged QT interval diagnosis suppression by a widely used computerized ECG analysis system. *CircArrhythmElectrophysiol*. 2013;6:76-83
14. Moss AJ, Kass RS. Long QT syndrome: from channels to cardiac arrhythmias. *J Clin Invest*. 2005;115(8):2018-24. doi: 10.1172/JCI25537
15. Ytting H, Henriksen JH, Fuglsang S, Bendtsen F, Møller S. Prolonged Q-T(c) interval in mild portal hypertensive cirrhosis. *J Hepatol*. 2005;43(4):637-644. doi:10.1016/j.jhep.2005.04.015
16. Kim SM, George B, Alcivar-Franco D, et al. QT prolongation is associated with increased mortality in end stage liver disease. *World J Cardiol*. 2017;9(4):347-354. doi:10.4330/wjc.v9.i4.347
17. Hajiaghahmohammadi AA, Daei MM, Zargar A, Ahmadi-Gooraji S, Rahban A, Attaran F. Q-T interval prolongation in cirrhosis: Relationship and severity. *Caspian J Intern Med*. 2018;9(3):239-243. doi:10.22088/cjim.9.3.239.
18. Lee ET, Welty TK, Fabsitz R, Cowan LD, Le NA, Oopik AJ, Cucchiara AJ, Savage PJ, Howard BV. The Strong Heart Study. A study of cardiovascular disease in American Indians: design and methods. *Am J Epidemiol*. 1990;132(6):1141-55. doi: 10.1093/oxfordjournals.aje.a115757
19. Koshy AN, Gow PJ, Testro A, Teh AW, Ko J, Lim HS, et al. Relationship between QT interval prolongation and structural abnormalities in cirrhotic cardiomyopathy: A change in the current paradigm. *Am J Transplant*. 2021 Jun;21(6):2240-2245. doi: 10.1111/ajt.16500