



A STUDY OF CARDIAC AUTONOMIC NEUROPATHY IN DIABETES MELLITUS AND ITS CORRELATION WITH QTC INTERVAL

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ABSTRACT

Only cases with typical symptoms and signs were included. Age group of less than 16 years was not included.

Objectives: To study the prevalence and association of cardiac autonomic neuropathy in diabetic with Corrected QT interval.

Methods : All patients of type 1 and 2 diabetes mellitus admitted in Department of General Medicine, Government General Hospital, Nizamabad were taken for the study considering the inclusion and exclusion criteria.

Results: Out of the 100 patients 76 (76%) were males and 24 (24%) were females. CAN was present in 56 patients (56%) out of 100 patients. This correlated with prevalence of CAN as stated by other studies. QTC interval was more prolonged in diabetic patients with severe CAN (467.14 ± 45.44 ms. 64 out of 100 diabetics had one or the other symptoms attributable to autonomic neuropathy.

KEYWORDS : Cardiac Autonomic Neuropathy, Diabetes Mellitus, Corrected QT interval.

INTRODUCTION

Diabetes mellitus is a chronic disease that requires long-term medical attention to limit the development of its devastating complications and to manage them when they do occur. Microvascular complications of diabetes include retinal, renal, and possibly neuropathic disease. Diabetic neuropathy affects autonomic and peripheral nerves cardiovascular autonomic neuropathy is a common form of autonomic neuropathy, causing abnormalities in heart rate control and central and peripheral vascular dynamics. Cardiovascular autonomic neuropathy has been linked to postural hypotension, exercise intolerance, enhanced intraoperative cardiovascular lability, increased incidence of asymptomatic ischemia, myocardial infarction, and decreased likelihood of survival after myocardial infarction. India leads the world with largest number of diabetic subjects earning the distinction of being termed the "diabetes capital of the world"¹.

Cardiovascular autonomic neuropathy occurs in 17% of patients with type 1 diabetes and 22% of those with type 2. An additional 9% of type 1 patients and 12% of type 2 patients have borderline dysfunction².

In the early 1970s, Ewing et al proposed five simple noninvasive cardiovascular reflex tests (Valsalva maneuver, heart rate response to deep breathing, heart rate response to standing up, blood pressure response to standing up, and blood pressure response to sustained handgrip) that have been applied successfully³.

A prolonged corrected QT interval and QT dispersion (the difference between the longest and shortest QT interval) indicates an imbalance between right and left sympathetic innervation.⁴

Electromyography and Nerve Conduction Studies

Nerve conduction studies (NCS) and electromyography (EMG) can document the characteristics of the neuropathy (eg, axonal, demyelinating) and the localization (eg, mononeuropathy versus radiculopathy or distal neuropathy) and possibly. These same panels recommend the use of nerve conduction velocity (NCV)/EMG procedures in clinical research studies. An appropriate array of electrodiagnostic tests includes both nerve conduction testing and needle EMG of the most distal muscles usually affected.

Risk Factors

Poor glycemic control, Advanced age, Hypertension, Long duration of DM, Dyslipidemia, Smoking, Heavy alcohol intake, HLA-DR3/4 phenotype, Tall height.

Aims & Objectives

- To study the prevalence of cardiac autonomic neuropathy in diabetic patients
- To study the association of cardiac autonomic neuropathy in diabetics with QTC interval.

MATERIAL & METHODS

All patients of type 1 and 2 diabetes mellitus admitted in Department of

General Medicine, Nizamabad General Hospital, Nizamabad were taken for the study considering the inclusion and exclusion criteria.

Inclusion Criteria

All type 1 and type 2 diabetes mellitus patients admitted to Government General Hospital, Nizamabad.

Exclusion Criteria

- Patients with diabetes mellitus with evidence of heart diseases, respiratory, renal, hepatic, and cerebrovascular diseases.
- Patients with diabetes mellitus having hypertension, electrolyte imbalance.
- Patients with diabetes mellitus with previously abnormal ECG's.
- Patients with diabetes mellitus who are taking drugs known to interfere with autonomic function tests and QTC interval.
- Patients with diabetes mellitus with history of alcohol consumption.

OBSERVATIONS & RESULTS

Out of the 100 patients 76 (76%) were males and 24 (24%) were females

Table-1: Sex ratio

	Number	Percentage
Male	76	76%
Female	24	24%

Table 2: Type of Diabetes Mellitus

	MALE	FEMALE	TOTAL
TYPE I	24	8	32
TYPE II	48	20	68

Out of 100 patients, there were 32 type I and 68 type II patients. Of 32 type I patients, 24 were male and 8 were female. Of 68 type II patients 48 were male and 20 were female.

Table : 3 CARDIAC AUTONOMIC NEUROPATHY(CAN) SCORE

Cardiac autonomic neuropathy (CAN) scoring is done based on ewings test, and distribution of patients based on CAN score.

	No. of Patients	Percentage
No CAN (0-0.5)	44	44%
Early CAN (1-2)	42	42%
Severe CAN (≥ 2.5)	14	14%

Table : 4 CORRELATION BETWEEN DURATION OF DIABETES AND CAN SCORE

Can Score	Duration of Diabetes (years)
No CAN	8.90 \pm 5.45
Early CAN	11.54 \pm 6.44
Severe CAN	14.92 \pm 6.23

DISCUSSION

Diabetes mellitus is a common disorder worldwide. The global prevalence of diabetes is estimated to increase, from 4% in 1995 to 5.4% in 2025. The WHO has predicted that the major burden will occur in the developing countries especially India. The greatest increase in prevalence of diabetes will be in India, from 19.4 million in 1995 to 57.2 million in 2025. It is estimated that out of every 5 diabetics in the world one will be an Indian.

Diabetic autonomic neuropathy is also one of the major complications of long standing diabetes. It is difficult to ascertain the exact prevalence of diabetic autonomic neuropathy since it is often asymptomatic or present's with vague symptoms.⁵

A number of tests based on cardiovascular reflexes are now available for detecting even minimal dysfunction of autonomic nervous system. Ewing while classifying autonomic abnormalities used three tests based on heart rate response (i.e. Sinus arrhythmia, Valsalva ratio, Postural tachycardia index) and two test based on B.P. response (Postural drop in Systolic BP, and Rise in Diastolic BP on sustained hang grip).

Patients were grouped as normal or early, definite, severe and atypical pattern of autonomic dysfunction. This method could assess even atypical pattern and avoid such over simplification regarding autonomic dysfunction as terming it as present or absent We have followed this scoring system in present study⁹

Cardiac autonomic function tests

Resting heart rate

- <100 beats/min → 0 points
- 100 – 110 beats/min → 0.5 point
- >110 beats/min → 1 point

Postural hypotension (fall in systolic B.P.)

- <20 mm Hg → 0 point
- 20 – 30mm Hg → 0.5 point
- >30 mm Hg → 1 point

Symptoms of Autonomic Neuropathy

	Lakhotia et al. ⁸	Krishna et al. ¹¹	Balachander et al. ¹²	Shetty et al. ¹³	Present study
Sweating	26%	38%	38%	7.2%	32%
Fullness	16%	34%	20%	2.7%	30%
Constipation	12%	-	-	1.8%	8%
Diarrhea	18%	28%	38%	5.4%	12%
Impotence	54%	9%	22.2%	30.9%	8%
Postural dizziness	44%	58%	46%	-	30%

- Sweating abnormalities were noted in 32% of our patients. This is in comparison with other studies as shown in the table.
- Fullness of stomach was noted in 30% of our patients. Similar results were obtained in other studies.
- Constipation was noted in only 8% of our patients which is similar to that mentioned by Lakhotia et al.
- Diarrhoea as a complaint was noted in only 12% of our patients which is lesser when compared to other studies mentioned.
- Similarly impotence was also less, 8% when compared to other studies.
- Postural dizziness was noted in 30% of our patients. Similar results were noted in other studies

QTC Prolongation

There is a well described association between abnormalities of autonomic function and QTC Prolongation. Bellavere et al, in their study mentioned that diabetic cardiac autonomic neuropathy should be included among long QT syndromes. In present study QTC interval was more prolonged in diabetic patients with severe CAN (467.14 ± 45.44 ms $P < 0.001$ significant) when compared to patients with early CAN (420.47 ± 55.33 ms $P < 0.2$ not significant) and no CAN (378.18 ± 38.86 ms $P < 0.2$ not significant). Similar observation were made by Barthwal et al⁹, (426 ± 24.4 ms), Veglio et al¹⁴, (421 ± 26 ms), Kumar et al, (423 ± 22 ms), Shimbakuro et al¹⁵, (449 ± 13 ms).

CONCLUSIONS

- The duration of diabetes, and fasting blood sugar values were significantly higher in patients with diabetes with severe CAN.
- Prolongation of QTC interval correlates well with degree of cardiac autonomic neuropathy in diabetics.

Valsalva ratio (longest RR interval : shortest RR interval)

- >1.2 → 0 point
- 1.2 – 1.10 → 0.5 point
- <1.10 → 1 point

Heart rate variability on deep breathing

- >15 beats/min → 0 point
- 10 – 15 beats/min → 0.5 point
- <10 beats/min → 1 point

Increase in diastolic blood pressure during sustained hand grip

- >15 mm Hg → 0 point
- 10 – 15 mm Hg → 0.5 point
- < 10 mm Hg → 1 point

CAN SCORE

- No CAN → 0 - 0.5 point
- Early CAN → 1 - 2 points
- Severe CAN → ≥ 2.5 points

Prevalence of Diabetic - CAN

In our study CAN was present in 56 patients (56%) out of 100 patients. This correlated with prevalence of CAN as stated by other studies.

Prevalence of diabetic-CAN

Nijhawan S et al ⁷	60%
Lakhotia M et al ⁸	64%
Barthwal et al ⁹	36.2%
Kumar M et al ¹⁰	60%
Krishna et al ¹¹	48%

AGE

Age of the patient does not correlate with severity of CAN. This was also seen in other studies.

Symptoms of Autonomic Neuropathy

64 out of 100 diabetics had one or the other symptoms attributable to autonomic neuropathy. Frequency of different symptoms have been listed out in comparison with other Studies.

- QTC prolongation may be considered as pointer towards diabetic cardiac autonomic neuropathy in the busy outpatient setting where it is not possible to perform the conventional battery of tests.
- Recognition of QTC prolongation may help identify diabetics with a high risk of sudden cardiac death.

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