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Original Research Article

A STUDY OF QTc PROLONGATION IN EPISODES OF HYPOGLYCEMIA IN CHRONIC DIABETICS

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Abstract

Background: The time it takes for the ventricular myocardium to repolarize after depolarizing is represented by QT on the surface ECG. Due to its potential arrhythmogenicity, QT interval prolongation is a risk factor for abrupt cardiovascular events and is a serious ECG anomaly that can be inherited or acquired. Both type 1 and type 2 diabetes mellitus have been studied to determine the prevalence of QT prolongation (DM).

Methods: Based on the inclusion and exclusion criteria a total of n=50 cases consecutive cases of hypoglycemia in diabetics were selected and included in the study. The baseline characteristics of the patient's age, sex, and diabetes (both type 1 and type 2) patients with symptoms of hypoglycemia with low glucose levels, duration of diabetes, and Q-T interval were recorded in proforma prepared according to the need of study. Corrected Q-T interval was calculated by using Bazett's formula [$QTcB = QT/RR^{1/2}$] Prolongation of corrected Q-T interval during the episodes of hypoglycemia (Normal QTc M=440ms, F=460ms).

Results: Q-T interval prolongation is depending on the severity of hypoglycemia. In our study 445.33 msec was a mean Q-T interval in Category I cases similarly, in category II cases the mean values were 468.92 msec and in category III the mean values were 503.64 msec and in category IV the mean values were 515.22 msec. The mean values of QTc prolongation with the severity of diabetes mellitus with ANOVA analysis found the p values <0.05 and hence considered significant.

Conclusion: The current study within its limitations found that severe hypoglycemia is more likely to cause QTc prolongation. In cases of severe hypoglycemia, repolarization irregularity is the most typical source of the arrhythmia. In cases of severe hypoglycemia, repolarization irregularity is the most typical source of the arrhythmia. An arrhythmia caused by a QTc interval of greater than 500 milliseconds might result in abrupt cardiac death.

Keywords: QT prolongation, hypoglycemia, Diabetes mellitus type I, Diabetes Mellitus type II.

Introduction:

Hypoglycemia in an adult human trigger a physiological reaction in the form of autonomic activation, primarily of the Sympathoadrenal system, which leads to adrenaline release and end-organ stimulation. The heart, brain, and splanchnic circulation all receive more blood.

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Our bodies will experience the following hemodynamic changes as a result of hypoglycemia: an increase in heart rate and peripheral systolic blood pressure; a decrease in central blood pressure; a reduction in peripheral arterial resistance; and an increase in myocardial contractility, stroke volume, and cardiac output. [1] The heart is briefly put under more strain. This brief cardiac stress can be tolerated by those with healthy cardiovascular systems. Nevertheless, individuals with DM and other risk factors are unable to withstand this brief myocardial stress and have consequences including life-threatening arrhythmias and sudden cardiac death. [2] In non-diabetic people, arteries become less rigid during a hypoglycemic condition, making them more elastic. Yet, in diabetic individuals, arterial wall stiffness is increased, and during hypoglycemia, arteries will become less elastic. These modifications lead to hemodynamic abnormalities, such as a [3] less dramatic drop in central aortic pressure. Myocardial perfusion is decreased, and myocardial ischemia is promoted by the arterial wall's growing stiffness. ST Segment alterations, a lengthened Q-T interval, and anomalies in cardiac repolarization are all brought on by hypoglycemia. The heart muscles contract in a coordinated manner as a result. Hypokalaemia results from excessive catecholamine release. All of these modifications lead to aberrant heart rhythms such as ventricular tachycardia and atrial fibrillation. [4] Viscosity anomalies due to vasoconstriction are brought on by an increase in sympathetic activity and the concomitant production of hormones such as endothelin. Increased erythrocyte concentration caused by viscosity. Factor VIII level increase, Von Willebrand factor, and coagulation-platelet activation CRP levels rising due to endothelial dysfunction. These modifications encourage thrombosis and intravascular coagulation. [5] The primary objective of the study was to assess the QTc interval during hypoglycemic episodes in diabetic patients concerning their baseline characteristics and duration of diabetes mellitus.

Material and Methods

This cross-sectional study was conducted in the Department of General Medicine, Kakatiya Medical College and MGM Hospital, Warangal, Telangana State. Institutional Ethical approval was obtained for the study. Written consent was obtained from all the patients of the study.

Inclusion criteria

1. Diabetic patients admitted to medical wards.
2. Reporting symptoms of hypoglycemia
3. Males and females
4. Blood sugar levels < 60mg/dl.

Exclusion criteria

1. Patients with electrolyte abnormalities.
2. Coronary artery disease.
3. Concurrent use of drugs that cause Q-T prolongation (quinidine, procainamide, Tri & Tetra cyclic antidepressant).

Based on the inclusion and exclusion criteria a total of n=50 cases consecutive cases of hypoglycemia in diabetics were selected and included in the study. The baseline characteristics of the patient's age, sex, and diabetes (both type 1 and type 2) patients with symptoms of hypoglycemia with low glucose levels, duration of diabetes, and Q-T interval were recorded in proforma prepared according to the need of study. Analyses of the digital 12-lead ECG recordings were performed at a ECG paper speed of 25 mm/sec was obtained

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from all the patients of the study during the episode of hypoglycemia RR and QT intervals were also measured for three consecutive cardiac cycles on the six thoracic leads. The dispersion of QTc was calculated using the difference between the maximal and the minimal QTc in any thoracic leads. Corrected Q-T interval was calculated by using Bazett's formula [$QTcB = QT/RR^{1/2}$] Prolongation of corrected Q-T interval during the episodes of hypoglycemia (Normal QTc M=440ms, F=460ms). [6] Hypoglycemia was tested using Point-of-Care Blood Glucose Testing for Diabetes Care in Hospitalized Patients, using Accu-Chek® Inform II system (Roche Diagnostics). Severe hypoglycemia was defined, in this study, as the condition requiring active medical assistance such as administering carbohydrate when serum glucose level was less than 60 mg/ dL. Serum Electrolytes and serum calcium levels were also estimated. Echocardiogram was also done for all the patients included in the study.

Statistical analysis: The data was collected and uploaded on an MS Excel spreadsheet and analyzed by SPSS version 21 (Chicago, IL, USA). Quantitative variables were expressed on mean and standard deviations and qualitative variables were expressed in proportions and percentages. Fisher's exact test has been used to find the difference between two proportions.

Results

In this study there we classified hypoglycemia into different categories based on blood sugar levels. Category I was (50 – 60 mg/dl), Category II (40 – 49 mg/dl), Category III (30 – 39 mg/dl) and category IV (< 30mg/dl) the distribution of cases based on the blood sugar levels and category has been depicted in figure 1.

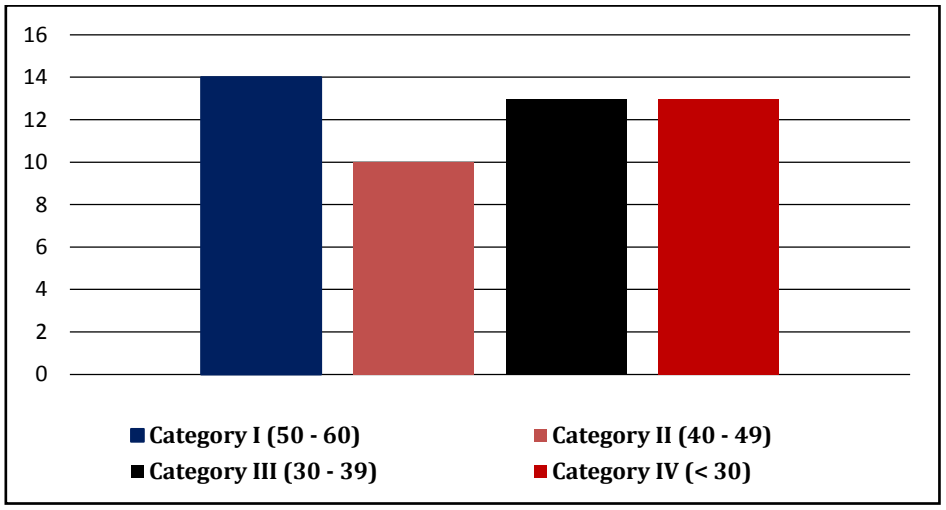

Figure 1: Category-wise distribution of cases in the study

Table 1: Sex-wise and category-wise distribution of the cases included in the study

	Male	*Females*	*Total (%)*
Category I	8	6	14 (28.00)
Category II	6	4	10 (20.00)
Category III	7	6	13 (26.00)
Category IV	8	5	13 (26.00)
Total	29	21	50 (100.0)

In the current study out of n=50 cases n=29(58%) cases were males and n=21 (42%) were females the details have been depicted in table 1. Similarly, based on the type of diabetes mellitus and category of the patients it was found that n=15(30%) cases were of type I diabetes mellitus and n=35(70%) were cases of type II diabetes mellitus the distribution of the cases has been depicted in table 2.

Table 2: Distribution of cases based on category and type of diabetes mellitus

	Type I	*Type II*	*Total (%)*
Category I	5	9	14 (28.00)
Category II	3	7	10 (20.00)
Category III	3	10	13 (26.00)
Category IV	4	9	13 (26.00)
Total	15	35	50 (100.0)

In the current study, we found QTc prolongation in n=13(26%) of all the cases. Based on the category we found most of the QTc prolongation occurred in category IV 38.46% followed by category III 30.77%, category II 20%, and category I 14.28%. The differences between the category and QTc prolongation were analyzed by ANOVA and the p-values were found to be <0.05 hence considered as significant details depicted in table 3.

Table 3: Distribution of cases of QTc prolongation in the study

	Frequency	QTc Prolongation	Percentage
Category I	14	2	14.28
Category II	10	2	20.00
Category III	13	4	30.77
Category IV	13	5	38.46
ANOVA (p-value)	------	0.037	

In the current study, we found a total of n=9/35 (25.71%) cases with type II having QTc prolongation similarly for type I cases 4/15(26.67%) cases with QTc prolongation. Therefore, it can be said that the incidence of Q-T prolongation is more with insulin treatment as noted that QTc prolongation occurs more commonly in type I diabetes cases as compared to type II diabetes mellitus cases as depicted in table 4.

Table 4: Distribution of cases of QTc prolongation based on the type of diabetes mellitus.

	Frequency	*Type I*	*Type II*	*QTc Prolongation*	*Percentage*
Category I	14	1	1	2	14.28
Category II	10	0	2	2	20.00
Category III	13	1	3	4	30.77
Category IV	13	2	3	5	38.46

Q-T interval prolongation is depending on the severity of hypoglycemia. In our study 445.33 msec was a mean Q-T interval in Category I cases similarly, in category II cases the mean

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values were 468.92 msec and in category III the mean values were 503.64 msec and in category IV the mean values were 515.22 msec (figure 2). The mean values of QTc prolongation with the severity of diabetes mellitus with ANOVA analysis found the p values <0.05 and hence considered significant. Hypoglycemia causes repolarization abnormality thereby increasing the interval of Q-T. This causes arrhythmias and SCD. In our study 2 patients in Category -III and 3 patients in Category- IV developed arrhythmias with a statistically significant p-value of 0.023.

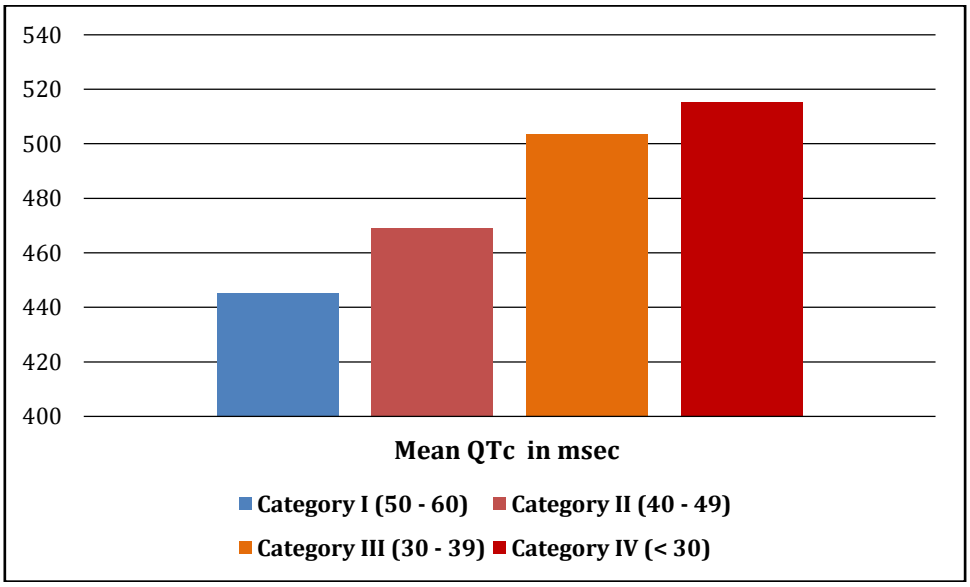

Figure 2: Distribution of cases and the mean QTc recorded in each category.

The analysis of the duration of diabetes mellitus with QTc prolongation revealed out of n=13 cases of prolongation n=2 cases with a duration of diabetes mellitus of 5 – 10 years and n=5 cases with a duration of diabetes mellitus of 11 – 20 years and n= 6 cases with diabetes mellitus duration of 21 – 30 years.

Discussion

One of the frequent side effects of diabetes patients receiving insulin treatment is hypoglycemia. QT prolongation brought on by hypoglycemia results in arrhythmias and abrupt cardiac death. In India, 1-2% of people have SCD brought on by hypoglycemia. For diabetic individuals, inappropriate repolarization during hypoglycemia is the leading cause of arrhythmias. [7] The most prevalent arrhythmias linked to hypoglycemia are ventricular tachycardia, fibrillation, and atrial fibrillation. [8] In our study, Type 2 DM exhibits higher hypoglycemia than Type 1 DM. However, in type-I DM, Q-T c prolongation is also more prevalent. Other risk factors for sudden cardiac mortality in type-2 DM patients include smoking, alcohol consumption, systemic hypertension, and obesity. [9] In our study, men had more hypoglycemia than women did. Patients with type-1 diabetes experience hypoglycemia episodes far more frequently than those with type-2 diabetes. Because people with type 1 diabetes depend on insulin. While initially responding to oral hypoglycemic medications, Type-2 individuals eventually need insulin or develop insulin dependence as a result of the disease's development. Around 50% of beta cells will be destroyed when Type-2 DM is diagnosed. [10] Individuals who have uncontrolled diabetes and are aging will need insulin to survive. [10] Moreover, the duration of diabetes is linked to an extended Q-T interval and sudden cardiac death. [11] Patients with very low glucose levels have a greater frequency of

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Q-T lengthening in our study. Arrhythmias are brought on more by repolarization anomalies in extreme hypoglycemia. In the current study, we found a total of n=9/35 (25.71%) cases with type II having QTc prolongation similarly for type I cases 4/15(26.67%) cases with QTc prolongation. Although it is well known that the sympathetic activation response to hypoglycemia raises heart rates [12], several studies found no such increase during hypoglycemia and suggested that this phenomenon was instead caused by the parasympathetic activation brought on by hypoglycemia itself. [13, 14] The QTc interval lengthening during hypoglycemia was hypothesized to be caused by altered brain control. [15] Even though none of the patients were using an alpha- or beta-adrenergic blocking drug, our investigation found no tachycardia and no appreciable variations in the participants' heart rates during bouts of acute hypoglycemia compared to the recovered stage. In type 2 diabetes patients, Lindstrom et al. [16] showed that ST depression and T wave flattening occur during periods of insulin-induced hypoglycemia. Prior reports have mentioned ischemic T wave inversion and ST segment depression linked to hypoglycemia without signs of myocardial infarction [17, 18] Nevertheless, during the periods of acute hypoglycemia in this investigation, ischemic alterations of the T wave and ST segment were not discovered. In type 2 diabetes patients, Lindstrom et al. [16] showed that ST depression and T wave flattening occur during periods of insulin-induced hypoglycemia. Prior reports have mentioned ischemic T wave inversion and ST segment depression linked to hypoglycemia without signs of myocardial infarction [17, 18]. Nevertheless, during the periods of acute hypoglycemia in this investigation, ischemic alterations of the T wave and ST segment were not discovered. Hypoglycemia and QT prolongation have been linked strictly in time, emphasizing the proarrhythmic risk brought on by dynamic alterations in cardiac repolarization. [19] So, it would have been ideal to comprehend the length of QT prolongation at various blood glucose levels. More blood glucose tests, especially non-hypoglycemic readings, would have helped to better understand this problem.

Conclusion

The current study within its limitations found that severe hypoglycemia is more likely to cause QTc prolongation. In cases of severe hypoglycemia, repolarization irregularity is the most typical source of the arrhythmia. In cases of severe hypoglycemia, repolarization irregularity is the most typical source of the arrhythmia. An arrhythmia caused by a QTc interval of greater than 500 milliseconds might result in abrupt cardiac death. Long-term diabetes mellitus also increases the risk of arrhythmia and abrupt cardiac death.

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