

## Original Research Article

# Detailed ECG analysis in type 2 diabetes mellitus: a predictor of multitude of complications

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### ABSTRACT

**Background:** Type 2 diabetes mellitus is a systemic disease with life-threatening complications and morbidity. The 12 lead ECG, an easily available investigation, when studied in detail can give a lot of information and predict various microvascular and macrovascular complications apart from coronary artery disease.

**Methods:** A random cross sectional study involving 100 patients of type 2 diabetes mellitus, in the age group of 18-80 years were included in study after applying various inclusion and exclusion criteria. They were subjected to ECG, 2D echocardiography and laboratory tests. Data were collected and analysed.

**Results:** Arrhythmia was not detected in any patient. A resting tachycardia (HR >100) in 30 patients correlated with Prolonged QTc (>440 miliseconds) (p=0.04). QRS amplitude was reduced in 26 patients. Prolonged QTc also correlated with presence of diabetic complications, retinopathy of NPDR type and nephropathy (p=0.004). Hence about 30% of the study group did show signs of early diabetic cardiac autonomic neuropathy and cardiomyopathy.

**Conclusions:** The statistically significant utility of electrocardiogram in predicting various complications of diabetes apart from coronary artery disease.

**Keywords:** Diabetes mellitus, Diabetic cardiac autonomic neuropathy, QTc prolongation, Resting tachycardia

### INTRODUCTION

Diabetes mellitus (DM) is a disease with effects on multiple organ systems primarily characterized by hyperglycaemia resulting from insufficient insulin secretion, inadequate insulin action or sometimes a combination of both. Diabetes can cause premature atherosclerosis affecting micro as well as macro-vasculature commonly presenting as coronary artery disease and as nephropathy at times. Heart is supplied by autonomic nervous system, which controls both rate and rhythm. Diabetes affects nerves and hence brings about changes in rate and rhythm and also contractility, by a direct toxic effect on the myocardium. The entire

presentation of this condition can be summed up as Diabetic Cardiac Autonomic Neuropathy (DCAN) and Cardiomyopathy.<sup>1</sup> The most lethal complication arising out of diabetic autonomic neuropathy is sudden cardiac death occurring secondarily to ventricular arrhythmias while a sinus tachycardia even at rest may invariably be the first manifestation of diabetic mellitus with cardiac autonomic neuropathy.<sup>2</sup>

Aim of the study was to study in detail the ECG of patients of type 2 diabetes mellitus, for heart rate variability, arrhythmias and other abnormalities and correlate them with macro and microvascular complications of diabetes.

**METHODS**

A random cross sectional observation study was conducted in a semi urban medical college hospital in western Maharashtra. The study was conducted over a period of 26 months from August 2017 to September 2019. 100 patients of type 2 diabetes mellitus who attended our general OPD and inpatient wards were selected randomly for the study after applying for exclusion and inclusion criteria. Written and informed consent was obtained from individual patients as well as their relatives in the vernacular language they understood the best. Institutional ethics committee clearance was obtained

**Inclusion criteria**

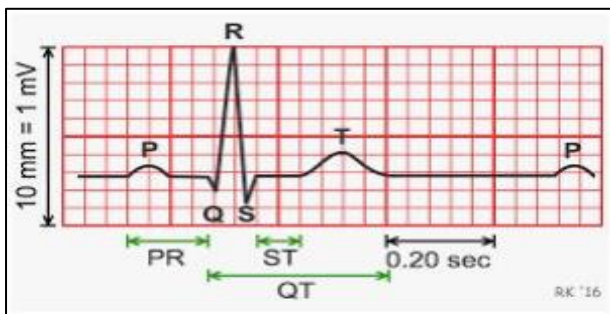
- Patients in the age group of 18-80 years, who are diagnosed to have diabetes mellitus (type II).

**Exclusion criteria**

- Autonomic neuropathy syndromes.
- Known as well as newly diagnosed cases of congenital heart disease.
- Known as well as newly diagnosed cases of rheumatic valvular heart disease.

ECG and 2D-echocardiography, funduscopy using direct ophthalmoscope, blood sugar fasting and post prandial, HbA1c, renal function test and urine protein creatinine ratio levels were done on all selected patients. 12 lead ECG of each patient was analysed for: heart rate, rhythm, P wave duration and height, PR interval, Q wave, amplitude of QRS complex, QT interval and calculated QTc and, T wave (Figure 1).

Data tabulated in Microsoft excel sheet and analysed in SPSS 20 software.



**Figure 1: ECG waves.**

Bazett’s formula for QTc:

$$QTc = \frac{QT \text{ interval in seconds}}{\sqrt{\text{cardiac cycle in seconds}}} = \frac{QT}{\sqrt{RR}}$$

**RESULTS**

In present study total 100 patients were there, out of which 48% were either 50 years or less than that in age while 52% were above 50 years of age with average age being 54.1 years. Among the participants 47% were males while the remaining 53% were females. 58% (n = 58) of the participants have had diabetes for a duration of 5 years and less than that while 42% have been suffering from diabetes mellitus for more than 6 years of duration. Out of them 23 % have had DM for more than 10 years with median duration of diabetes being 5.4 years.

In present study no arrhythmia was noted in study. 44% patients had prolonged QTc of more than 440 msec. Prolonged QTc did not correlate with age of the patients. Prolonged QTc correlated with mean HbA1c of 9.7% (p=0.04). QTc prolongation in the study did not correlate with duration of diabetes mellitus. Prolonged QTc correlated significantly with high mean fasting blood sugar levels of 176.9mg/dl (p <0.007). QTc prolongation is a well-established marker of diabetic cardiac autonomic neuropathy.

In present study 30% patients had resting tachycardia of more than 100 beats per minute. Resting tachycardia did not correlate with either HbA1c (p = 0.48) or duration of diabetes mellitus (p = 0.19). Significant correlation was seen between resting tachycardia and prolonged QTc (p = 0.003) Table 1. Resting tachycardia is one of the earliest sign of diabetic autonomic neuropathy.

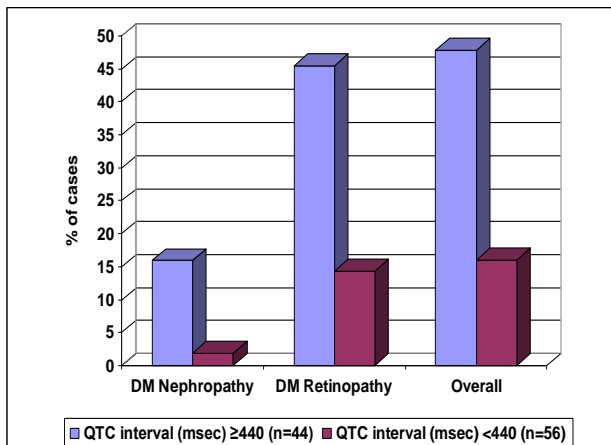
**Table 1: Association between QTC interval and HR in study group.**

HR (beats per minute)	QTC interval (msec)		Total
	≥440	<440	
≥100	20	10	30
<100	24	46	70
Total	44	56	100

Chi-square = 8.94, P=0.003

Out of the 100 study subjects 8 were diagnosed with diabetic nephropathy while 28 suffered from diabetic retinopathy as well. Out of the 8 subjects with diabetic nephropathy, 7 had prolonged QTc ( p = 0.015). Of the 28 subjects with diabetic retinopathy 2 had Proliferative diabetic retinopathy while 26 had non-proliferative diabetic retinopathy. Both the patients with proliferative retinopathy had prolonged QTc interval while 20 out of total 26 patients with NPDR had prolonged QTc (p = 0.0004) Figure 2.

Correlation between other ECG attributes like P-wave duration, PR-interval prolongation with duration of diabetes mellitus and HbA1c as well as other complications of complications was not significant.



**Figure 2: Association between QTC interval and nephropathy retinopathy in study group.**

On 2D echocardiography 19 patients showed Grade 1 Diastolic dysfunction and borderline LVH.

## DISCUSSION

Diabetic neuropathy can affect autonomic supply of the heart and can cause abnormalities with respect to control of heart rate, central and peripheral vascular dynamics. Multiple studies at various time points have postulated sinus tachycardia, prolonged QTc, HRV, ST-T changes, LV hypertrophy and all as signs of Early CAN (cardiac autonomic neuropathy) and that these are due to slow progressive fibrosis of myocardium.<sup>3</sup>

Ana de Santiago in her PhD concluded that ECG findings can be predictors of more serious events which could be aggressively prevented.<sup>4</sup> Prolongation of QTc was studied by Chugh S et al, Nelson MR et al, Okin PM individually and concluded that prolonged QTc is indeed a sign of CAN and a predictor of cardiovascular mortality in Type 2 diabetes.<sup>5-7</sup>

Seyerle A in her dissertation using GWAS (genome-wide association studies) felt that QT is heritable and may be responsible for cardiac events like SCD (sudden cardiac death), TdP (Torsades de Pointes), but there are non-cardiac acquired causes of QT prolongation like diabetes, liver cirrhosis and hypothyroidism. All QT prolongations though are prone to arrhythmia, both the highly prevalent atrial fibrillation or the highly fatal Torsades de pointes.<sup>8</sup>

Voulgari C et al, in Athens Greece felt that subtle ECG changes may be the only way to diagnose Early Diabetic cardiomyopathy.<sup>9</sup> Franconi E et al, studied sex-gender differences in cardiovascular events in diabetics.<sup>10</sup> Gupta S et al, felt ECG abnormalities were more in older diabetics.<sup>11</sup> CAN initially can be sub-clinical in most cases and in some cases may get evident only with fatal arrhythmias.<sup>12-14</sup> This further necessitates the need for a simpler screening test like ECG for asymptomatic subjects.

Chang YC et al, from university of Taiwan studied early myocardial repolarization heterogeneity using magnetocardiography and found changes in diabetics who did not have overt cardiac disease.<sup>15</sup> Insulin resistance in type 2 DM have been directly correlated with this cardiac in-homogeneity and sympathetic overactivity, ultimately increasing the risk of arrhythmias.<sup>16,17</sup>

Balkrishnan VK et al studied and correlated BNP and NT-BNP > 600 as an indication to investigate further with 2Decho and TMT.<sup>18</sup> Diastolic dysfunction has been reported to occur in diabetic subjects with autonomic neuropathy and retinopathy. This finding again correlates with the duration of diabetes, HbA1c levels.<sup>19</sup> Benichou T et al studied HRV (heart rate variability) as an index of CAN.<sup>20</sup> Moningi S et al, felt that ECG changes in diabetics could have anesthetic implications and thus overall effects on outcomes of surgery and hence should be looked into carefully in pre-anesthetic assessments.<sup>21</sup> Negishi K from Hobart Australia studied 2D echo findings of LVH and diastolic dysfunction in diabetics and concluded that these predict a limited cardiac reserve.<sup>22</sup>

## CONCLUSION

The study showed resting tachycardia and prolongation of QTc. Prolonged QTc did not correlate with age, gender, duration of diabetes. However it did correlate with mean high fasting blood glucose and diabetic control (HbA1c). The correlation between prolonged QTc and retinopathy (NPDR) was significant and so also nephropathy and retinopathy. And 19 patients showed grade 1 diastolic dysfunction and LVH on 2D echocardiography. Thus it was concluded that about 30% of the patients did show signs of early Diabetic Cardiac Autonomic Neuropathy and Cardiomyopathy (DCAN).

Hence a detailed study of the ECG, a cheap and easily available investigation must be performed in all asymptomatic Type 2 diabetic patients regularly which can serve as a guide for further extensive investigations to prevent a spectrum of cardiovascular, renal and ophthalmic complications.

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*Ethical approval: The study was approved by the Institutional Ethics Committee*

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