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A cross-sectional study of cardiovascular autonomic neuropathy associated with Type 2 Diabetes Mellitus with reference to QT interval

Dr Anubhav Gupta [1], Dr Kalpana Tiwari [2],Dr Lalan Pratap Singh [3],Dr Badri Vishal Singh[4]*

1. Senior Resident, Department of Medicine, Shyam Shah Medical College, Rewa (MP)
2. PHD scholar, IMS department Pharmacology BHU.
3. Assistant Professor , Superspecility Hospital , Shyam Shah Medical College, Rewa (MP)
4. Senior Resident, Department of Medicine, Shyam Shah Medical College, Rewa (MP)

Corresponding Author Details

Dr Badri Vishal Singh

Senior Resident,

Department of Medicine,

Shyam Shah Medical College, Rewa M.P.

EMAIL- bdr.vshl.sngh@gmail.com

ABSTRACT.

Background: Silent myocardial infarction and sudden death in diabetics are caused by the presence of cardiac autonomic neuropathy (CAN). Therefore, detecting cardiac dysautonomia early—when it is asymptomatic—will aid in slowing or stopping its progression.

Methods A cross-sectional study was conducted to assess the prevalence of cardiovascular autonomic neuropathy in people with type 2 diabetes, correlate it with the duration of the disease, and explore into 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

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, CAN

INTRODUCTION:

Diabetes mellitus is a heterogeneous group of metabolic disorders characterized by hyperglycemia due to defects in insulin secretion, insulin action or both. Type 2 Diabetes is one of the major health problems all over the world.(1)

Heart failure and related morbidity and mortality are increasing at an alarming rate, in large part, because of increases in aging, obesity, and diabetes mellitus. The clinical outcomes associated with heart failure are considerably worse for patients with diabetes mellitus than for those without diabetes mellitus(2)

The concept of diabetic cardiomyopathy was first introduced by Rubler et al(3). and has subsequently been widely used by epidemiologists and clinicians. CAN is one of the underdiagnosed DM complications and one of the major risk factors for CVD in people with DM . It is known as the impairment of the nerve innervated by the autonomic nervous system (ANS) that regulates the heart and the blood vessels attributable to coronary artery disease (CAD) or hypertension.(4)It is important to note that in many patients, particularly those with Type 2 diabetes, diabetes associated changes are amplified by the existence of these co-morbidities, which likely will augment the development of left ventricular hypertrophy, increase the susceptibility of the heart to ischemic injury and increase the overall likelihood of developing heart failure(5). A relationship between a prolonged QTc interval and cardiac autonomic neuropathy was first identified in 1980, which made it possible to design a rapid, accurate method for detecting cardiac autonomic neuropathy. Different methodologies and tests to examine CAN have led to this variance in prevalence. Various studies.showes that Prolonged QTc interval is associated with cardiac dysautonomia in diabetes mellitus. So, it was determined whether there was a connection between CAN

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and QT indices in T2DM patients (6)The goal of the current study is to assess the prevalence of cardiovascular autonomic neuropathy and its relationship to long-term Type 2 Diabetes.

MATERIALS AND METHODS:

STUDY POPULATION: study comprised 90 patients with Type 2 diabetes who were admitted to the medicine ward of the index medical college hospital and research centre and met the inclusion and exclusion criteria. After thoroughly discussing the research method, all patients who agreed to participate in the study signed a permission form.

STUDY DURATION: study was conducted for a period of 1 year from April 2020 to March 2021.

STUDY DESIGN: cross-sectional study to determine prevalence of CAN in people with T2DM and its relationship to diabetes duration.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:

Type 2 diabetics already on treatment and newly diagnosed T2DM patients.

EXCLUSION CRITERIA :

Age > 60 years, Documented IHD, Documented valvular/CHD Hypertension,COPD, Uraemia, Parkinsonism

STATISTICAL ANALYSIS:90 patients, were classified based on their age, gender, diabetes duration, & autonomic dysfunction score. The data were interpreted, & the QTc interval was examined. For comparing the means of more than two groups, a one-way analysis of variance (ANOVA) was used. The Chi-square (x2) statistic was used to determine significance of the difference in proportions. Student Ttest was used to determine significance of the difference in mean between groups. If <p0.05, variables were judged significant. Pearson's R-value correlation was used for intervariate analysis.

RESULTS :90 patients with Type 2DMwere listed according to age variation and sex distribution of the study group. As per Table 1 mean age of patients with less than 5-year diabetes was 50.20 years. Mean age of the patients with diabetes from 5 to 10 year was 52.06 years and more than 10 years was 54.83years.Among 90 patients, 52.22% (47)of patients were men. The remaining 47% (43) patients were women. Mean age of patients in the groups A, B and C were 50.20, 52.06, and 54.83 respectively. This demonstrates that the three groups differ significantly in age.

TABLE – 1 AGE VARIATION AMONG STUDY GROUPS

Diabetes duration	Number of patients	Mean Age	Standard deviation
< 5 yrs	29	50.20	2.86
5-10 yrs	31	52.06	2.79
>10 yrs	30	54.83	2.86

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TABLE – 2 STUDY GROUPS GENDER DISTRIBUTION TABLE

Diabetes duration		<5 yrs		5-10 yrs		>10 yrs	
		n	%	N	%	N	%
GENDER	MALE	15	51.72	17	54.83	15	50
	FEMALE	14	48.27	14	45.16	15	50
Total		29	100	31	100	30	100

Graph 1: Gender distribution amongst study groups

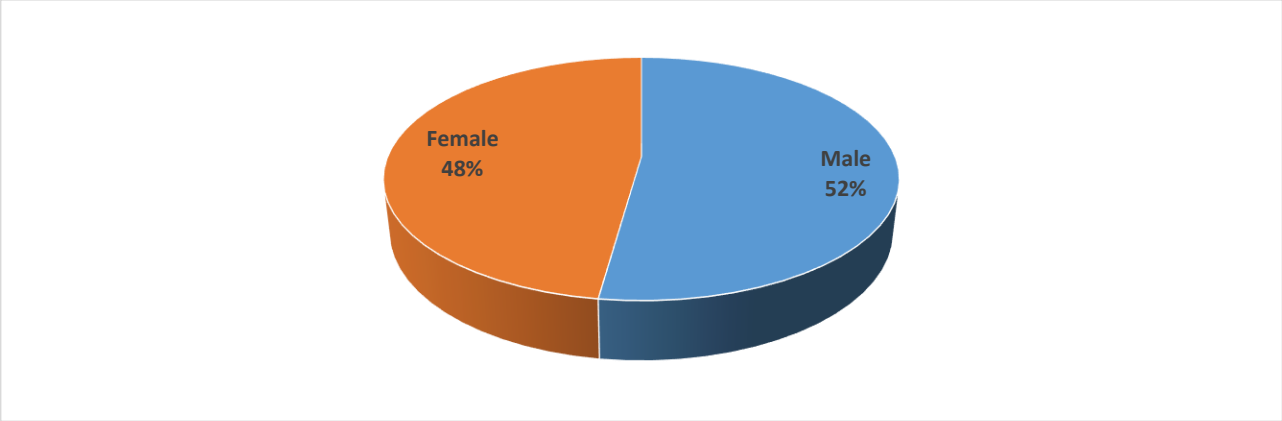

TABLE – 3 Correlation between can and qtc prolongation in total patients of diabetes

QT c inm-sec	DEFINITECAN	%	BORDER-LINE CAN	%	NO CAN	%	p value
>440	22	75.86	4	25	11	24.44	0.0023
<440	7	24.12	12	75	34	75.55	

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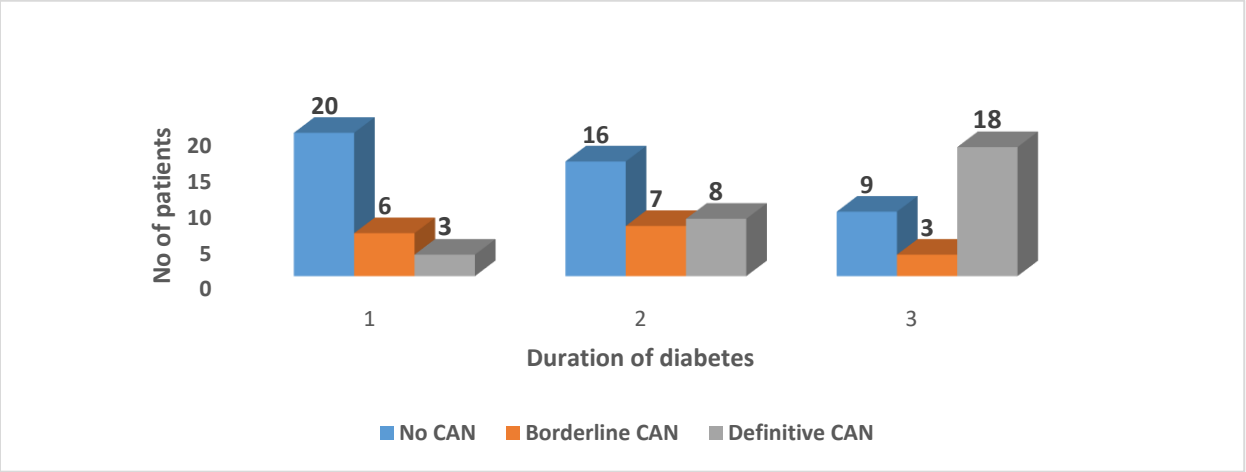
Graph 2: Frequency distribution of patients on the basis of CAN score



DISCUSSION: The findings of this study highlight the importance of identifying and monitoring CAN in patients with T2DM, as it is associated with a prolonged QT interval. Prolongation of the QT interval is known to increase the risk of life-threatening ventricular arrhythmias, including torsades de pointes and sudden cardiac death. The underlying mechanisms linking CAN and QT interval prolongation are likely multifactorial. Autonomic dysfunction can disrupt the balance between sympathetic and parasympathetic control of the heart, leading to altered repolarization and subsequent QT prolongation.The findings of this study show that cardiac autonomic malfunction is widespread in diabetic individuals, and that its incidence rises with diabetes duration. Previous investigations performed in India and other countries have shown similar results.(7),(8
)Using well-validated basic CV autonomic function test, this study found severe anomalies in autonomic function. Result of study on the sensitivity of autonomic function test performed on 3516 patients with Type1DM and Type 2 DM. HRV sensitivity during the course of deep breath testing and Valsalva was determined to be 98 %and 93 %, respectively.(7)
. In our study, Heart rate variability during deep breathing is abnormal in 29 patients with definite CAN, with a sensitivity of 100 %, and Valsalva is abnormal in 27 of 29 patients with definite CAN, with a sensitivity of 93.10 %.. Early autonomic neuropathy is characterized by abnormal HRV during deep breathing. Result of another study shows 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.
another study shows that the prevalence of CAN in 336 patients with NIDDM looked at the P of CAN in 336 T2DM2 patients. The prevalence of CAN increased as duration of diabetes increased. Autonomic dysfunction was found to be prevalent in 28.2 % of children aged zero to 5.(9) In our study, autonomic dysfunction was found in 28% of the children aged zero to 5, with 8% having definite CAN and 20% having signs of borderline/early CAN.
the clinical significance of autonomic neuropathy in NIDDM importance of autonomic neuropathy in Type 2 diabetes was investigated At baseline, 5 and 10 years following diagnosis, a total 133 patients with newly diagnosed T2DM (70 males) and 144 control participants (62 men) were evaluated.
The P of autonomic dysfunction was 4.9 % at baseline, 19.6 % at 5 years, and 65% at 10 years. The P of definite CAN in our study at 5 years, 5-10 years, and >10 years is 10%, 25%, and 60 %, respectively, which is close to the aforementioned studies. (10).
With increasing diabetes duration, prevalence of CAN rose (p=0.023). the incidence of CAN in 100 people with Type1DM &Type2DM DM in south India study using Ewing's technique and the 5 autonomic function tests. CAN was found to be prevalent in 60% of the population, which is similar to the findings of this study (51 %).(4)
CONCLUSION: The prevalence of cardiovascular autonomic neuropathy will rise as the diabetic duration increases. After 10 years, around 50% of Type 2 diabetes patients develop autonomic dysfunction. CV autonomic dysfunction & QTc prolongation have a substantial relationship. With reasonable sensitivity and specificity, the QTc interval in ECG can be utilized to detect CAN.

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Limitations of this study include its cross-sectional design, which limits the establishment of causal relationships. Longitudinal studies are needed to validate these findings and determine whether the presence of CAN and QT prolongation predicts adverse cardiovascular events in individuals with T2DM. Additionally, the study did not investigate the impact of specific treatment interventions or glycemic control on the association between CAN and QT interval prolongation, which warrants further investigation.

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