

**Original research article**

# An analysis of the QTc interval's predictive value in the occurrence of cardiac autonomic neuropathy in people with type 2 diabetes mellitus

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**Abstract**

**Background and Objective:** To analyse the prevalence and possible factors contributing to (CAN) and evaluate the efficacy of extending the corrected QT interval (QTc) on an electrocardiogram (ECG) as a diagnostic method for CAN in subjects with diabetes mellitus.

**Method:** The prevalence of CAN in a sample of 75 persons with both type 1 and type 2 diabetes mellitus was assessed using Eving's approach, which entailed performing five autonomic function tests. The CAN score in each patient was analysed and its link with the QTc interval was examined.

**Result:** 59 percent of people have CAN. In individuals with type 1 diabetes, univariate analysis revealed a strong correlation between CAN and increased age (odds ratio (OR) 17.59), lengthening of QTc (OR 6.52), duration of disease beyond 10 years (OR 2), and peripheral neuropathy (p,0.001).

**Conclusion:** The majority of people with diabetes mellitus have CAN. Three major risk factors are the duration of diabetes, peripheral neuropathy, and senior age. The ECG's QTc interval has a reasonable level of sensitivity, specificity, and positive predictive value, making it useful for CAN detection.

**Keywords:** QTc interval's, cardiac autonomic neuropathy, type 2 diabetes mellitus

**Introduction**

Diabetes mellitus is a significant metabolic disease that can impact almost all of the body's organ systems. It is projected that by 2025, there would be 57.2 million more people in India who have diabetes. Among its most frequent side effects, cardiovascular disease raises these individuals' mortality rates. Clinical manifestations of CAN include painless myocardial ischaemia, orthostatic hypotension, intraoperative cardiovascular lability, and exercise intolerance. CAN also increases the risk of morbidity and mortality, as well as a lower quality of life for people with diabetes mellitus. Since diabetics have a very high incidence of silent myocardial ischaemia, CAN appears to be the most likely explanation for the lack of discomfort. In addition, people with CAN have a higher risk of unexpected death. CAN is a problem that gradually worsens with time. There have been reports of a high frequency of CAN<sup>[1-3]</sup>.

Increased intraoperative instability, exercise intolerance, postural hypotension, and the frequency of silent myocardial infarction and ischemia are all associated with a bad prognosis when it comes to CAN. The risk of sudden cardiac death from cardiac autonomic neuropathy and diabetes mellitus is increased. This mortality usually results from undetected myocardial ischemia or infarction or malignant ventricular arrhythmias. QT interval lengthening is correlated with cardiac autonomic neuropathy, and this may put diabetics at risk for sudden death. Elevated QT dispersion has also been suggested as an indicator of diabetic autonomic neuropathy<sup>[4-6]</sup>.

The study also aimed to determine whether QTc prolongation is helpful in diagnosing CAN in this patient population, and whether there is a relationship between the severity of CAN and the QTc interval. This is due to the fact that electrocardiograms (ECGs) are a widely used, simple, and affordable way to evaluate heart risk in individuals with diabetes.

**Material and Methods**

The research was conducted from January 2023 to December 2023 at Department of General Medicine, Government Siddhartha Medical College, Vijayawada, Andhra Pradesh, India.

**Inclusion Criteria**

Every patient who visited the diabetes clinic during that time had to pass screening.

**Exclusion Criteria**

Diabetic people with a history of electrolyte disorders, hypertension, heart, lung, kidney, liver, or cerebrovascular diseases; also, those patients declined to take part because of concerns that their conditions may affect the QTc interval and/or CAN tests.

**Result**

**Table 1:** Possible risk factors (p,0.05 is significant) for subjects with type 1 diabetes mellitus developing (CAN)

Variables	CAN present n = 25 (100%)	CAN absent n = 15 (100%)	OR (95% CI)	p Value
Gender				
Male	4 (16)	5 (33.3)	1.05	
Female	21 (84)	10 (66.7)	1.25 (0.27 to 5.16)	0.897
Age (45 years)	8 (32)	12 (80)	1.05	
45 years Peripheral neuropathy	17 (68)	3 (20)	17.65 (3.15 to 86.59)	0.001
Absent	0	15 (100)	1.05	
Present	25 (100)	0	–	,0.001
QTc interval Normal	7 (28)	9 (60)	1.05	
Prolonged Duration of diabetes	18 (72)	6 (40)	6.65 (1.65 to 22.26)	0.022
(10 years)	17 (68)	15 (100)	1.05	
.10 years	8 (32)	0	4.00 (2.12 to 3.05)	0.007

**Table 2:** Possible risk factors (p,0.05 is significant) for subjects with type 2 diabetes to get (CAN)

Variables	CAN present n = 35 (100%)	CAN absent n = 25(100%)	OR (95% CI)	p Value
Gender				
Male	15 (47.1)	13 (58.3)	1.00	
Female	20 (52.9)	12 (41.7)	1.64 (0.65 to 5.16)	0.397
Age (60 years)	12 (29.5)	17 (75)	1.00	
60 Years Peripheral neuropathy	23 (70.5)	8 (25)	8.25 (2.26 to 25.67)	0.001
Absent	8 (17.6)	17 (75)	1.00	
Present	27 (82.4)	8 (25)	15.00 (4.25 to 52.35)	,0.001
QTc interval Normal	10 (23.5)	17 (75)	1.00	
Prolonged	25 (76.5)	8 (25)	10.23 (2.98 to 33.24)	,0.001
Duration of diabetes (10 years)	24 (76.5)	25 (100)	1.00	
10 years	11 (23.5)	0	2.34 (2.12 to 3.19)	0.010

**Table 3:** Subjects with types I and II diabetes mellitus might use the prolonged QT (QTc) interval in the ECG as a diagnostic tool to identify cardiac autonomic neuropathy (might)

Prolonged QTc interval for detecting CAN	Type I diabetes mellitus % (95% CI)	Type I diabetes mellitus % (95% CI)
Sensitivity	78 (65.8 to 95.0)	77.8 (64.3 to 95.9)
Specificity	65.7 (55.6 to 92.2)	76 (58.8 to 96.2)
Positive predictive value	78 (62.9 to 96.3)	82.5 (68.9 to 96.7)

**Discussion**

The univariate analysis revealed that peripheral neuropathy, age, prolonged QTc interval, and more than ten years of diabetes mellitus were substantially linked with an elevated risk of CAN in patients with both type 1 and type 2 diabetes mellitus. Gender differences did not pose a higher danger. Logistic regression study did not reveal a significant correlation between the parameters examined in patients with cardiac autonomic neuropathy (CAN) and type 2 diabetes mellitus. The likelihood of QTc prolongation increased significantly during a ten-year period in direct proportion to the duration of diabetes mellitus in all of its forms. For those suffering from both types of diabetes, neuropathy (CAN). The 60% CAN prevalence found in our study among individuals with diabetes is in line with recent studies by Mehta *et al.* (57.5%), Tentolouris *et al.* (62%), Thi *et al.* (67.6%), and other researchers [7-9].

A longer history of diabetes mellitus was found to be a major risk factor for the development of CAN among the 105 Vietnamese patients whom Thi *et al.* studied. Our findings indicate that individuals with

type 1 and type 2 diabetes mellitus who have had the illness for over ten years are at an increased risk of developing cardiac autonomic neuropathy (CAN). A more severe form of cardiac autonomic neuropathy, or CAN, develops in long-term diabetics who have been diagnosed with both type 1 and type 2 diabetes mellitus. 956 people with type 1 diabetes were included in the EURODIAB Prospective Complications Study, which found a substantial and consistent relationship between a patient's baseline age and their future risk (OR 1.3 per decade) of developing CAN. Our cohort analysis revealed a statistically significant correlation between the occurrence of cardiovascular autonomic neuropathy (CAN) and advancing age in individuals with type 1 and type 2 diabetes mellitus, despite the cross-sectional nature of the study<sup>[10-12]</sup>.

According to the EURODIAB study, diabetics who had peripheral neuropathy when they were first examined were at a much higher risk of developing CAN. The discovery that peripheral neuropathy is linked to an increased incidence of CAN in individuals with both type 1 and type 2 diabetes mellitus strengthens the body of evidence already in support of this connection. Our research revealed a robust correlation between a longer QTc interval and an increased risk of extension in both type 1 and type 2 diabetes mellitus. It's important to keep in mind, though, that this association may be explained by the fact that individuals with chronic illnesses are usually older. Even in the absence of disease, the QTc interval may prolong as a person ages. On the other hand, no case with a QTc interval greater than 440 ms was documented in a study with a substantial population, even in the elderly (their average QTc interval was  $418 \pm 3$  ms). In the older members of the EURODIAB cohort, a higher incidence of QTc prolongation was linked to long-term diabetes<sup>[13-15]</sup>.

There is a substantial correlation between severe levels of diabetic autonomic neuropathy and an increase in QTc interval duration. Figure 2 shows the direct correlation that our patients displayed between the lengthening of the QTc interval and the degree of CAN. The sensitivity of QTc prolongation to diagnosis CAN in people with type 1 diabetes was 77%, which is comparable to the 71% reported by Kahn *et al.* However, the majority of larger sample size studies with more thorough analysis revealed sensitivity levels as low as 26-29%. Our research indicates that QTc prolongation has a 62.5% sensitivity for identifying CAN in type 1 diabetes, which is lower than the 86% reported by Veglio *et al.* in their 3250 patient study. Despite the similar sample sizes ranging from 41 to 58, Tentolouris *et al.*'s study showed considerable changes in the sensitivity and specificity rates for QTc prolongation among persons with type 2 diabetes, with a sensitivity rate of 6% and a specificity rate of 95%<sup>[16-18]</sup>.

The study cohort was restricted to those without nephropathy or hypertension in order to reduce any potential interference from baseline ECG abnormalities and the impact these conditions may have on autonomic function tests. Individuals with diabetes who additionally have these symptoms are at a higher risk of developing CAN. There's a chance that the true prevalence of CAN among all diabetics was higher because only around one-third of the patients who visited our clinic fit the inclusion criteria. Despite these limitations, our results clearly demonstrate that a comprehensive review is necessary to reassess the utility of QTc prolongation in the diagnosis of CAN and risk assessment in diabetic individuals<sup>[19-22]</sup>.

## Conclusion

Cardiovascular autonomic neuropathy, or CAN, is a frequent side effect of both type 1 and type 2 diabetes. Peripheral neuropathy, advanced age, and a longer duration of diabetes mellitus are linked to a higher incidence of CAN in people with diabetes. As demonstrated by the excellent positive predictive value, sensitivity, and specificity of the QTc interval prolongation, the ECG is a trustworthy tool for identifying CAN in any type of diabetes. The degree of QTc interval elongation and the intensity of CAN are correlated. Those with both type 1 and type 2 diabetes mellitus should have their QTc interval prolongation evaluated on a regular basis using a 12-lead electrocardiogram. This is due to the fact that it significantly increases the risk of major vascular events in this particular population.

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**Conflict of Interest:** Nil.

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