A Study on Prevalence of Cardiovascular Autonomic Neuropathy in Type 2 Diabetes and Utility of Corrected Qt Interval for Its Diagnosis

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KEYWORDS	ABSTRACT:
cardiovascular autonomic neuropathy, type 2 diabetes, QT interval, diagnosis	Background: Diabetes Mellitus, a cluster of metabolic disorders, is distinguished by elevated blood glucose levels resulting from insulin secretion or action issues. Type 2 Diabetes is a major global health concern, impacting a substantial portion of the population. According to the World Health Organization, India had 31.7 million diabetics in 2000, and this figure is projected to reach 79.4 million by the year 2030. Materials & Methods: This is hospital based cross sectional observational study which was conducted in the Department of general medicine of Private medical college with study period of 1 year. The total sample size of the study was 100 patients. The collected data was entered in Microsoft Excel. Coding of the variables was done. Analysis was done using SPSS software (Version 27, IBM). Results: The average age of the individuals is 50.3 years, with a standard deviation of 24.68 years with gender distribution of 53% males and 47%females . Diabetic duration - 20% of patients are below 5 years duration, 30% are between 5 and 10 year duration, and 50%, is more than 10 years of duration. Relationship between QTc interval values and Cardiac Autonomic Neuropathy (CAN) scores, with a p-value of 0.000, indicates a highly significant association. Conclusion: The prevalence of Cardiovascular Autonomic Neuropathy is high among type 2 diabetics in our hospital, and it increases with the duration of diabetes. Approximately half of patients with type 2 diabetes develop autonomic dysfunction after ten years. A strong correlation exists between Cardiovascular autonomic dysfunction and QTc prolongation. QTc interval on an ECG can be used to diagnose Cardiovascular Autonomic Neuropathy.

INTRODUCTION

Diabetes Mellitus is a cluster of metabolic disorders characterized by elevated blood glucose levels due to insulin secretion or action problems[1]. Type 2 Diabetes is a major global health concern, affecting a substantial number of individuals. The World Health Organization reports that in the year 2000, India had 31.7 million diabetics, and this number is predicted to reach 79.4 million by the year 2030[2].

Diabetic patients often experience autonomic dysfunction, although symptomatic autonomic neuropathy is not as prevalent. Cardiac Autonomic Neuropathy (CAN) is a significant contributor to the occurrence of silent myocardial infarctions and sudden deaths in individuals with diabetes. It is essential to recognize cardiac dysautonomia early, when it is asymptomatic, to slow or halt its development[3].

Diabetic neuropathy is a common complication of diabetes, and autonomic neuropathy can affect several systems. Diabetic autonomic neuropathy (DAN) is a

serious and frequent complication of diabetes that frequently coexists with other peripheral neuropathies and other diabetic complications. DAN may be isolated, often preceding the detection of other complications. Despite its association with an increased risk of cardiovascular mortality and its connection to multiple symptoms and impairments, the significance of DAN has not been fully comprehended[4].

The widespread use of autonomic function tests is crucial for the evaluation of autonomic function. These tests are non-invasive and do not require advanced equipment. To perform the tests, an electrocardiogram machine, heart rate monitor, and sphygmomanometer are all that are necessary. This highlights the significance of simple, non-invasive tools, such as ECG and sphygmomanometer, in diagnosing asymptomatic cardiac autonomic neuropathy.

It is noteworthy that type 2 diabetic patients with abnormal cardiovascular reflex tests may have higher mortality rates, and those with postural hypotension have even higher mortality rates than those without[5].

In 1980, the association between a prolonged QTc interval and cardiac autonomic neuropathy was first established, which opened up the possibility of a rapid, objective method for detecting cardiac autonomic neuropathy. Further research demonstrated a correlation between a prolonged QTc interval and cardiac dysautonomia in diabetes mellitus[6].

This study aims to estimate the prevalence of cardiovascular autonomic neuropathy in relation to the duration of diabetes and to assess the usefulness of the corrected QT interval in diagnosing it.

MATERIALS & METHODS

This is hospital based cross sectional observational study which was conducted in the Department of general medicine of Meenakshi medical college hospital with study period of 1 year. The total sample size of the study was 100 patients. Inclusion criteria – 1)) Type 2 diabetes already on treatment and newly diagnosed patients. Exclusion criteria – 1) Age above 60 years 2) Documented ischaemic heart disease 3) Documented valvular or congenital heart disease 4) Hypertension 5) COPD 6) Uraemia 7) Parkinsonism. The study was approved by Institutional Ethics Committee of the private medical college. A written informed consent was obtained from all the patients. Detailed clinical history was taken from each patient and a complete review of their case notes was performed. A complete clinical examination of the cardiovascular system was done for each patient.

The collected data was entered in Microsoft Excel. Coding of the variables was done. Analysis was done using SPSS software (Version 27, IBM). Descriptive statistics was used. Association between categorical tests. The outcomes of the treatment groups were compared using a test to reach the hypothesis, a P value less than 0.5 was considered significant.

RESULT

This is hospital based cross sectional observational study which was conducted in the Department of general medicine of Private medical college with study period of 1 year. The total sample size of the study was 100 patients.

Table 1: Demographic details

Variables		Frequency (%) / Mean ± SD
Age		50.3 ± 24.68
Gender	Male	53%
	Female	47%
Duration of DM	<5years	20%
	5-10 years	30%
	>10 years	50%

The average age of the individuals is 50.3 years, with a standard deviation of 24.68 years, indicating a wide range of ages within the group. The gender distribution shows a slight predominance of males, who make up 53% of the sample, while females constitute 47%. According to age group classifications, 20% of individuals are less than 5

years duration, while 30% fall between 5 and 10 years duration. However, the largest segment, comprising 50% of the population, have more than 10 years duration. **(Table 1, Chart1, Chart 2)**

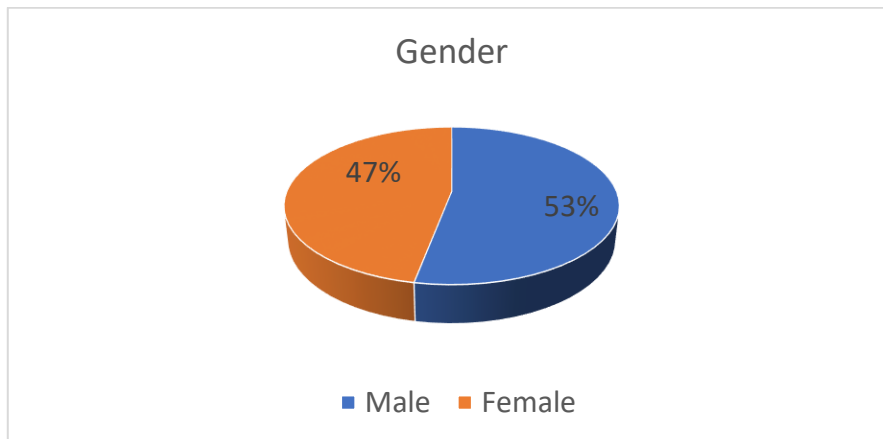**Chart 1: A pictorial representation of gender**
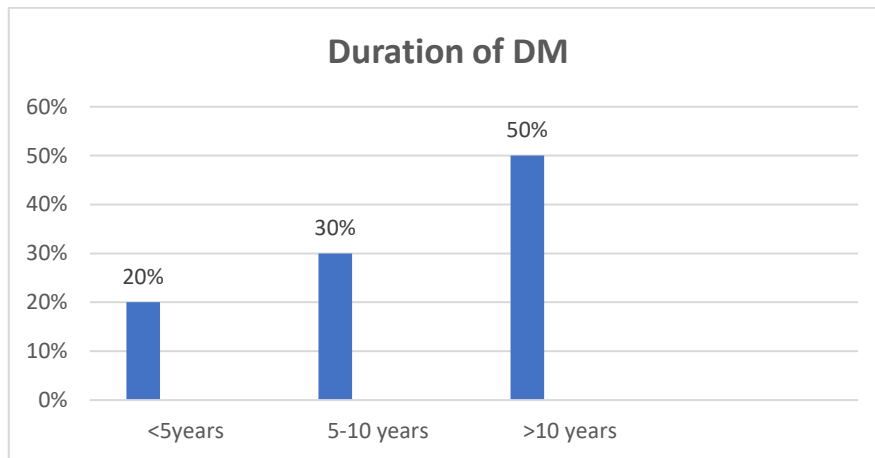

Chart 2: Duration of DM

Table 2: Simple bedside tests for cardiac autonomic neuropathy diagnosis

Score	Heart rate variability test			Blood pressure test	
	Deep breathing	Valsalva ratio	Response to standing	Response to handgrip	Response to standing
0	>15	>1.30	>16	>14	<10
1	11-15	1.01-1.30	12-16	11-14	11-30
2	<11	<1.01	<12	<11	>30

For the heart rate variability tests, scores range from 0 to 2. The "Deep breathing" test scores 0 for a variability greater than 15, 1 for 11-15, and 2 for less than 11. The "Valsalva ratio" scores 0 for greater than 1.30, 1 for 1.01-1.30, and 2 for less than 1.01. The "Response to standing" test scores 0 for a variability greater than 16, 1 for 12-16, and 2 for less than 12. For the blood pressure tests, the "Response to handgrip" scores 0 for a response greater than 14, 1 for 11-14, and 2 for less than 11. The "Response to standing" blood pressure test scores 0 for a

response less than 10, 1 for 11-30, and 2 for greater than 30.

Table 3: Cardiovascular autonomic neuropathy scoring

Score	Frequency	Percentage
Normal (0-1)	40	40%
Borderline (2-4)	30	30%
Abnormal (>5)	30	30%
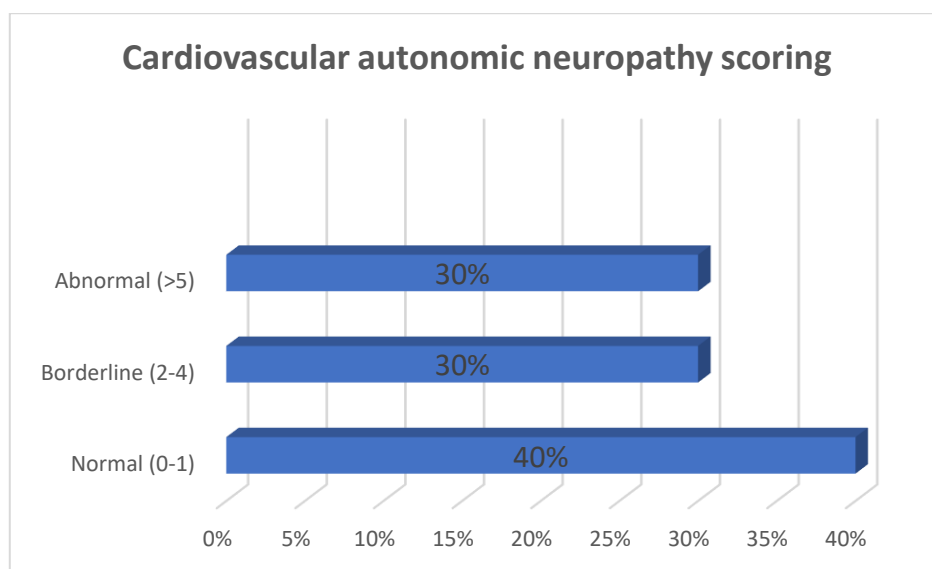
Chart 3: Cardiovascular autonomic neuropathy scoring

The distribution of scores reveals that 40% of the individuals scored in the normal range (0-1), indicating typical results. Meanwhile, 30% of the individuals scored in the borderline range (2-4), suggesting potential concerns that may require monitoring. Lastly, 30% of the individuals scored in the abnormal range (>5) (Table 2, Chart 3).

Table 4: Association between duration of DM with cardiovascular autonomic dysfunction

Duration of DM	CAN Score			P value
	Normal (0-1)	**Borderline(2-4)**	**Abnormal(>5)**	
<5years	16%	5%	4%	**0.001***
5-10 years	14%	9%	7%	
>10 years	10%	16%	19%	

The relationship between the duration of diabetes mellitus (DM) and the Cardiac Autonomic Neuropathy (CAN) scores, with an associated p-value of 0.001, indicating a statistically significant difference. For individuals with diabetes for less than 5 years, most (16) have a CAN score of 0-1, while fewer (5 and 4) have scores of 2-4 and >5, respectively. Among those with diabetes for 5-10 years, the distribution shifts, with 14 having a score of 0-1, 9 with a score of 2-4, and 7 with a score >5. For those with diabetes for more than 10 years,

the trend reverses: fewer individuals (10) have a score of 0-1, while higher numbers (16 and 19) have scores of 2-4 and >5, respectively. This suggests that longer duration of diabetes is associated with higher CAN scores.

Table 5: Mean ± Standard deviation of QTc with duration of DM

Duration of DM	QTc
<5years	399 ± 4.44
5-10 years	422 ± 3.00
>10 years	438 ± 2.56

The QTc interval in relation to the duration of diabetes mellitus (DM). Individuals with diabetes for less than 5 years have an average QTc interval of 399 milliseconds, with a standard deviation of 4.44 milliseconds. For those with diabetes lasting between 5 and 10 years, the average QTc interval increases to 422 milliseconds, with a smaller standard deviation of 3.00 milliseconds. The longest duration group, those with diabetes for more than 10 years, has the highest average QTc interval of 438 milliseconds, with a standard deviation of 2.56 milliseconds. This trend indicates that as the duration of diabetes increases, the QTc interval tends to lengthen, suggesting a potential worsening of cardiac function over time.

Table 6: Association between CAN and QTc

QTc	CAN Score			P value
	Normal (0-1)	Borderline(2-4)	Abnormal(>5)	
<400	16%	10%	13%	0.000*
>400	24%	18%	19%	

The relationship between QTc interval values and Cardiac Autonomic Neuropathy (CAN) scores, with a p-value of 0.000, indicates a highly significant association. For individuals with a QTc interval of less than 400 milliseconds, the distribution of CAN scores is as follows: 16 have normal scores (0-1), 10 have borderline scores (2-4), and 13 have abnormal scores (>5). Conversely, for individuals with a QTc interval greater than 400 milliseconds, there is a notable increase in CAN scores: 24 have normal scores, 18 have borderline scores, and 19 have abnormal scores. This suggests that higher QTc intervals are associated with higher CAN scores, indicating a correlation between prolonged QTc intervals and increased severity of cardiac autonomic neuropathy.

DISCUSSION:

The study on native Indian population reveals that cardiac autonomic dysfunction is common among diabetic patients and becomes more prevalent with the duration of diabetes. Previous studies conducted in India and other countries have shown similar findings. The current study demonstrated significant abnormalities in autonomic function using validated cardiovascular autonomic function tests.

Mohan et al[7] investigated the prevalence of CAN in 336 patients in south India, and found an increase in the prevalence of CAN with the duration of diabetes. In the 0-5 years group, the prevalence of autonomic dysfunction was 28.2%.

According to a study conducted by Toyry J P et al[8], the clinical significance of autonomic neuropathy in NIDDM was investigated. 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 at 10 years was 4.9%, 19.6%, and 65%, respectively.

Researchers, including Pappachan JM et al[9], investigated the prevalence of cardiovascular autonomic neuropathy (CAN) among 100 individuals with type 1 and type 2 diabetes mellitus in South India by employing the five autonomic function tests as per Eving's methodology. The prevalence of CAN was 60%, which is consistent with the findings of this study. Additionally, Vinik et al[10]. discovered that parasympathetic damage tends to occur earlier than sympathetic damage in diabetic cardiovascular autonomic neuropathy.

Chen et al.[4] investigated the 8-year survival rates for individuals with abnormal CVR tests, which were 63.6% for males and 76.4% for females, compared to 80.9% and 93.3% for those with normal CVR tests. These findings indicate that Type 2 diabetic patients with abnormal CVR tests may have increased mortality, and those with postural hypotension have higher mortality rates than those without. Abnormal CVR tests may serve as crucial predictors of mortality in Type 2 diabetes mellitus. It is important to note that subclinical autonomic dysfunction can occur within a year of diagnosis in Type 2 diabetes patients and within two years in Type 1 diabetes patients. Additionally, Massin et al.[11] suggested that early puberty is a critical period for the development of CAN and recommended screening all Type 1 diabetic patients for CAN beginning at the first stage of puberty.

The authors Vinik et al[12] suggested that measuring Heart rate variability (HRV) at the time of type 2 diabetes diagnosis and within five years of type 1 diabetes diagnosis (excluding cases where individuals exhibit symptoms of autonomic dysfunction earlier) can establish a baseline for future comparison with 1-year interval tests.

In a study conducted by C P Mathur et al[13], 50 patients with diabetes and 20 healthy controls were examined to investigate the connection between CAN and the QTc interval. Among the 19 diabetic patients with CAN, 15 (78.94%) had QTc prolongation, while none of the diabetics without CAN or control subjects exhibited this prolongation.

CONCLUSION:

The Prevalence of Cardiovascular Autonomic Neuropathy is high in type 2 diabetics in our hospital. The prevalence of CAN will increase with the 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.

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