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ORIGINAL RESEARCH

A Study of corrected QT interval in Asymptomatic type 2 Diabetes Mellitus patients.

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ABSTRACT
Introduction – Diabetes mellitus is a medical condition characterized by insufficient regulation of glucose levels in the blood. It is caused by abnormalities in the secretion of insulin, the action of insulin, or both, leading to a range of metabolic diseases. Cardiovascular diseases are frequent long-term consequence of type 2 diabetic mellitus (T2DM). The corrected QT interval is a reliable measure of the time it takes, for the ventricular myocardium to depolarize and repolarize. The aim of present study was to assess the corrected QT interval in asymptomatic type 2 Diabetes Mellitus patients.
Material and methods- The present prospective cross-sectional study was conducted at a B.J. Medical College, Ahmedabad and 200 asymptomatic diabetes mellitus patients were subjected to study. All the laboratory and clinical parameters were noted. ECG of patients were done according to protocol and corrected QT interval was measured.
Results – The mean age of patients was 53.9±10.8 years. The number of female patients (60%) was higher in number as compared to male (40%). The mean value of HbA1c (%) among patients was 9.50±3.25 and mean value of corrected QT interval (ms) was 493.48 ± 67.4. 35% of patients had prolonged corrected QT interval in ECG whereas 65% had normal ECG. Several factors were found to be significantly associated with an increased odds of prolonged corrected QT interval ($p<0.05$).
Conclusion-Abnormalities in the resting corrected QT interval in patients with type 2 diabetes mellitus (T2DM) suggest the beginning of cardiovascular alterations that worsen as the duration of the disease rises. Regular surveillance of individuals with T2DM using ECG can aid in the prompt identification of cardiovascular diseases.
Keywords – cardiovascular diseases, complications, diabetes mellitus, ECG, QTc interval

INTRODUCTION

Alarming statistics from epidemiological data indicate a worrying projected future for Type 2 Diabetes Mellitus. In 2019, diabetes caused the death of 4.2 million individuals and impacted 463 million people aged 20 to 79, as reported by the International Diabetes Federation (IDF).[1]. It is projected that the number of individuals with diabetes globally would reach 700 million by 2045. With a prevalence of 90% among diabetic patients, Type 2 Diabetes Mellitus has emerged as a significant health concern in the twenty-first century. [2,3]
Cardiovascular disease (CVD) is the primary reason for illness and death in those with Type 2 Diabetes Mellitus. These patients have a 15% higher risk of mortality from any cause compared to individuals without diabetes.[4]
Type 2 Diabetes Mellitus is a highly widespread metabolic illness worldwide. It is a condition where the pancreatic islet β-cells do not produce enough insulin, insulin resistance in the tissues and a lack of compensatory insulin release response. This type of diabetes accounts for over 90% of all instances of diabetes mellitus.[4] Complications arising from diabetes mellitus can impact multiple organ systems. Retinopathy, nephropathy, and neuropathy are the outcomes of microvascular complications. Coronary artery disease, peripheral artery disease, and cerebrovascular illness are classified as macrovascular disorders. Gastroparesis, infections and skin problems are nonvascular consequences.
According to World J Diabetes 2021, coronary artery disease, cardiac autonomic neuropathy, and diabetic cardiomyopathy are all constituents of diabetic heart disease. Individuals with diabetes are at a greater risk of premature mortality due to a higher occurrence of cardiac complications at a younger age and more severe illness linked with coronary artery disease in Diabetes Mellitus. [5]

QT interval analysis is a possible technique for categorizing the level of risk in patients with diabetes. QT abnormalities can predict cardiac death in several illness conditions, such as chronic heart failure, systemic hypertension, and peripheral vascular disease. In 2012, Giunti et al conducted a study on this topic using QT interval analysis [6,7].

The prevalence of corrected QT interval prolongation in Type 2 Diabetes Mellitus is 26%.[8,9] The lengthening of the QT interval in diabetes is caused by multiple factors, such as insulin resistance, glucose tolerance, glycemic management, and diabetic comorbidities. Therefore, the reason of QT interval prolongation in diabetes is multifactorial.[10] Hence the present study was conducted with a primary objective to study the corrected QT interval abnormalities in type 2 DM patients. Secondary objectives were (1) to early detection of cardiovascular changes and (2) to study the effect of duration of disease and glycemic control on corrected QT interval.

MATERIAL AND METHODS

The present prospective cross-sectional study was conducted in asymptomatic diabetes mellitus patients who were attending the diabetic clinic at B.J. Medical college, Ahmedabad and duration of the study was 6 months. Ethical permission was taken from institutional ethics committee before commencement of study. Patients were asked to sign an informed consent form after explaining them the complete procedure of the study.

Through consecutive sampling a total of 200 diabetes patients who visited to OPD were selected after fulfilling the inclusion and exclusion criteria.

Inclusion criteria-

- Patients between the age group of 30-60 years.
- Diagnosed cases of T2DM as given by the American Diabetes Association (ADA)
  Patients who fulfil the following criteria for the diagnosis of diabetes mellitus:
  a. Symptoms of diabetes plus random blood glucose (RBS) concentration ≥ 11.1 mmol/l (200mg/dL) or
  b. FBS ≥7.0 mmol/L (126 mg/dL) or
  c. HbA1c ≥6.5% or
  d. PPBS ≥ 11.1 mmol/L (200 mg/dL) during an OGTT.
- Patients having no cardiovascular complaints.
- Co-operation and willing to participate in the study.

Exclusion criteria-

- Patients with existing microvascular complications of diabetes such as retinopathy, neuropathy, and nephropathy.
- Known cases of cardiovascular disorders such as hypertension, coronary artery disease and congestive cardiac failure.
- Presence of any other concomitant diseases disrupting cardiovascular homeostasis like thyroid disorders, pheochromocytoma, chronic renal failure due to any cause, respiratory disorders, and dyselectrolytemia.
- With history of any kind of drug intake such as vasodilators, diuretics, anti-arrhythmic, beta-blockers, alpha agonist or alpha blockers.

Patients were instructed to recline comfortably in the ECG recording room. The resting ECG parameters of the patients were then recorded, following the detailed sampling procedure, only after obtaining their informed consent based on the inclusion criteria. All relevant information, including the patient's name, age, and sex, was documented according to the case study format. Thorough clinical examination was done and baseline laboratory data including fasting and postprandial blood glucose and plasma insulin, HbA1c and urine microalbumin were also collected. The following ECG parameter were assessed using Standardization (Calibration): 10 mm = 1 mV QT interval – 0.39 ± 0.04 s/390 ± 40 ms RR interval – 60-100/min QTc interval was calculated using the formula

$$\text{QTc interval} = \frac{QT\ interval}{\sqrt{RR\ interval}}$$

The data were analyzed using SPSS 23.0. A p-value was generated to determine the significance of the difference in ECG parameters. A significance level of $P < 0.05$ was deemed to be statistically significant. An analysis was conducted to determine the correlation between the corrected QT interval, HbA1c level, and duration of disease.

RESULTS

Out of 200 patients the mean age of patients were53.9±10.8 years. The number of female patients (60%) were higher in number as compared to male (40%). The mean value of HbA1c (%) among patients were9.50±3.25 and mean value of QTc interval were493.48 ± 67.4ms as shown in table 1.

Table 1: **shows Mean HbA1c level and Mean corrected QT interval in T2DM patients.**

PARAMETERS	MEAN ± SD
HbA1C (%)	9.50±3.25
QTc interval (ms)	493.48 ± 67.4

Figure 1: **shows correlation graph of duration of disease with corrected QT interval (P= 0.023).**

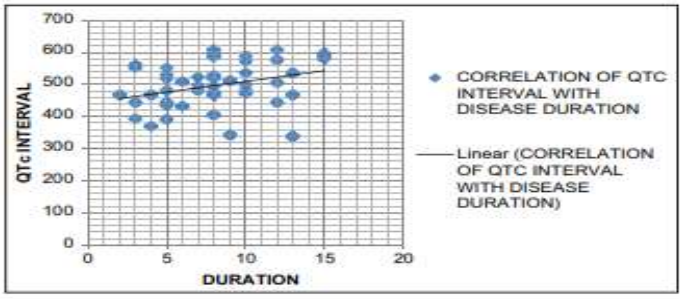
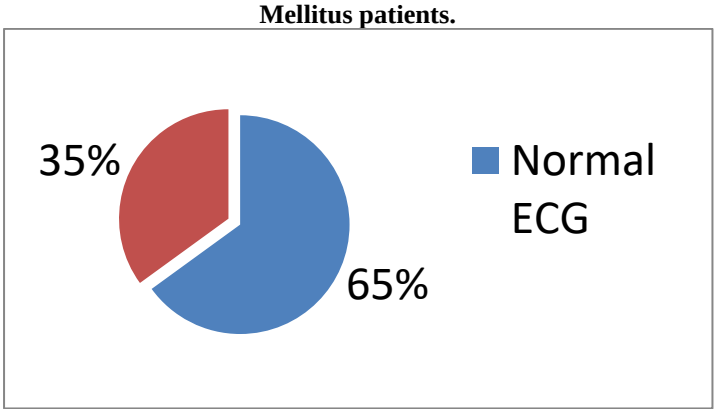


Figure 2: **shows Pie chart representation of percentage of prolong corrected QT interval in type 2 diabetes Mellitus patients.**



After adjusting for age and gender in multivariate regression analysis, several factors were found to be significantly associated with an increased odds of prolonged corrected QT interval. These factors include lower height, higher waist circumference, increasing diastolic blood pressure levels, higher postprandial glucose levels, higher fasting insulin levels, and the presence of microalbuminuria as shown in table 2.

Table 2 Multivariate regression analysis for risk factors of prolonged corrected QT interval.

Risk factor	Regression coefficient	OR	95% CI	P value
Height	-1.856	0.157	0.031-0.758	0.030
Waist circumference	0.024	1.026	1.020-1.040	0.002
Diastolic blood pressure	0.019	1.017	1.008-1.027	0.000
PP blood glucose	0.050	1.050	1.023-1.060	0.000
Fasting plasma insulin	0.015	1.015	1.004-1.029	0.010
Microalbuminuria	0.235	1.267	1.033-1.558	0.024

DISCUSSION

The corrected QT interval is a measure of the duration of myocardial refractoriness and electrical stability. The lengthening of it was linked to ventricular fibrillation and abrupt cardiac death [11]. The occurrence of extended QT interval is more frequent in people with type 1 or type 2 diabetes compared to patients without diabetes [12-14]. The incidence of QT prolongation has been documented to be as high as 16% in individuals with type 1 diabetes [12] and

26% in those with type 2 diabetes [13]. In the present study we conducted a prospective cross-sectional research of 6 months to assess the corrected QT interval in 200 asymptomatic type 2 Diabetes Mellitus patients.

Their blood glucose readings were assessed and a resting electrocardiogram (ECG) was taken. The corrected QT interval was measured in order to observe any potential changes in these patients. The corrected QT interval was extended in patients with type 2 diabetes. There was a direct relationship between the HbA1c level and corrected QT interval, however the relationship did not have enough statistical evidence to be considered significant. The length of duration of disease showed a strong positive relationship with the corrected QT interval (P = 0.023). The extended QTc presence suggested the initiation of cardiovascular problems, which worsened with higher HbA1c levels and longer disease duration. An extended corrected QT interval heightens the likelihood of ventricular arrhythmias including ventricular fibrillations.

A study conducted in two referral centers in Nigeria including 200 patients revealed that 25.5% of individuals with diabetes mellitus had a prolonged corrected QT interval. The average duration of the disease in this study was 20 years.[15] In 1991, Ewing et al. shown in their research that diabetes individuals commonly experience degradation of ECG characteristics specifically in the QT region of the ECG.[16] Rossing et al. reported in their study that the corrected QT interval was notably extended in individuals with diabetes.[17] In their study, Maser et al. found that individuals with diabetes had a higher likelihood of experiencing ventricular arrhythmias, as seen by a longer corrected QT interval.[18] In their study, Khoharo and Halepoto found a strong correlation between corrected QT prolongation and autonomic dysfunction in patients with diabetes mellitus. They concluded that corrected QT prolongation is a particular indicator of autonomic cardiac dysfunction and is associated with a significant risk of mortality.[19] The study conducted by Chugh et al. and Nelson et al. separately investigated the prolongation of corrected QT interval. Both studies indicated that prolonged corrected QT is a reliable indicator of cardiac autonomic neuropathy (CAN) and a predictor of cardiovascular death in individuals with type 2 diabetes. [20,21].

The literature has identified several risk factors for prolonged corrected QT interval in patients with diabetes, including age, gender, components of insulin resistance syndrome such as BMI, hypertension, insulin concentration, hyperglycemia, diabetic microvascular complications such as diabetic retinopathy, neuropathy, microalbuminuria, and preexisting coronary heart disease [22-25]. While there may be discrepancies among research on the numerous risk variables, hypertension was consistently identified as an autonomous risk factor by the majority of studies. Our study revealed that the presence of hypertension, particularly an increase in diastolic blood pressure, was associated with a significantly higher incidence of prolonged corrected QT interval. This finding aligns with earlier research.

The results of our study highlight the importance of regular electrocardiogram (ECG) monitoring in diabetic patients, as it revealed a prolonged corrected QT interval even in those who showed no symptoms of cardiovascular disease. Timely care of diabetes and strict control of HbA1c levels can effectively prevent additional cardiac problems. It is recommended that all individuals diagnosed with type 2 diabetes undergo screening for cardiovascular abnormalities using a basic 12 lead ECG at the time of diagnosis and regularly thereafter. This practice aims to decrease the occurrence of cardiovascular morbidity and mortality.

CONCLUSION

The presence of a prolonged corrected QT interval in patients with type 2 diabetes mellitus, even in the absence of any symptoms, suggests the development of cardiovascular disease and an elevated risk for cardiac arrhythmias. Regular electrocardiogram (ECG) monitoring can assist in the detection of cardiovascular problems in asymptomatic people with type 2 diabetes mellitus (T2DM). Regular evaluation of electrocardiogram (ECG) measurements and maintaining rigorous control over blood sugar levels might postpone the development of cardiovascular problems in diabetes patients who do not exhibit symptoms.

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