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**Original Research Article**

# A study of cardiological autonomic neuropathy in Type 2 Diabetes Mellitus with reference to QT interval for its diagnosis

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## ABSTRACT

**Background:** Presence of cardiac autonomic neuropathy (CAN) is responsible for silent myocardial infarction and sudden death in diabetics. Hence recognizing cardiac dysautonomia early, which is asymptomatic will help to delay or arrest its progression.
**Methods:** A cross-sectional study to evaluate the Prevalence of Cardiovascular Autonomic Neuropathy in Type 2 diabetes and correlate it with duration of Diabetes and to investigate the relationship between cardiac autonomic dysfunction and corrected QT interval.
**Results:** In the study population, the prevalence of definite CAN was 8%, 24% and 58% in group A, B and C respectively. The prevalence of definite CAN increases with increase in duration of diabetes. P value <0.001 significant.
**Conclusions:** A significant correlation is present between Cardiovascular autonomic dysfunction and QTc prolongation. QTc interval in the ECG can be used to diagnose Cardiovascular autonomic neuropathy with a reasonable sensitivity and specificity.

**Keywords:** Autonomic neuropathy, Type 2 diabetes mellitus, QT interval

## INTRODUCTION

Diabetes mellitus is a heterogenous group of metabolic disorders characterized by hyperglycemia resulting from defects in insulin secretion, insulin action or both.[1] Type 2 Diabetes is one of the major health problems all over the world.

Presence of cardiac autonomic neuropathy (CAN) is responsible for silent myocardial infarction and sudden death in diabetics. Hence recognizing cardiac dysautonomia early, which is asymptomatic will help to delay or arrest its progression. DAN (Diabetic Autonomic Neuropathy) frequently coexists with other peripheral neuropathies and other diabetic complications, but DAN may be isolated, frequently preceding the detection of other complications. Despite its relationship to an increased risk of cardiovascular mortality and its association with multiple symptoms and impairments, the significance of CAN has not been fully appreciated.[3] Type 2 diabetic patients with abnormal CVR tests may have increased mortality, and those combined with postural hypotension have higher mortality than those without.[4]

In 1980, for the first time, an association of prolonged QTc interval with cardiac autonomic neuropathy was given, thereby opening the possibility of a rapid objective

method for detecting cardiac autonomic neuropathy. Furthermore, studies are needed to demonstrate an association of prolonged QTc interval with cardiac dysautonomia in diabetes mellitus.[5,6]

Hence, present study focuses on prevalence of cardiac autonomic neuropathy and utility of corrected QT prolongation for its diagnosis in type 2 Diabetes mellitus. Present study has been designed to evaluate the prevalence of cardiovascular autonomic neuropathy and its correlation with duration Type 2 Diabetes.

## METHODS

### *Study population*

A total of 120 patients satisfying all the inclusion and exclusion criteria were enrolled for the study from the population of Type 2. Written consent was obtained from all the patients participating in the study after clearly explaining the study procedure.

### *Study duration*

This study was conducted for a period from May 2017 to August 2018 in Konaseema Institute of Medical Sciences and RF.

### *Study design*

A cross-sectional study to evaluate the prevalence of cardiovascular autonomic neuropathy in Type 2 diabetes and correlate it with duration of diabetes. To investigate the relationship between cardiac autonomic dysfunction and corrected QT interval.

### *Tests for autonomic functions*

Blood pressure was recorded manually using standard sphygmomanometer. The heart rate variation was calculation using standard Heart rate monitor, Pulse oximeter and continous ECG recording. A baseline ECG was taken with a Standard ECG machine for calculation of QTc interval. QT interval was taken from the onset of QRS complex to the end of T wave. QT was then corrected for heart rate using the Bazette's formule44.

QTc interval=QT/√(R-R). A QTc interval more than 440 Millisecond is considered prolonged.

Inclusion criteria was type 2 diabetes, already on treatment and newly diagnosed patients.

### *Exclusion criteria*

- Age above 60 years
- Documented ischemic heart disease and congenital heart disease.
- Hypertension
- COPD
- Uremia.

## RESULTS

### *Population characteristics*

The study group consists of 150 patients with Type 2 diabetes. The following tables lists the information about the age variation and sex distribution of the study group. The patients in the groups <5 years, 5-10 years and >10 years were taken as group A, B and C respectively.

As per Table 1 mean age of patients with less than 5-year diabetes was 50.08 years. Mean age of the patients with diabetes from 5 to 10 year was 52.76 years and more than 10 years was 55.76 years.

**Table 1: Age variation among study groups.**

| Duration of DM | N | Mean age | Mean QTc | SD |
|---|---|---|---|---|
| <5 years | 40 | 50.08 | 416.84 | 4.251 |
| 5-10 years | 40 | 52.76 | 426.55 | 3.217 |
| >10 years | 40 | 55.16 | 441.64 | 2.881 |

**Table 2: Sex distribution among study groups.**

| Duration of DM | | <5 years | | 5-10 yrs | | >10 years | |
|---|---|---|---|---|---|---|---|
| | | n | % | n | % | n | % |
| Sex | Male | 27 | 54 | 29 | 58 | 28 | 56 |
| | Female | 23 | 46 | 21 | 42 | 22 | 44 |
| Total | | 50 | 100 | 50 | 100 | 50 | 100 |

**Table 3:Frequency distribution of normal (0-1), borderline (2-4), abnormal (≥5).**

| CAN | | Group | | | | | | Significance |
|---|---|---|---|---|---|---|---|---|
| | | <5 years | | 5-10 years | | >10 years | | |
| | | n | % | n | % | n | % | |
| Score | 0-1 | 28 | 72 | 18 | 48 | 12 | 26 | P <0.001 Significant |
| | 2-4 | 8 | 20 | 12 | 28 | 7 | 16 | |
| | ≥5 | 4 | 8 | 10 | 24 | 21 | 58 | |
| Total | | 40 | 100.0 | 40 | 100.0 | 40 | 100.0 | |

**Table 4: Correlation between autonomic neuropathy (an) and QTc prolongation in total diabetic patients.**

| QTc in msec | Definite CAN | % | Borderline CAN | % | No CAN | % |
|---|---|---|---|---|---|---|
| ≤440 | 6 | 20 | 16 | 68.8 | 50 | 79.5 |
| >440 | 30 | 80 | 6 | 31.2 | 12 | 20.5 |
| Total | 36 | | 22 | | 62 | |

Among 120 patients, 67 patients were men accounting for 56% of total patients. The remaining 53 (44%) patients were women. Mean age of patients in the groups A, B and C were 50.8, 52.76 and 55.16 respectively. This shows there is no significant variation in age among the three groups.

From the Table 4, it is clear that, QTc interval prolongation occurs with development of CAN. Prolongation of QTc interval is well correlated with Cardiac Autonomic Neuropathy. P value <0.001.

## DISCUSSION

The results of this study on native Indian population illustrate the fact that cardiac autonomic dysfunction is common in Diabetic patients and its prevalence increases with duration of diabetes. Similar results have been reported in previous studies conducted in India and other countries.[7] This study demonstrated significant abnormalities in autonomic function using basic cardiovascular autonomic function tests, which have well been validated.

Vinik et al, studied and published a data of sensitivity of Autonomic function tests done on a population of 3516 patient with type 1 and type 2 Diabetes.[3] The calculated sensitivity of HRV during deep breath testing and valsalva was 98% and 93% respectively. In our study, Heart rate variability during deep breathing is abnormal in 44 out of 45 patients with definite CAN giving a sensitivity of 97.7% and valsalva is abnormal in 42 of 45 patients with CAN giving a sensitivity of 93% which correlates with given values. Abnormal HRV in one test is indicative of early autonomic neuropathy3. Meta-analyses of published data demonstrate that reduced cardiovascular autonomic function as measured by heart rate variability (HRV) is strongly (i.e., relative risk is doubled) associated with an increased risk of silent myocardial ischemia and mortality.[3]

Mohan et al, studied the prevalence of CAN in 336 patients with NIDDM in south India.[8] There was an increase in prevalence of CAN with duration of diabetes. In 0-5 years group the prevalence of autonomic dysfunction was 28.2%. In our study, the prevalence of autonomic dysfunction in 0-5 years group is 28% of which 8% had definite CAN and 20% had evidence of borderline/early CAN.

Toyry JP et al, studied the clinical significance of autonomic neuropathy in NIDDM. Toyry JP et al, studied the clinical significance of autonomic neuropathy in NIDDM.[9] A total of 133 patients with newly diagnosed NIDDM (70 men) and 144 control subjects (62 men were examined at baseline and after 5 and 10 years of follow-up. The frequency of autonomic dysfunction at baseline, at 5 years and 10 years was 4.9%, 19.6% and 65% respectively. In our study, the prevalence of definite CAN at <5 years, 5-10 years and >10 years is 8%, 24% and 58% respectively which is comparable to the above study. Also, the prevalence of cardiovascular autonomic neuropathy increases with increase in duration of diabetes (p<0.001).

Pappachan JM et al, studied the prevalence the CAN among 100 type 1 and type 2 diabetes mellitus, in south India assessed by the five autonomic function tests by Eving's methodology.[10] The prevalence of CAN was 60% which is comparable to the results obtained in this study.

## CONCLUSION

Authors concluded that prevalence of CAN will increase with increase in the duration of diabetes. About half of the patients with type 2 diabetes have autonomic dysfunction after ten years. A significant correlation is present between Cardiovascular autonomic dysfunction and QTc prolongation. QTc interval in the ECG can be used to diagnose Cardiovascular autonomic neuropathy with a reasonable sensitivity and specificity.

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