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Prolonged QTc Interval in Diabetes Mellitus: Frequency and Correlation with Glycemic Control

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ABSTRACT

Background: Prolonged QTc interval is a known predictor of ventricular arrhythmias and sudden cardiac death. Diabetic patients are at increased risk of QTc prolongation due to underlying autonomic neuropathy and metabolic disturbances. Identifying its frequency and correlation with glycemic control can aid in early detection and prevention of cardiac complications. **Objective:** To determine the frequency of prolonged QTc interval in diabetic patients attending follow-up at the Outpatient Department of Medicine, and to compare mean HbA1c levels between patients with and without QTc prolongation. **Material and Methods:** A cross-sectional analysis was conducted at Department of Medicine, Jinnah Hospital, Lahore, from January to June 2023, involving 362 adult patients with type 2 diabetes mellitus attending follow-up appointments. Demographic and clinical data including age, sex, body mass index (BMI), duration of disease, and HbA1c levels were recorded. Each participant underwent a 12-lead electrocardiogram (ECG) to determine QTc interval, which was corrected for heart rate using Bazett's formula. Prolongation was defined as QTc ≥450 ms in males and ≥470 ms in females. Statistical evaluation was performed using SPSS version 25, applying chi-square and independent t-tests, with a significance threshold set at $p < 0.05$. **Results:** Prolonged QTc was observed in 112 (30.9%) patients. Although not statistically significant, a higher frequency of QTc prolongation was seen in females and those with uncontrolled diabetes. Mean HbA1c was higher in patients with prolonged QTc (8.17 ± 1.39%) than those with normal QTc (7.89 ± 1.41%) ($p = 0.087$). **Conclusion:** QTc prolongation is common in diabetic patients, particularly in those with poor glycemic control. Routine ECG monitoring is advisable for early risk identification.

INTRODUCTION

Diabetes mellitus (DM) remains a major global health issue and is closely linked with numerous cardiovascular disorders. Among these, prolongation of the corrected QT (QTc) interval on an electrocardiogram (ECG) is an underrecognized but clinically important finding. This prolongation signifies disturbances in ventricular repolarization and has been associated with serious arrhythmic events such as torsades de pointes and sudden cardiac death [1]. In both type 1 and type 2 diabetes, QTc prolongation has emerged as a potential indicator of cardiac autonomic neuropathy (CAN), particularly in patients with long-standing disease or inadequate glycemic control [2].

Recent studies have highlighted that poor glycemic control, reflected by elevated glycated hemoglobin (HbA1c) levels, is closely associated with QTc prolongation. A study by Arya et al. found that QTc interval variations were observed across a broad spectrum of diabetic patients, regardless of age and treatment history, suggesting a systemic metabolic effect on cardiac electrophysiology [3]. Similarly, a study in Ugandan outpatients reported that higher mean HbA1c levels and elevated arterial pressure were significantly associated with prolonged QTc intervals, indicating poor metabolic control and hypertension as compounding factors [4].

QTc prolongation has been frequently observed even in pediatric populations with type 1 diabetes. El-Walili et al. reported that one-third of diabetic children had QTc intervals ≥0.45 seconds, and nearly all of them exhibited poor glycemic control (HbA1c >7.5%) [5]. These findings emphasize the critical role of glycemic management from an early age in preventing cardiovascular risks.

Further reinforcing this association, Rochmah et al. demonstrated significant positive correlations between QTc interval and HbA1c, as well as with serum potassium

levels, suggesting that both metabolic control and electrolyte balance influence QT prolongation in type 1 diabetic children [6]. Additionally, Su et al. reported that long-term variability in postprandial glucose, rather than sustained hyperglycemia alone, independently predicted prolonged QTc duration in patients with type 2 diabetes [7]. This finding emphasizes the need to monitor glycemic fluctuations in addition to average glucose levels.

Importantly, the presence of QTc prolongation correlates with the severity of diabetic complications. In a recent study, QTc interval was significantly prolonged in patients diagnosed with cardiac autonomic neuropathy, with higher prevalence observed in those with longer diabetes duration and worse glycemic control [8]. Similarly, Yadav et al. reported a 58% prevalence of QTc prolongation among diabetic patients with CAN, further supporting the clinical utility of QTc as a screening tool [9].

Glycemic variability has also been shown to contribute to QTc abnormalities. Pertseva and Moshenets demonstrated that hypoglycemic episodes were associated with acute QTc prolongation, independent of HbA1c levels, indicating the dynamic nature of glucose on cardiac function [10].

Prolonged QTc interval is a well-recognized electrocardiographic marker associated with an increased risk of ventricular arrhythmias and sudden cardiac death, particularly in individuals with diabetes mellitus. Chronic hyperglycemia, cardiac autonomic neuropathy, and metabolic imbalances common in diabetic patients are believed to contribute to QTc prolongation. Despite this, QTc monitoring remains underutilized in routine diabetes care, especially in resource-limited settings. Identifying the frequency of QTc prolongation and its correlation with glycemic control, as reflected by HbA1c levels, may offer valuable insights into subclinical cardiovascular risk and guide preventive strategies. This study was conducted to address the gap in local data and to determine whether poor glycemic control in type 2 diabetic patients is associated with QTc abnormalities, thereby supporting the need for routine ECG screening as part of diabetes management.

MATERIALS AND METHODS

This was a descriptive, cross-sectional study conducted at Department of Medicine, Jinnah Hospital, Lahore from January to June 2023. The study aimed to determine how frequently QTc interval prolongation occurs in patients with type 2 diabetes and to examine its association with glycemic control. A total of 362 patients were selected using non-probability consecutive sampling. The sample size was calculated based on a 38% expected prevalence of prolonged QTc interval, with a 95% confidence level and a 5% margin of error, as reported by Noor et al. [11].

Inclusion criteria involved patients aged 18 years or older with a known diagnosis of type 2 diabetes mellitus who were presenting for routine follow-up. Written informed consent was obtained from all participants. Patients were excluded if they had congenital long QT syndrome, existing cardiovascular diseases (such as ischemic heart disease, arrhythmia, or heart failure), electrolyte imbalances, end-stage renal disease, or were using QT-prolonging medications like fluoroquinolones, macrolides, or antipsychotics.

Data were collected through a predesigned proforma documenting variables including age, sex, BMI, duration of diabetes, and HbA1c levels. A 12-lead ECG was performed while the patient was at rest in a supine position. The QT interval was corrected for heart rate using Bazett's formula ($QTc = QT/\sqrt{RR}$). Prolongation was defined as QTc ≥450 ms in men and ≥470 ms in women. Blood samples were drawn for HbA1c testing, which was performed using high-performance liquid chromatography (HPLC). Glycemic control was analyzed both as a continuous variable (HbA1c%) and categorically (<7% controlled, ≥7% uncontrolled).

Statistical analysis was carried out using SPSS version 25. Means and standard deviations were calculated for continuous variables, while categorical data were summarized as frequencies and percentages. Associations between QTc status and categorical variables (e.g., gender, BMI category, diabetes control) were examined using chi-square tests. Independent samples t-tests were used to compare mean HbA1c levels between QTc groups. A p-value of less than 0.05 was considered statistically significant.

RESULTS

A total of 362 diabetic patients were included in the study. The mean age of participants was 56.08 ± 9.88 years, with an average duration of diabetes of 7.80 ± 3.97 years. The mean body mass index (BMI) was 28.19 ± 3.80 kg/m^2, and the mean glycated hemoglobin (HbA1c) level was 7.98 ± 1.41%, indicating a predominance of poor glycemic control among participants. The mean corrected QT interval (QTc) was recorded as 450.27 ± 23.26 milliseconds.

Of the total participants, 112 (30.9%) had a prolonged QTc interval, while 250 (69.1%) had a normal QTc. Gender distribution was equal, with 181 (50.0%) males and 181 (50.0%) females. The majority of patients were non-obese (266; 73.5%), while 96 (26.5%) were classified as obese. Glycemic control status showed that 269 (74.3%) had uncontrolled diabetes (HbA1c ≥7%), and only 93 (25.7%) had controlled diabetes (HbA1c <7%), highlighting a substantial burden of poor glycemic control and QTc prolongation in the study population (Table 1).

The association between QTc status and baseline characteristics was evaluated. Among male participants, 131 (72.4%) had normal QTc and 50 (27.6%) had prolonged QTc, while among females, 119 (65.7%) had normal QTc and 62 (34.3%) had prolonged QTc. Although the difference was not statistically significant (p = 0.172), a higher proportion of QTc prolongation was observed in females. Stratification by age showed no meaningful difference: in the 30–50 year group, 69 (69.0%) had normal QTc and 31 (31.0%) had prolonged QTc, while in the 51–75 year group, 181 (69.1%) had normal and 81 (30.9%) had prolonged QTc (p = 0.988). Similarly, diabetes duration showed no significant association with QTc status. Among patients with 1–10 years of diabetes, 188 (69.4%) had normal and 83 (30.6%) had prolonged QTc, whereas in those with 11–20 years of diabetes, 62 (68.1%) had normal and 29 (31.9%) had prolonged QTc (p = 0.825). In relation to obesity, 69 (71.9%) of obese patients had normal QTc and 27 (28.1%) had prolonged QTc,

compared to 181 (68.0%) with normal and 85 (32.0%) with prolonged QTc among non-obese patients (p = 0.487). The association between BMI category and QTc prolongation was not statistically significant. Analysis of glycemic control revealed that among patients with controlled diabetes, 70 (75.3%) had normal and 23 (24.7%) had prolonged QTc. In contrast, among those with uncontrolled diabetes, 180 (66.9%) had normal and 89 (33.1%) had prolonged QTc (p = 0.133). Although not statistically significant, this trend suggests a possible relationship between poor glycemic control and QTc prolongation (Table 2).

Lastly, comparison of mean HbA1c levels showed that patients with prolonged QTc had a higher mean HbA1c (8.17 ± 1.39%) compared to those with normal QTc (7.89 ± 1.41%), although this difference did not reach statistical significance (p = 0.087) (Table 3). Nevertheless, the direction of association reinforces the potential role of poor glycemic control in QTc interval prolongation.

Table 1

Distribution of Study Variables (n = 362)

Variable	Category	Frequency (n)	Percentage (%)
QTc Status	Normal	250	69.1
	Prolonged	112	30.9
Gender	Male	181	50.0
	Female	181	50.0
Obesity Status	Obese	96	26.5
	Non-obese	266	73.5
Diabetic Status	Controlled	93	25.7
	Uncontrolled	269	74.3

Table 2

Association of Baseline Variables with QTc Status (n = 362)

Variable	Category	QTc Normal n (%)	QTc Prolonged n (%)	p-value
Gender	Male	131 (72.4%)	50 (27.6%)	0.172
	Female	119 (65.7%)	62 (34.3%)	
Age Group	30–50 years	69 (69.0%)	31 (31.0%)	0.988
	51–75 years	181 (69.1%)	81 (30.9%)	
Duration of Diabetes	1–10 years	188 (69.4%)	83 (30.6%)	0.825
	11–20 years	62 (68.1%)	29 (31.9%)	
Obesity Status	Obese	69 (71.9%)	27 (28.1%)	0.487
	Non-obese	181 (68.0%)	85 (32.0%)	
Diabetic Status	Controlled	70 (75.3%)	23 (24.7%)	0.133
	Uncontrolled	180 (66.9%)	89 (33.1%)	

Table 3

Comparison of Mean HbA1c Levels between QTc Status Groups

QTc Status	n	Mean HbA1c (%)	SD	p-value
Normal	250	7.89	1.41	0.087
Prolonged	112	8.17	1.39	

DISCUSSION

In this study, prolonged QTc interval was observed in 30.9% of diabetic patients, with a higher, though statistically non-significant, frequency in females and patients with poor glycemic control. While the association between HbA1c and QTc prolongation did not reach statistical significance (p = 0.087), the upward trend in mean HbA1c in patients with prolonged QTc (8.17%) compared to those with normal QTc (7.89%) suggests a clinically relevant link between hyperglycemia and ventricular repolarization abnormalities.

This finding aligns with the study by Noor et al**.**, who reported a significantly higher prevalence of prolonged QTc (38%) in diabetic patients, with a statistically significant association between elevated HbA1c and QTc prolongation (p = 0.024) [11]. Their data support the hypothesis that poor glycemic control plays a key role in cardiac autonomic dysfunction, particularly in younger patients and those with dyslipidemia.

Similarly, Ruhangisa et al**.** found a prolonged QTc interval in 32% of diabetic patients, with poor glycemic control, hypertension, dyslipidemia, high BMI, and duration of diabetes as significant contributors [12]. Their multivariate model emphasized poor glycemic control and combined insulin/oral hypoglycemic regimens as strong predictors. These factors, although not statistically significant in our dataset, showed parallel trends.

The study by Ninkovic et al. further underscores the importance of chronic hyperglycemia and comorbidities such as coronary heart disease in prolonging QTc intervals. They reported a 44.1% prevalence of QTc >440 ms and identified hyperglycemia, sulfonylurea therapy, and female gender as independent predictors of QTc prolongation [13]. Our study also found a higher frequency in females, consistent with this observation, though not statistically significant.

Alam et al. observed that QTc increased significantly with both rising HbA1c levels and diabetes duration, with a mean QTc elevation of 0.39 ms per 1% increase in HbA1c [14]. This reinforces the relevance of long-term glycemic control in modulating cardiac electrophysiological parameters. Although our results did not find a significant relationship with diabetes duration, similar directional trends were seen.

In contrast, the ACCORD trial found no significant association between intensive glycemic control and QTc prolongation [15]. This suggests that while chronic hyperglycemia may contribute to QTc changes, rapid fluctuations from aggressive glycemic control may not be the sole mechanism underlying cardiovascular risk.

Kacheva et al. highlighted another important aspect—insulin-induced hypoglycemia significantly prolonged QTc and increased QT dispersion, mediated by hypokalemia and elevated catecholamines [16]. This supports the idea that both hyper- and hypoglycemia can contribute to QTc variability, making stable glucose levels a crucial target.

Other regional studies have identified varying prevalence and risk factors. Aburisheh et al. reported a lower prevalence (13%) of QTc prolongation in a Saudi cohort, with cardiovascular disease and loop diuretic use being independent predictors [17]. Similarly, Li et al. in China reported a prevalence of 30.1%, identifying high postprandial glucose, microalbuminuria, and elevated diastolic blood pressure as significant factors [18].

Finally, Lafqih et al. found a 27.77% prevalence of prolonged QTc and identified smoking, use of diuretics, and longer diabetes duration as key risk factors [19]. These findings further affirm the multifactorial etiology of QTc prolongation, where metabolic control, comorbidities, and pharmacological therapy all contribute.

Collectively, the current study aligns with existing literature in demonstrating a high prevalence of QTc prolongation among diabetic patients and a possible association with poor glycemic control. While our findings did not reach statistical significance, the clinical implications are notable. Routine ECG monitoring, especially in patients with elevated HbA1c and long-standing diabetes, may help identify high-risk individuals and guide interventions to reduce arrhythmic complications.

CONCLUSION

This study found that nearly one-third of diabetic patients exhibited prolonged QTc intervals, with a higher proportion observed among females and those with uncontrolled glycemic status. Although the associations between QTc prolongation and variables such as gender, age, duration of diabetes, obesity, and HbA1c levels did not reach statistical significance, consistent trends suggest a potential link between poor glycemic control and QTc abnormalities. These findings highlight the importance of routine ECG monitoring in diabetic patients, particularly those with elevated HbA1c levels, to identify subclinical cardiac risk and prevent adverse cardiovascular events. Further studies with larger sample sizes and multivariate analysis are recommended to establish stronger associations.

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