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Original Research Article

Prolonged QTC Interval as an Indicator of Cardiac Autonomic Neuropathy in Diabetes Mellitus Patients

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Abstract:

Introduction: Due to its high risk of cardiac arrhythmias and sudden death from silent myocardial ischaemia, CAN is a significant source of morbidity and mortality in diabetes individuals. Numerous studies have shown that the electrocardiogram's corrected QT interval (QTc) prolongation is a specific, quick, and reliable way to identify cardiac autonomic neuropathy. The objective of the current study was to assess the relationship between the QTc interval and diabetic cardiac autonomic neuropathy.

Material and Methods: Between April 2020 and March 2021, 60 patients with type 2 diabetes mellitus who met the inclusion and exclusion criteria were studied. The patients underwent five cardiovascular autonomic function tests as described by Ewing et al, and they were classified according to Ewing's criteria. The QTc interval was computed using Bazett's formula.

Results: Out of 60 type2 Diabetic patients, CAN was found in 35 (58.3%) patients. Early CAN was seen in 54.3%, Definite CAN in 28.6%, and Severe CAN in 17.1% patients. Patients with CAN had a mean QTc458 ± 12.8 ms, whereas patients without CAN had a mean QTc407 ± 11.8 ms which was statistically significant ($p<0.05$).

Conclusion: Early detection of CAN aids in the prevention of cardiovascular disease-related mortality and morbidity. In diabetic patients, the prolonged QTc interval is a relatively simple, fast, and reliable indicator for identifying CAN.

Keywords: Diabetes mellitus, cardiovascular autonomic neuropathy, QTc interval, Ewing's criteria.

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Introduction

Chronic hyperglycemia along with abnormalities in the metabolism of carbohydrates, fats, and proteins brought on by deficiencies in insulin secretion, insulin action, or both are characteristics of diabetes mellitus.[1]By 2040, the global number of persons suffering from diabetes mellitus is expected to climb from 415 million to 642 million. The number of people with type 2 diabetes mellitus is increasing in every country, with developing countries accounting for 75% of the total.[2]With an increasing global prevalence, diabetes mellitus is expected to be a prominent cause of illness and mortality in the future.[3]

Diabetic neuropathy affects around 50% of persons with long-term type 1 and type 2 diabetes mellitus. It may exhibit symptoms of autonomic neuropathy, polyneuropathy, or both. Cardiac autonomic neuropathy (CAN) is a typical and frequently neglected complication of diabetes. CAN is caused by damage to the autonomic nerve fibres that innervate the heart and blood vessels, which causes anomalies in heart rate control and vascular dynamics. The prevalence of CAN in people with type 2 diabetes ranges from 20% to 73%. Because it is associated with an increased risk of cardiac arrhythmias and sudden death due to silent myocardial ischemia,[4]

CAN is a substantial source of morbidity and mortality in diabetics. Early subclinical identification and management of CAN are critical

for risk stratification in preventing sudden death from silent myocardial infarction. [5] Several non-invasive diagnostic methods for CAN have been described. While sensitive and repeatable, these tests are time-consuming and inadequate for screening a large number of diabetic patients. Many studies have indicated that Prolongation of corrected QT interval (QTc) in the electrocardiogram (ECG) is a quick and specific way of identifying CAN. [6]The present study aims to evaluate the correlation between QT interval and diabetic cardiac autonomic neuropathy.

Materials and Methods

Study Design

The study was a cross sectional study in which the patients were selected as per the inclusion and exclusion criteria.

Source of Data

60 patients of Type 2 diabetes mellitus visiting the medicine outpatient department and admitted in wards of the Department of Medicine, Panimalar Medical College Hospital and Research Institute, Chennai, Tamilnadu during the period of April 2020 to March 2021 were taken for the study.

Inclusion Criteria

Type 2 diabetes mellitus patients in the age range of 20-70 years of both sexes

Exclusion Criteria

1. Patients of type 2 diabetes mellitus with evidence of heart failure, hypertension, cardiac arrythymias and other cardiaovascular diseases.
2. Patients of type 2 diabetes mellitus with Anemia, COPD, renal failure, liver diseases, electrolyte abnormalities, and cerebrovascular diseases.
3. Patients on drugs known to interfere with autonomic function tests and QT interval.
4. Patients on alpha blockers, beta blockers and vasodilators.
5. Patient with clinically overt neuropathy due to causes other than diabetes.

Cardiac autonomic neuropathy was assessed by cardiovascular responses to non-invasive cardiac autonomic function tests as recommended by Ewing et al.[7]

These are as follows:

a) Heart rate variability during deep breathing (by doing ECG)(normal response > 15 beats/minute, borderline 11-14 beats/minute; abnormal response < 10 beats/minute).
b) Immediate heart rate response to standing (by doing ECG)(normal responseif > 1.04; borderline between 1.01 and 1.03; and abnormal if <1.00).
c) Heart rate response to Valsalva manoeuvre (by doing ECG)(Normal ratio is>1.21, abnormal 1.20 or less).
d) Blood pressure response during sustained hand grip (normalresponse >16mmHg, borderline response 10-15mmHg, abnormal response<10mmHg).
e) Blood pressure response to standing (normal response <10mmHg, borderline response 11-29mmHg, abnormal response>30mmHg).

Based on the results of the above tests, the autonomic dysfunction in Type -2 diabetes mellitus patients is categorized as none, early, definite, and severe.[11]

None: All tests normal or 1 test borderline.

Early: One of 3 heart rate tests abnormal or 2 borderline.

Definite: Two heart rate test abnormal.

Severe: 2 heart rate tests abnormal with one or both blood pressure tests abnormal or both borderline.

The QTc interval was determined by Bazett's formula (QTc =QT/√R-R), and a value exceeding 440 msec. was considered prolonged.[8]

Statistical Methods

SPSS software-22 was used for analysis. Continuous measurements were presented as Mean ± SD and categorical measurements were presented as percentages.

Chi-square test was used to assess differences between categorical variables and Student's t-test was used to assess differences between continuous variables. p value < 0.05 was considered to be significant.

Result

The mean age of diabetic patients was 48.76 ± 10.27 years (range: 20-70 years). The majority of the cases were in the age group of 30-60 years.

The mean age in the group with CAN was 48.657 ± 10.134 years. The mean age in the group without CAN was 48.66 ± 11.3116 years which was not significant statistically

Table 1: Age distribution of patients with and without CAN

Age group	Without CAN	With CAN	Total	p-value
20-30	2	1	3	0.164
31-40	10	5	15	
41-50	8	12	20	
51-60	8	7	15	
>60	3	4	7	
Total	25	35	60	

There were 25 (42%) males and 35(58%) females. Total number of male and female among CAN positive were 13 (37%) & 22 (63%) respectively as shown in Table 2

Table 2: Gender distribution of patients with and without CAN

Gender	Without CAN	With CAN	p-value
Male	10	13	0.354
Female	15	22	

Out of 60 patients, CAN was found in 35 (58.3%) patients as shown in fig.1

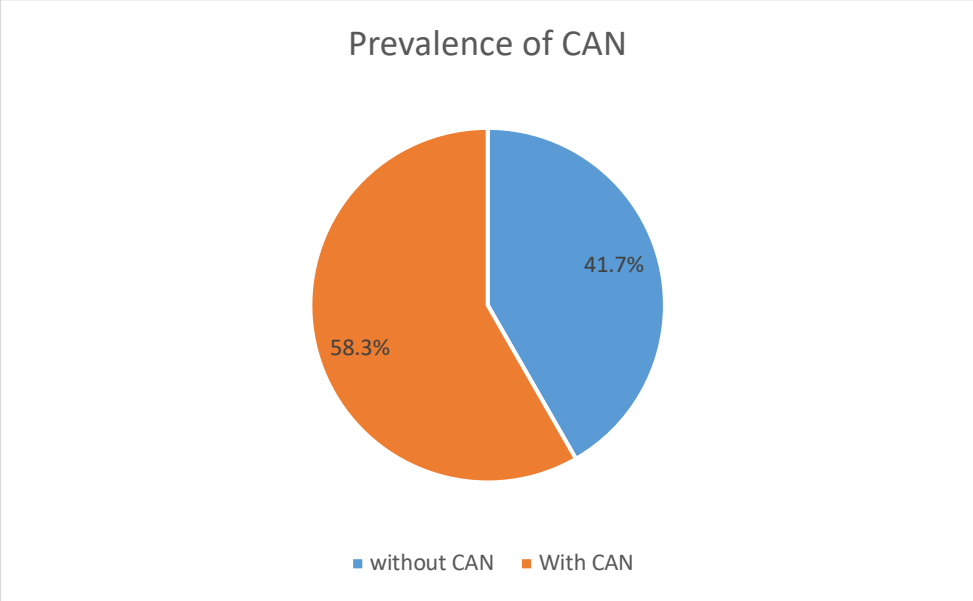

Figure 1: Prevalence of CAN

We categorized the abnormal autonomic function tests as per Ewing's criteria where the abnormality was sub-grouped as early, definite and severe. The observation revealed that 54.3% of our diabetic patients had early, 28.6% had definite and 17.1% had severe CAN.

Table 3: Percentage of CAN in different stages

	number	Percentage
Early	19	54.3
Definite	10	28.6
Severe	6	17.1

The mean QT_C interval among CAN positive was 458 ± 12.8msand among CAN negative was 407 ± 11.8ms which was statistically significant.

Table 4: comparison of QT_C interval between CAN negative and CAN positive groups

CAN	QT_C interval	p-value
CAN negative	407 ± 11.8ms	0.003*
CAN positive	458 ± 12.8ms	

*significant

Discussion

Cardiac Autonomic Neuropathy is a serious and often undiagnosed consequence of diabetes. After exploring the numerous inclusion and exclusion criteria, a total of 60 type 2 diabetes mellitus patients were included in this study. In this study, 41.7% (25) of the patients did not have CAN. Positive autonomic dysfunction tests were found in 58.3% (35) of the patients. Early CAN was detected in 54.3% (19) of the 35 patients, definite CAN in 28.6% (10), and severe CAN in 17.1% (6) of the patients.

Mathur CP et al.[9] used Ewing's criteria to assess 50 diabetics for autonomic neuropathy. A normal study was observed in 42% of cases, early CAN in 20% of cases, definite in 30% of cases, severe in 4% of cases. Pillai JN et al [10] performed autonomic function testing on 50 type 2 diabetes mellitus patients and discovered that 21 (42%) had severe autonomic neuropathy and 12 (24%) had early autonomic neuropathy. Taha mahwi et al. [11] found CAN in 106 of 150 cases in their study. 35 patients had early CAN, 40 had definite CAN, and 31 had severe CAN. In their study, Agarwal et al[12] found that 70% of patients had CAN. Early neuropathy was detected in 37% of patients, definite neuropathy in 40%, and severe autonomic dysfunction in 22.9%.

Patients with CAN had a mean QTc interval of 418.76± 38.01 msec, whereas patients without CAN had a QTC interval of 394.88 ± 28.91 msec. This indicates that the QTC interval was longer in CAN patients, and the difference was statistically significant (p =0.031).

In their study of 50 diabetic patients, Mathur et al. [9] confirmed that prolonged QTc is linked with cardiac dysautonomia. According to Pillai JN et al. [10] and Barthwal et al. [13], diabetics with autonomic neuropathy had significantly greater QTc mean values than diabetics without autonomic neuropathy. In line with the previous studies, the current study found a substantial association between cardiac autonomic neuropathy and QTc interval prolongation.

Conclusion

CAN is a prevalent complication of diabetes that is underdiagnosed. CAN plays a role for the development of asymptomatic myocardial ischaemia. Effective prevention of cardiovascular disease-related morbidity and mortality is facilitated by early detection of CAN. As described by Ewing et al., cardiovascular autonomic function tests are simple but time-consuming. Identifying CAN in diabetic patients is relatively simple, fast, and reliable by measuring the QTc interval.

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