# Effect of Alcohol Dependence on QTc Interval - A Case Control Study

Kadappa Jaligidad[1], Ajinkya Dilip Auti[2], Appu Patil[3]

[1, 2, 3] Department of General Medicine, SNMC & HSK Hospital, Bagalkot, Karnataka, India.

**ABSTRACT**

**BACKGROUND**

Deleterious effects on the cardiovascular system like alcoholic cardiomyopathy and severe heart failure has been seen in those who are having chronic or heavy alcohol consumption. Majority of the clinical studies were based on selected group of patients like severe heart failure, as compared to that, the study among asymptomatic alcoholics were not well studied. Chronic and heavy alcohol consumption leads to adverse effects like arrhythmias such as atrial fibrillation and life-threatening re-entrant ventricular arrhythmias which can be predicted by studying QTc interval. The purpose of this study was to observe the effect of alcohol dependence on QTc interval.

**METHODS**

This is a Hospital based case control study conducted among patients admitted in SNMC & HSK hospital with diagnosis as Alcohol Dependence Syndrome (ADS) according to International classification of diseases (ICD) 10 criteria from October 2020 to December 2020. 30 alcohol dependence cases and 30 age matched controls above 18 years of age were selected. The ECG was recorded in lying down and resting position. The ECG results were analysed for QTc interval. Sample size estimation was done using open epi Software version 2.3.1.

**RESULTS**

Among the 30 cases, 53.3 % had prolonged QTc interval. Out of these, 11 were in the age group of 18 - 35 years, 17 were in 36 - 55 years while 2 were in the age group > 55 years while in 30 controls only 1 had prolonged QTc in the age group of 36 - 55 years.

**CONCLUSIONS**

A prolonged QTc interval was observed in 16 out of 30 cases which provides the evidence, that prolonged QTc interval was significant in alcohol dependence patients. Hence, early detection of ECG changes like prolonged QTc interval will help in preventing the adverse cardiovascular events and comorbidities associated with it.

**KEYWORDS**

QTc Interval, ECG, Alcohol Dependence

*Corresponding Author:*
*Dr. Ajinkya Dilip Auti,*
*SNMC PG Boys Hostel, Room No. 140,*
*SNMC and HSK Hospital,*
*Bagalkot - 587103, Karnataka, India.*
*E-mail: ajinkyaauti@gmail.com*

*DOI: 10.18410/jebmh/2021/288*

*How to Cite This Article:*
*Jaligidad K, Auti AD, Patil A. Effect of alcohol dependence on QTc interval - a case control study. J Evid Based Med Healthc 2021;8(20):1521-1525. DOI: 10.18410/jebmh/2021/288*

*Submission 22-12-2020,*
*Peer Review 02-01-2021,*
*Acceptance 30-03-2021,*
*Published 17-05-2021.*

## BACKGROUND

Chronic heavy alcohol consumption can result in systolic and diastolic dysfunction, left ventricular dilatation, conduction abnormalities, and decreased ejection fraction resulting in alcoholic cardiomyopathy. Alcoholism is one of the important causes for mortality associated with it. Early changes of alcoholic cardiomyopathy can be reversed by absolute abstinence from alcohol which prevents further myocardial damage. Arrhythmias are one of the important causes of mortality associated with alcoholism. This is accomplished primarily by persuading the patient to cease drinking. Total abstinence is absolutely necessary. Heavy alcohol consumption leads to serious problems like cardiac dysfunction, stroke, arrhythmias and sudden cardiac death. Patients with acute alcohol intoxication can result in atrial fibrillation, while some may develop arrhythmias like supraventricular, ventricular arrhythmia etc. Abnormalities of electrolytes (hypomagnesemia, hypokalaemia), increased sympathetic tone and catecholamine secretion, as well as cardiac cellular infiltrate, hypertrophy, and fibrosis are frequently seen in chronic alcoholism, which may all cause changes in QT interval.[1,2]

Many studies confirm that electrocardiographic changes such as prolonged QTc occur prior to symptomatic cardiac disorders. These will help in predicting the early ongoing effects of alcohol which are reversible during the early stages. These early changes will be detected by non invasive investigations like Electrocardiography that will later help in preventing the alcoholic dilated cardiomyopathy. Alcohol toxicity to myocardial cells happen in the form of inhibiting mitochondrial respiration and inhibition of activity of enzymes in the tricarboxylic acid cycle and interfering in mitochondrial calcium up taking and binding. The heart muscle does not contain alcohol dehydrogenase that's why ethanol profoundly affects myocardial lipid metabolism. Acetaldehyde diminishes myocardial protein synthesis and inhibits Ca + + - activated myofibrillar ATPase.[3]

Leakage of isocitric and malic dehydrogenase into coronary sinus blood was found in men chronically consuming large amounts of alcohol, both at rest and after exercise, regardless of whether or not clinical evidence of heart disease was present.[4] After acute ingestion of alcohol by chronic alcoholics, isocitric and malic dehydrogenase increased in coronary sinus blood in association with a decrease in myocardial extraction of free fatty acids without a change in extraction of triglycerides.[5] Ingestion of alcohol also increases potassium and phosphate in coronary sinus blood, with an increase in serum transaminase and a decrease in triglyceride uptake.[6] Thus, it is conceivable from these data that important metabolic changes may result from chronic ingestion of alcohol.

Acute alcohol intoxication and alcohol withdrawal will lead to electrolyte abnormalities such hypomagnesaemia and hypokalaemia which predispose to VT, torsades de pointes and Sudden cardiac death.

The purpose of this study was to evaluate the effect of alcohol dependence on QTc interval.

## METHODS

### Study Design

It is a hospital based case control study involving patients admitted in HSK hospital, Bagalkot with diagnosis as Alcohol Dependence according to ICD 10 criteria between October 2020 and December 2020. ECG taken at the time of admission of patients fulfilling the inclusion and exclusion criteria of our study was evaluated. A 12 lead ECG which was taken & evaluated for ECG parameters like QTc interval. Ethical clearance was taken for the above study with IECHSR NO 2020 – 2021 / A – 14 / 1.1. Consent prior to study was taken for both cases and controls.

Bazett's formula was used to calculate the corrected QT interval (QTc):

$$QTc\ in\ seconds = QT\ interval\ in\ second\ \sqrt{RR\ interval\ in\ seconds},$$

$$QTcnormal\ range\ = 0.33 - 0.44\ secs$$

### Inclusion Criteria

Patients above the age of 18 yrs. with alcohol dependence syndrome according to ICD - 10 criteria and age and sex matched non-alcoholic individuals as controls.

### Exclusion Criteria

Patients with Ischaemic heart disease (IHD), T2DM, any cardiac illness, history of consumption of psychoactive substances or any other comorbidities.

### Statistical Analysis

Sample size estimation was done using open EPI software version 2. 3. 1 and sample size 30 for case and 30 for controls was taken. Group comparisons were made using Fischer exact test for categorical data. The data were tabulated and statistically analysed. P < 0.05 was taken as statistically significant.

## RESULTS

Cases and controls were group matched and all the participants in the study were males above the age group of 16 years. Table 1 shows group statistics for case and control along with their mean, P values.

| | Group | N | Mean | Std. Deviation | t | P |
|---|---|---|---|---|---|---|
| Age | Control | 30 | 39.7 | 11.612 | 0.21 | 0.83 |
| | Case | 30 | 40.3 | 10.442 | | |
| QTc | Control | 30 | 0.4173 | 0.03051 | 2.8 | 0.007* |
| | Case | 30 | 0.4507 | 0.05729 | | |

***Table 1. Group Statistics***

*indicates statistically significant difference

| | < 35 Yrs. | > 36 Yrs. |
|---|---|---|
| Mean prolong QTc | 2 (6.7 %) | 14 (47 %) |
| Mean normal QTc | 7 (23.3 %) | 7 (23.3 %) |

***Table 2. Occurrence of Mean Prolonging of QTc Interval According to Age in Cases***

Chi square test $x^2 = 5$, P = 0.01 Significant

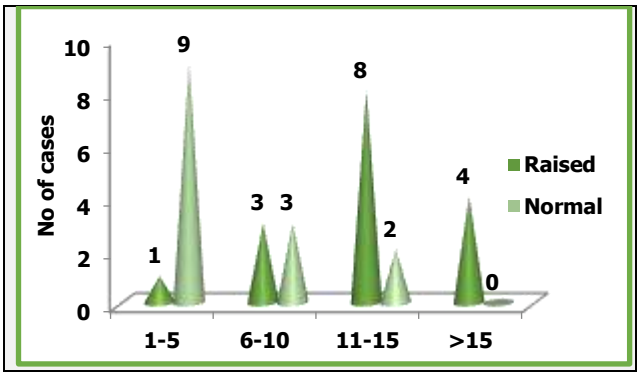


***Figure 1. Duration of Alcohol and QTc Prolongation among 30 Cases***

Out of 30 cases, 2 (6.7%) were in the age group < 35 yrs. while 14 (47 %) were in the age group of > 36 yrs. which had mean prolong QTc interval (chi square test, P = 0.01, significant). Also there was correlation between duration of alcohol and prolonged QTc interval. Figure 2 shows that out of 30 controls only 1 (3.4 %) had prolonged QTc prolongation in the age group 36 – 55 yrs. Table no 4 shows that the prolonged QTc interval was more seen in cases compared to that of controls which was statistically significant.

| QTc Prolonged | Alcohol Dependence | |
|---|---|---|
| | Yes n (%) | No n (%) |
| Yes | 16 (53.3 %) | 14 (46.7 %) |
| No | 01 (3.3 %) | 29 (96.7 %) |

***Table 3. QTc Prolongation among Those with and with No Alcohol Dependence***

$\chi^2$ = 18.49, P = 0.001. Odds Ratio = 31.27 statistically significant

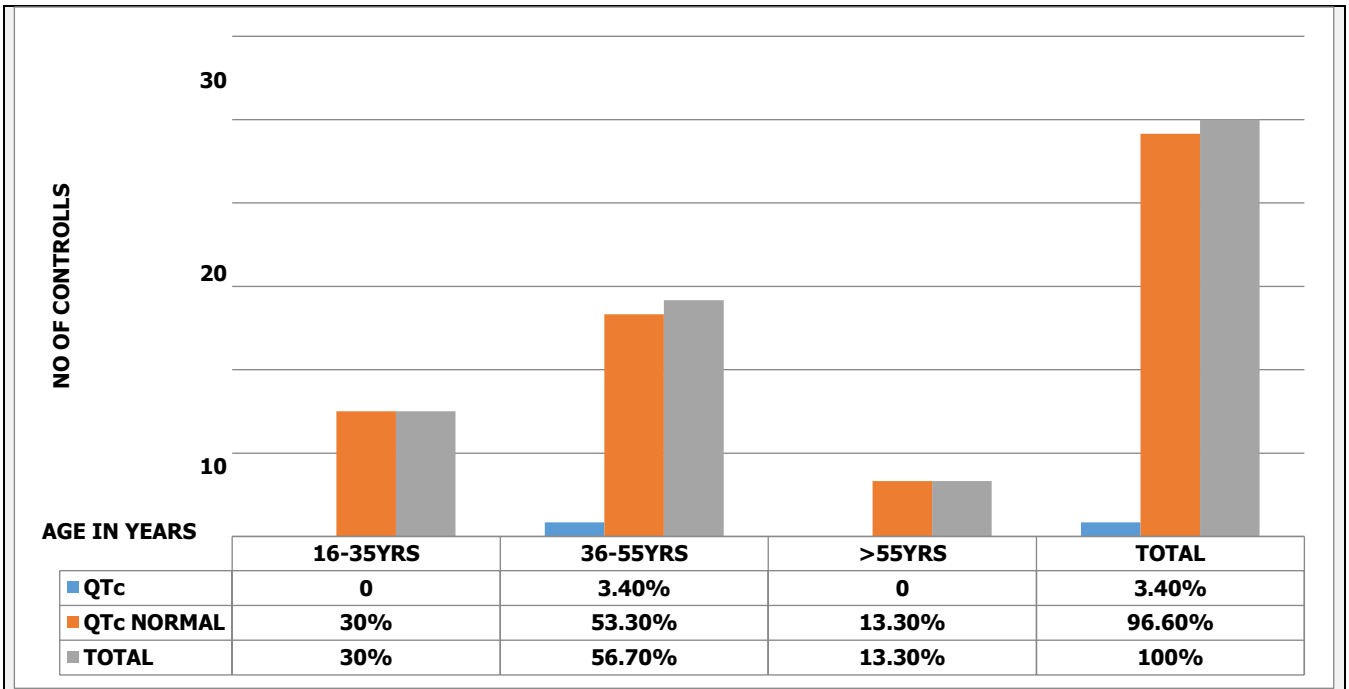


***Figure 2. QTc Results among Controls***

## DISCUSSION

Alcoholic cardiomyopathy type of non-ischaemic dilated cardiomyopathy has been associated with regular heavy alcohol consumption, which have been attributed to its cardiotoxin effect. In general, alcoholic patients consuming regularly for 5 years are at risk of developing asymptomatic alcoholic cardiomyopathy, which is clinically expressed as an impairment of left ventricular function, those who continue to drink for longer period may become symptomatic and develop signs and symptoms of heart failure.[7]

Alcohol consumption causes ECG changes which include cardiac conduction abnormalities, prolongation of the QT interval, prolongation of ventricular repolarization and sympathetic stimulation.[8] The reason for changes in QT intervals include electrolyte abnormalities of magnesium & potassium like hypomagnesemia, hypokalaemia, increased sympathetic tone , catecholamine secretion, cardiac cellular infiltrate, hypertrophy, and fibrosis which are frequently seen in chronic alcoholism.[1,2] Hence the adverse cardiovascular events like sudden cardiac death, atrial fibrillation and ventricular tachycardia can be detected and prevented early with the use of electrocardiographic changes.

The cardiac toxicity of ethanol is augmented and supplemented by that of acetaldehyde. The inotropic and chronotropic effects resulting from acetaldehyde induced release of catecholamines may explain the occurrence of cardiac arrhythmias observed after ingestion of ethanol.[9,10] Acetaldehyde also results in vitro in a marked decrease in myocardial protein synthesis.[11,12] This finding is significant in light of the observation by Zuihlke and co-workers that inhibition of myocardial protein synthesis leads to the development of myocardial failure in hearts with increased afterload.[13] Additional damaging effects of acetaldehyde may be due to the inhibition of Ca + + - activated myofibrillar ATPase. This could be partially responsible for

the diminished cardiac contractility observed after the ingestion of ethanol. Further reduction in myocardial contractility could arise from diminished Ca + + uptake and binding by sarcoplasmic reticulum induced by ethanol. Earlier detection of ECG changes is useful in preventing the adverse cardiovascular events like sudden cardiac arrest, Atrial Fibrillation, Ventricular Tachycardia.

A recent study established that QT prolongation may predict the risk of sudden death in chronic alcoholics. QT prolongation is a known risk factor for lethal arrhythmias in other circumstances, and may reflect myocardial alterations capable of supporting either re-entry and/or triggered automaticity.

Also according to study conducted by Lorsheyd et al., it showed significant correlation between alcohol consumption and QTc interval.[14]

According to study conducted by Day et al. Simultaneous 12 - lead electrocardiographic recordings were obtained from 69 patients with histologically proven alcoholic liver disease (without evidence of structural heart disease), and from 40 healthy non-drinking controls matched for age and sex. Maximum QT intervals were longer in alcoholics than in controls (QTcub 450 vs 439, P = 0.016). QT intervals were prolonged in the 14 patients who died compared with survivors (QTcub 471 vs 446, P = 0.007).

According to study conducted by Kino et al. 145 alcoholics without known causes of heart disease, who were serially admitted to the alcohol detoxification centre, were studied to see the incidence of cardiac abnormalities and dose related effects of ethanol. Patients were divided into heavy (consumed more than three equivalent amount of 125 ml of pure ethanol daily for 10 years or more) and moderate drinkers (consumed 75 to 125 ml of ethanol daily). All of them were ambulatory and free from cardiac symptoms. There was no difference among heavy and moderated drinkers in the incidence of abnormalities detected by the electrocardiogram sand chest x-ray films. In the alcoholics, the most frequent finding was a prolonged QTc interval of more than 0.44 son the electro cardiogram (62 patients, 42.8 %).[15]

According to study conducted by Yokoyama et al., which showed that alcohol causes dysfunction of the autonomic nerves as well as worsening QT prolongation, and this may predispose such patients to sudden cardiac death.[16]

Berger et al., developed the QT variability index (QTvi), calculated by normalizing the QT to heart rate variability as a non-invasive marker of cardiac repolarization lability. In a study of patients experiencing acute alcohol withdrawal, Bär et al. found that QT variability index (QTvi) was increased in alcohol withdrawers compared to controls.[17] various mechanism of increase QTvi have been proposed like increased sympathetic activity in alcohol withdrawal, hypokalaemia, hypomagnesaemia direct myocardial damage from alcohol.

## CONCLUSIONS

The incidence of electrocardiographic changes like prolonged QTc interval will be higher in patients with alcohol dependence of longer duration even in the absence of cardiomegaly or heart disease. Our study results showed that alcohol dependants were prone for electrical abnormality of the heart leading to sudden cardiac arrest. These changes may be considered as an early indicator of the effects of alcohol abuse on electrical activity of heart. Precautions need to be taken in the alcohol dependence in the form of complete stoppage of alcohol consumption or moderation of alcohol consumption to prevent the onset of alcohol induced arrhythmias. Further research is required to provide the significance for these electrocardiographic changes in alcoholics.

Data sharing statement provided by the authors is available with the full text of this article at jebmh.com.
Financial or other competing interests: None.
Disclosure forms provided by the authors are available with the full text of this article at jebmh.com.
Our sincere thanks to all the colleague faculty members for their valuable guidance and their cooperation at each stage of this study. Also sincere gratitude to all our cases and controls who volunteered to participate in this clinical study. We are also thank full to HOD of our general medicine department in helping and guiding for these study.

## REFERENCES

[1] Schenk EA, Cohen J. The heart in chronic alcoholism. Clinical and pathologic findings. Pathol Microbiol (Basel) 1970;35(1):96-104.
[2] Hognestad J, Teisberg P. Heart pathology in chronic alcoholism. Acta Pathol Microbiol Scand A 1973;81(3):315-322.
[3] Bing RJ. Cardiac metabolism: its contributions to alcoholic heart disease and myocardial failure. Circulation 1978;58(6):965-970.
[4] Wendt VE, WU C, Balcon R, et al. Hemodynamic and metabolic effects of chronic alcoholism in man. Am J Cardiol 1965;15:175-184.
[5] Wendt VE, Ajluni R, Bruce TA, et al. Acute effects of alchohol on the human myocardium. Am J Cardiol 1966;17(6):P804-P812.
[6] Regan TJ, Levinson GE, Oldewurtel HA, et al. Ventricular function in non cardiacs with alcoholic fatty liver: role of ethanol in the production of cardiomyopathy. J Clin Invest 1969;48(2):397-407.
[7] Urbano-Marquez A, Estruch R, Navarro-Lopez F, et al. The effects of alcoholism on skeletal and cardiac muscles. N Engl J Med 1989;320(7):409-415.
[8] Rossinen J, Sinisalo J, Partanen J, et al. Effects of acute alcohol infusion on duration and dispersion of QT interval in male patients with coronary artery disease and in healthy controls. Clin Cardiol 1999;22(9):591-594.
[9] James TN, Bear ES. Effects of ethanol and acetaldehyde on the heart. Am Heart J 1967;74(2):243-255.
[10] McCloy RB Jr, Prancan AV, Nakano J. Effects of acetaldehyde on the systemic, pulmonary and regional circulations. Cardiovasc Res 1974;8(2):216-226.

[11] Schreiber SS, Oratz M, Rothschild MA, et al.. Alcoholic cardiomyopathy. II. The inhibition of cardiac microsomal protein synthesis by acetaldehyde. J Mol Cell Cardiol 1974;6(2):207-213.
[12] Zuhlke V, de Rochemont DW, Gudbjarnason S, et al. Inhibition of protein synthesis in cardiac hypertrophy and its relation to myocardial failure. Circ Res 1966;18(5):558-572.
[13] Day CP, James OF, Butler TJ, et al. QT prolongation and sudden cardiac death in patients with alcoholic liver disease. The Lancet 1993;341(8858):1423-1428.
[14] Lorsheyd A, de Lange DW, Hijmering ML, et al. PR and OTc interval prolongation on the electrocardiogram after binge drinking in healthy individuals. Neth J Med 2005;63(2):59-63. Erratum in: Neth J Med 2005;63(4):136.
[15] Kino M, Imamitchi H, Morigutchi M, et al. Cardiovascular status in asymptomatic alcoholics, with reference to the level of ethanol consumption. Heart 1981;46(5):545-51.
[16] Yokoyama A, Ishii H, Takagi T, et al. Prolonged QT interval in alcoholic autonomic nervous dysfunction. Alcoholism: Clinical and Experimental Research 1992;16(6):1090-1092.
[17] Bär KJ, Boettger MK, Koschke M, et al. Increased QT interval variability index in acute alcohol withdrawal. Drug and Alcohol Dependence 2007;89(2-3):259-266.