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Study of Qt_c Prolongation in Diabetes Mellitus - As an Indicator of Cardiac Autonomic Neuropathy

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Abstract: ***Background and Objectives:*** ***Autonomic neuropathy is a well known complication of long standing Diabetes Mellitus. Cardiac Autonomic Neuropathy (CAN) is a common Diabetic autonomic neuropathy leads to silent Myocardial Infarction and sudden death, prolongation of QTc interval in ECG is rapid and specific method in detecting CAN.*** ***Methodology:*** ***70 patients were included in the study. Cardiac autonomic function tests, routine investigations, ECG for QTc interval were done for all the patients.*** ***Result:*** ***Among 70 patients included 36 patients had CAN and they had significantly prolonged QTc interval.*** ***Interpretation & Conclusion:*** ***Recognition of QTc prolongation may help identify diabetics with CAN.***

Keywords: Diabetes Mellitus; Autonomic neuropathy; Cardiac Autonomic neuropathy; QTc interval

1. Introduction

Diabetes mellitus affects 8% of the world's population. After the advent of oral hypoglycaemic drugs and insulin therapy the survival of diabetic patients is increasing and they have prolonged longevity[1]. Autonomic neuropathy is a well known complication of long standing diabetes. Although insidious in onset, it may be associated with substantial morbidity and mortality. Infact, sudden death and silent myocardial ischemia has been attributed to cardiac autonomic dysfunction. Diabetic autonomic neuropathy has wide spread involvement and it is much commoner than originally thought[1]. The cardiovascular complications of diabetes mellitus can be classified into three groups – atherosclerotic coronary artery disease, diabetic cardiomyopathy, and cardiac autonomic neuropathy (CAN) [2]. Prolongation of the corrected QT interval (QTC) in the electrocardiogram (ECG) has been found to be a specific, rapid and objective method for detecting cardiac autonomic neuropathy in most studies. The present study aims to evaluate the correlation between QTC interval and diabetic cardiac autonomic neuropathy[2]. CAN is a common form of diabetic autonomic neuropathy and causes abnormalities in heart rate control as well as central and peripheral vascular dynamics. The incidence of silent myocardial ischemia and sudden death is also high in patients with CAN[2].

2. Methodology

2.1 Study design

The study is a cross sectional study in which patients were selected taking into consideration inclusion and exclusion criteria.

2.2 Source of Data

All patients of type 1 and 2 diabetes mellitus admitted in Department of General Medicine, Adichunchanagiri Institute of Medical Sciences, B G Nagar, during the period of September 2013 to August 2014 were taken for the study considering the inclusion and exclusion Criteria.

a) Inclusion criteria:
Type 1 and type 2 diabetes mellitus patients in the age range of 20 to 70 yrs.

b) Exclusion criteria:
1) Patients with diabetes mellitus with evidence of heart diseases, respiratory, renal, hepatic, and cerebrovascular diseases.
2) Patients with diabetes mellitus having hypertension, electrolyte imbalance.
3) Patients with diabetes mellitus with previously abnormal ECG's.
4) Patients with diabetes mellitus who are taking drugs known to interfere with autonomic function tests and QTC interval.

2.3 Method of Collection of Data

The study group comprised of 70 patients with Diabetes Mellitus (Selected according to Inclusion Criteria) belonging to age group of 23 to 70 years (average 45.7 ± 14.03 years). Among these 30 were males (42%) & 40 were females (58%), 5 patients were type 1 (7%) and 65 were Type 2 (93%). Detailed history and clinical examination was done as per the proforma and necessary investigations were done. The following tests for the detecting CAN were performed as described by Ewing, et al[3], in each of the enrolled participants (1) resting heart rate (2) blood pressure for postural or orthostatic hypotension (3) heart rate response to valsalva manoeuvre (4) heart rate response to deep breathing (5) diastolic blood pressure to an isometric exercise. The results of each of the five tests for the detection of CAN were classified into three separate groups based on the severity of abnormality detected, and each of them were given a definite point as described by Bellavere, et al[4]. CAN is considered absent, early, definite or severe if the CAN scores were 0, 1, 2 or 3 respectively. QT interval was calculated by electrocardiograph. The QTC were

determined with Bazett's formula (QTC = QT / √RR) and a value exceeding 440 m sec were considered prolonged. The results were analysed by appropriate statistical methods. Hb%, TC, DC, ESR, Urine Routine, FBS, PPBS, BI.Urea, Sr.Creatinine, Sr.Electolytes, Sr. Bilirubin, AST, ALT, Chest X-ray - PA-view is done for all patients.

2.4 Statistical Methods

Results were expressed as Mean ± Standard Deviation. Students "t" test was used tocompare Mean's of different groups. P value < 0.05 was considered significant.

3. Results

Our study included 70 patients, of which 30 were males (42%) and 40 were females (52%). 5 patients had Type 1 Diabetes Mellitus and 65 patients had Type 2 Diabetes Mellitus. Majority were in the age group of 41-50 years.

Table 1: Sex Ratio

	Male	Female
Number	30	40
%	42	58

Table 2: Type of Diabetes

	Male	Female	Total
Type 1	3	2	5 (7%)
Type 2	27	38	65 (93%)

Table 3: Distribution by age

Age in years	Number	Percentage
21-30	2	3
31-40	7	10
41-50	28	40
51-60	19	27
61-70	14	20
Total	70	100

Table 4: Distribution of patients according to CAN score

No CAN (0-0.5)	34(49%)
Early CAN (1-2)	23(33%)
Severe CAN (>2.5)	13(18%)

Table 5: Correlation between duration of DM and CAN score

CAN Score	Duration of Diabetes(Years)
No CAN	5.1765±2.68
Early CAN	9.30±4.53
Severe CAN	15.53±3.97

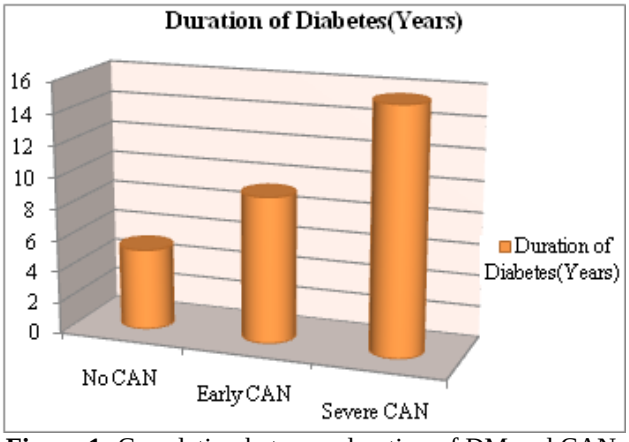

Figure 1: Correlation between duration of DM and CAN score

Table 6: Resting heart rate in CAN

CAN SCORE	Resting heart rate (beats/min)
No CAN	78.63 ±6.30
Early CAN	89.24 ± 6.18
Severe CAN	102.2 ± 8.24

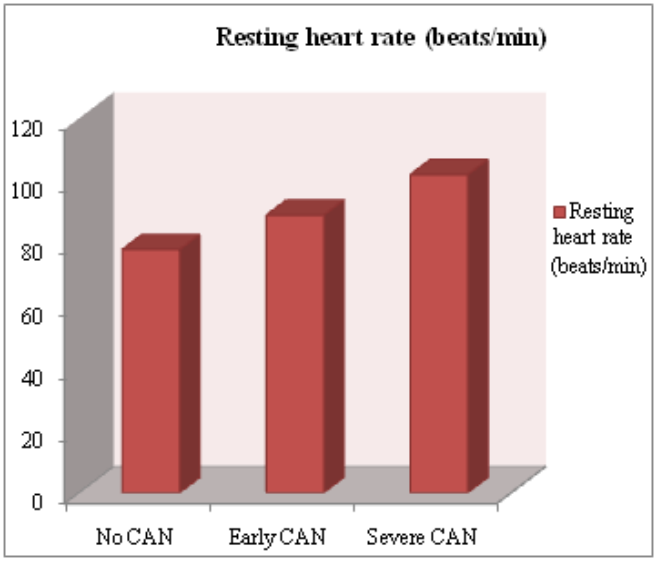

Figure 2: Resting heart rate in CAN

Table 7: Valsalva ratio in CAN

CAN SCORE	Valsalva Ratio
No CAN	1.30 ± 0.10
Early CAN	1.17 ± 0.062
Severe CAN	1.05 ± 0.058

Table 8: Heart rate variability on deep breathing

CAN SCORE	HRV on deep breathing(beats/min)
No CAN	15.86 ± 1.16
Early CAN	11.85 ± 3.07
Severe CAN	9.14 ± 2.19

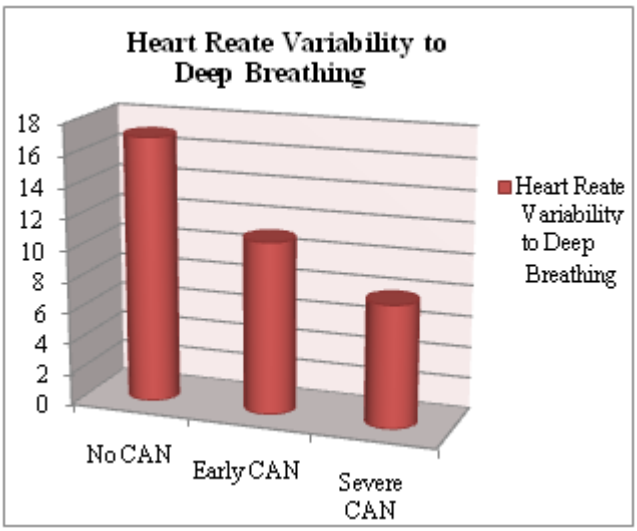

Figure 3: Heart rate variability on deep breathing

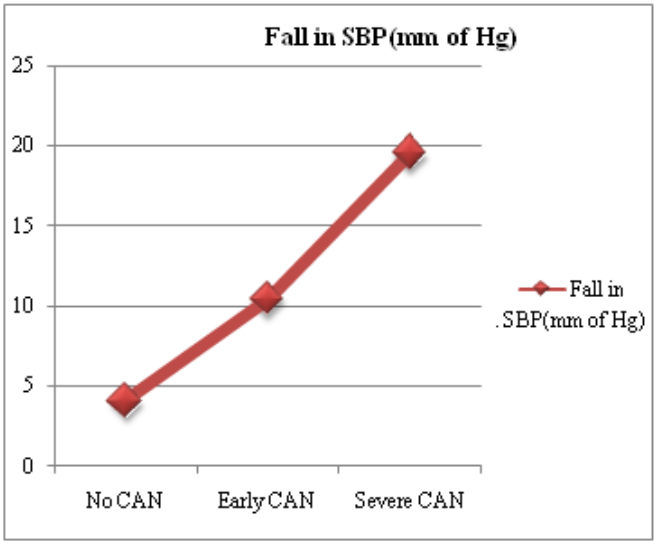

Figure 4: SBP response to standing

Table 9: SBP response to standing

CAN SCORE	Fall in SBP (mm of Hg)
No CAN	4.06 ±2.76
Early CAN	10.43 ± 3.85
Severe CAN	19.54 ± 5.62

Table 10: DBP response to sustained hand grip

CAN SCORE	*Rise in DBP (mm of Hg)*
No CAN	15.03 ± 2.12
Early CAN	14 ± 2.33
Severe CAN	10.94 ± 3.20

Table 11: Standing 30:15 Ratio of Heart Rate

CAN SCORE	*Standing 30:15 Ratio of Heart Rate*
No CAN	1.11 ± 0.073
Early CAN	1.06 ± 0.059
Severe CAN	1.02 ± 0.029

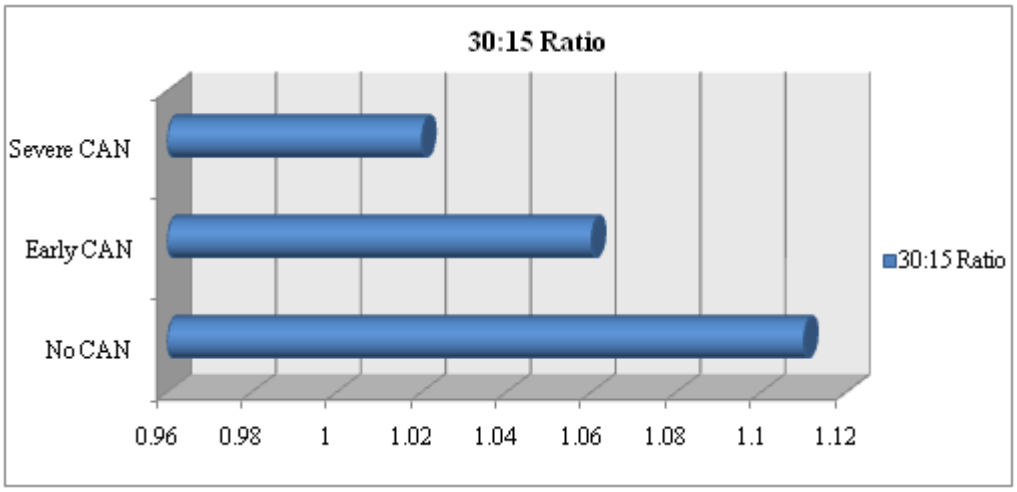

Figure 5: Standing 30:15 Ratio of Heart Rate Variation

Table 12: QTC interval in diabetic patients

CAN SCORE	QTc (ms)
No CAN	412.38 ± 17.05
Early CAN	436.7 ± 18.07
Severe CAN	488.15 ± 14.72

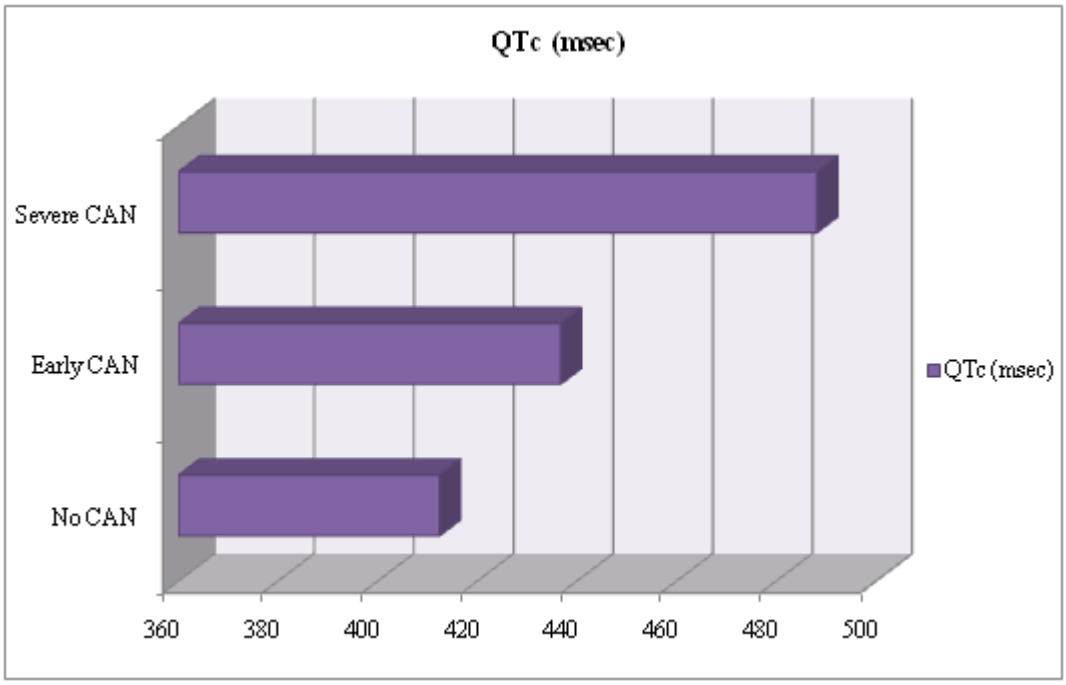

Figure 6: QTC –interval in diabetic patients

4. Discussion

In our study CAN was present in 36 patients (51.5%) out of 70 patients. This correlated with prevalence of CAN as stated by other studies like Krishna et al[5] 48%, Kumar et al[6] 60%, Nijhawen S et al[7] 60% and Barthwal et al[8] 36.2%. In our study we found that the duration of diabetes correlates with the severity of CAN, which is simlar in other sudies also.

Table 13: Correlation between duration of DM and severity of CAN

	Without CAN	With CAN
Kumar et al[6]	3.19 ± 2.81	11.52 ±6.26
Barthwal et al[8]	3.51 ± 2.81	7.11 ± 3.49
Shimbakuro et al[9]	5.3± 2.1	13.6±1.1
Present study	5.17 ± 2.68	15.53 ± 3.97

There is a well described association between abnormalities of autonomic function and QTC Prolongation. Bellavere et al[4], 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 (488.15 ± 14.72 ms P <0.001 significant) when compared to patients with early CAN (436.7 ± 18.07 ms P<0.2 not significant) and no CAN (412.38 ± 17.05 ms P <0.2 not significant). Similar observation were made by Barthwal et al[8](426 ± 24.4 ms), Veglio et al[10](421 ± 26 ms), Kumar et al[6] (423 ± 22 ms), Shimbakuro et al[9] (449 ± 13 ms) and Mathur CP et al[11], (449.31± 21.9).

5. Conclusion

Cardiovascular autonomic neuropathy was studied in 70 diabetic patients. Patient's age ranged from 23 to 70 yrs. Majority of them were in the age group of 41-50 years. Mean age was 45.76 ± 14.17 years. The duration of diabetes ranged from 1-30 years with a mean duration of 11.2±6.75 years. Patients with severe CAN had longer duration of diabetes than those with early and no CAN. 36(51.5%) patients had cardiac autonomic neuropathy of which 13(18%) had severe CAN and 23(33%) had early CAN. Patients with cardiac autonomic neuropathy had significantly prolonged QTc interval. Prolongation of QTC interval correlates well with degree of cardiac autonomic neuropathy in diabetics. 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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