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A Study of Cardiac Autonomic Neuropathy Among Type-II Diabetic Patients

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ABSTRACT

Background: Though very common, CAN is a least understood complication of diabetes which is often under-diagnosed. In diabetes mellitus patients, CAN leads to silent myocardial infarction and sudden death. So by identifying CAN early, which is asymptomatic will help to delay or arrest its progression.

Aim: To find out the prevalence and the associated risk factors of Cardiac autonomic neuropathy (CAN) among type-II Diabetes Mellitus patients in a tertiary care hospital.

Materials & Methods: A total of 273 type-II diabetic participants were selected after taking into consideration of inclusion & exclusion criteria. The prevalence of CAN was assessed by ewings and clarkes on invasive cardiac autonomic neuropathy reflex tests. The association of risk factors with the presence of CAN was analysed by using the Pearsons chi-square test. Data were analysed by using SPSS 16. The accepted level of significance was set below 0.05 (P<0.05).

Results: The prevalence of CAN among type-II diabetic patients in this study was found to be 34%. Prevalence of CAN increased in the participants with male gender, increased age, and increased BMI, increased duration of diabetes, poor glycaemic control, dyslipidemia, smokers and hypertension and it is statistically significant.

Conclusion: In this study, it is observed that the prevalence of CAN increased with old age, male gender, poor glycemic control, increased duration of diabetes, Dyslipidemia, higher BMI, Hypertension & smoking. So risk factors associated with the CAN be detected and treated at an early stage to further reduce morbidity and mortality.

Key Words: Cardiac Autonomic Neuropathy (CAN), Diabetes Mellitus, Ewings test, Risk factors, Prevalence, Cardiac autonomic function tests (CAFT)

INTRODUCTION

Diabetes is a metabolic disorder characterized by hyperglycemia that occurs either due to decreased insulin level or insulin resistance Diabetic Autonomic Neuropathy¹ can involve the entire autonomic nervous system (ANS). It is manifested by dysfunction² of one or more organ systems. (e.g., cardiovascular, gastrointestinal, genitourinary, sudomotor, or ocular) Cardiac Autonomic Neuropathy (CAN) is a serious complication of Diabetes Mellitus (DM) that is among the least recognized and understood. Not only does it affect the survival and quality of life in diabetics³⁻⁵ it is also a major source of increased cost in diabetic care. Currently, a consensus exists that CAN is an independent risk factor for cardiovascular events⁶. Its high mortality rate is related to

cardiac arrhythmias, silent myocardial ischemia, sudden death, perioperative cardiovascular, and cardiorespiratory instability.⁷ The autonomic fibres innervating heart and blood vessels are affected in CAN and causes disturbances in cardiovascular dynamics⁸ and anatomy⁹ It is recommended by several professional bodies,¹⁰⁻¹² to perform a subclinical assessment of CAN by utilizing CARTs as soon as T2DM is diagnosed. Ewing's CARTs are considered as Gold standard in CAN, therefore, consistently been used for its subclinical assessment.^{13,14} Hyperglycemia, obesity, dyslipidemia, hypertension, and smoking which are the modifiable risk factors are among the proposed risk factors for Cardiac autonomic neuropathy^{15,16-20} No clear evidence supports glucose-lowering intervention to prevent CAN in type 2 diabetes²¹. On the other hand in the steno-2 trial,

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multifactorial therapy decreased the development of CAN up to 68%.²²

The present study was planned to find out the prevalence of Cardiac autonomic neuropathy and the risk factors associated with CAN among type-II Diabetes Mellitus participants in a tertiary care hospital.

MATERIAL AND METHODS

This cross-sectional study was conducted at the department of General medicine OPD, Viswabharathi medical college from December 2019 to November 2020. 273 type-II Type-II DM patients with ≥ 3 years of the duration of both the sexes aged between 35-80 years were selected for this study by purposive sampling technique. Participants with other diseases associated with the autonomic nervous system, Patients on drugs like sympathomimetics, and antiarrhythmics, patients with underlying cardiac illness, uncooperative and physically disabled patients were excluded from this study.

This study was approved by the Institutional Ethics Committee having approval number VMC/IEC/2/2018 and an informed consent form was obtained from the study participants.

STUDY PROTOCOL

A questionnaire That included socio-demographic details such as age, sex; anthropometric details such as height, weight; duration of diabetes, smoking & Hypertension history was administered to each patient.

clinical and laboratory parameters such as BMI, Blood pressure, HbA1c, serum cholesterol, serum triglycerides were collected from each patient

BMI: by dividing weight in kilograms by the square of height in meters BMI was calculated.

Blood pressure was measured with a standard mercury manometer and if their blood pressure values were $>140/90$ mmHg or they were taking any antihypertensive drugs were considered to have arterial hypertension after an overnight fasting Venous blood was drawn in the morning. using the automatic analyzer. Serum cholesterol and serum triglycerides Were measured and Glycosylated haemoglobin (HbA1c) was measured by the high-performance liquid chromatography.

Ewings Cardiovascular Reflex Tests (CRT): All the patients selected for the study underwent Cardiovascular

Reflex Tests (CRT) for evaluation of cardiac autonomic neuropathy. Standard 12 lead ECG was taken and heart rate was measured by continuous ECG recording using lead II.

Instruments:

1. ECG instrument (CONTEC ECG300G) with a paper speed of 25mm/sec
2. Diamond Sphygmomanometer BP instrument

All five Ewing's tests were performed as following for the detection of DCAN (diabetic cardiac autonomic neuropathy):

I. Tests for assessing parasympathetic function

- 1) Heart rate response to deep breathing test:
- 2) Heart rate response to Valsalva maneuver
- 3) Heart rate response to standing

II. Tests for assessing sympathetic function:

- 1) Blood pressure response to sustained handgrip
- 2) Blood pressure response to standing

The results were then categorized into one of the four groups

Normal

Early CAN - One of three parasympathetic tests abnormal or two borderline

Definite CAN- Two parasympathetic tests abnormal

Severe CAN- Two parasympathetic tests abnormal + one or both sympathetic tests abnormal

Statistical Analysis: Data analysis was done by using Software Package of Social Sciences (SPSS) trial version 16. Continuous data were analysed by using the Student unpaired t-test. The association of risk factors with the prevalence of CAN was analysed by using the Pearsons chi square test. The accepted level of significance was set below 0.05 ($P < 0.05$).

RESULTS

A total of 273 type-II diabetes patients were included. Out of which 142 were males and 131 were females

Prevalence of CAN-based on Ewings tests criteria

Fig. 1 is showing the Prevalence of CAN-based on Ewings tests criteria. The prevalence of CAN is 34% among type-2 diabetes mellitus patients.

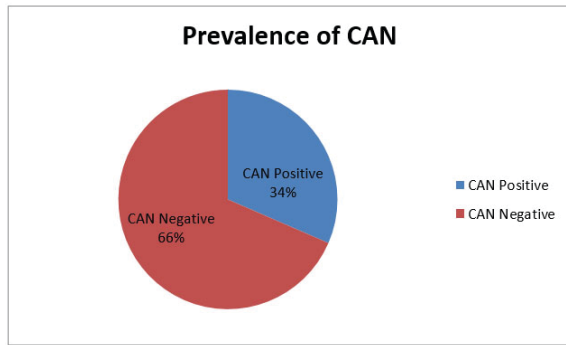


Figure 1: Prevalence of CAN-based on Ewings tests criteria.

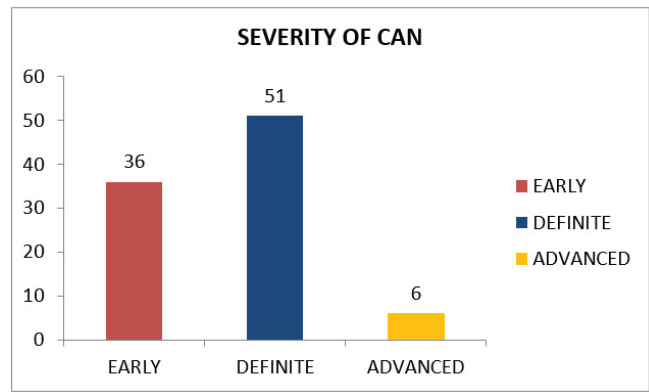


Figure 2: Severity of CAN.

Severity of CAN

Fig. 2 is showing the severity of CAN. Out of 93 T2DM participants with cardiac autonomic neuropathy, 36 (39%) individuals had ‘early’, 51 (55%) had ‘definite’ and 6 (6%) had ‘advanced’ Cardiac autonomic Neuropathy

Comparison of continuous variables between CAN & Non-CAN participants was described in Table-1.

Table 1: comparison of continuous variables between CAN & NON CAN participants:

| Demographic variable | | CAN positive Patients (n=93) | CAN Negative Patients (n=180) | P-value |
|------------------------------|-----------|------------------------------|-------------------------------|------------|
| Age (Years) | Mean±SD | 57.83±10.38 | 53.23±8.73 | p< 0.001** |
| BMI (kg/m²) | Mean± SD | 27.83±3.68 | 24.18±3.67 | P< 0.001** |
| Duration of Diabetes (Years) | Mean± SD | 8.64±4.034 | 6.87±3.038 | P< 0.001** |
| HbA1c (%) | Mean ± SD | 6.48±.51 | 5.79±.44 | P< 0.001** |
| SBP (mmHg) | Mean ± SD | 134.28±15.98 | 127.34±16.58 | P< 0.05* |
| DBP (mmHg) | Mean ± SD | 84.30±9.36 | 80.68±10.09 | P< 0.05* |
| Serum triglycerides (mg/dl) | Mean ± SD | 141.3±25.55 | 132.85±19.03 | P< 0.001** |
| Serum cholesterol (mg/dl) | Mean ± SD | 201.32±41.6 | 174.56±31.6 | P< 0.001** |

the mean age BMI duration of diabetes HbA1c SBP DBP serum triglycerides serum cholesterol were higher in CAN patients than non CAN patients

The association between various risk factors and prevalence of CAN was described in Table 2

Table 2: Association between various risk factors and prevalence of CAN

| Demographic variable | | NO can | CAN Positive | Total | P-value |
|----------------------|-----------|------------|--------------|-------|------------|
| Age (years) | <40 | 0 | 16 | 16 | P<0.001* |
| | 40-49 | 17 (24.6%) | 52 (75.4%) | 69 | |
| | 50-59 | 36 (35.6%) | 65 (64.4%) | 101 | |
| | 60-69 | 27 (38.6%) | 43 (61.4%) | 70 | |
| | ≥70 | 13 (76.5%) | 4 (23.5%) | 17 | |
| Gender | female | 35 (26.7%) | 96 (73.3%) | 131 | P<0.05* |
| | male | 58 (40.8%) | 84 (59.2%) | 142 | |
| BMI (kg/m²) | <18.5 | 1 (16.7%) | 5 (83.3%) | 6 | P< 0.001** |
| | 18.5-24.9 | 20 (15.4%) | 110 (84.6%) | 130 | |
| | 25-29.9 | 46 (46.9%) | 52 (53.1%) | 98 | |
| | ≥30 | 26 (66.7%) | 13 (23.3%) | 39 | |

Table 2: (Continued)

| Demographic variable | | NO can | CAN Positive | Total | P-value |
|------------------------------|-------------------|------------|--------------|-------|------------|
| Duration of Diabetes (years) | <6 | 24 (23.8%) | 17 (76.2%) | 101 | P< 0.05** |
| | 6-10 | 44 (34.4%) | 84 (65.6%) | 128 | |
| | >10 | 25 (56.8%) | 19 (43.2%) | 44 | |
| HbA1c (%) | <6.5 | 33 (17%) | 161 (83%) | 194 | P< 0.001** |
| | ≥6.5 | 60 (75.9%) | 19 (24.1%) | 79 | |
| Hypertension | Non-Hypertensives | 36 (22.2%) | 126 (77.8%) | 162 | P< 0.001** |
| | Hypertensives | 57 (51.4%) | 54 (48.6%) | 111 | |
| | ≥200 | 58 (70.7%) | 24 (59.3%) | 82 | |
| dyslipidemia | Absent | 29 (16.2%) | 150 (83.8%) | 179 | P< 0.001** |
| | Present | 64 (68.1%) | 30 (31.9%) | 94 | |
| Smoking | Non Smokers | 40 (20.4%) | 156 (79.6%) | 196 | P< 0.001** |
| | Smokers | 53 (68.8%) | 24 (31.2%) | 77 | |

Prevalence of CAN increased in the participants with male gender, increased age, and increased BMI, increased duration of diabetes, poor glycaemic control, dyslipidemia, smokers and hypertension and it is statistically significant.

DISCUSSION

In the present study, the prevalence of CAN was found to be 34%. DAN study in 2014 reported the prevalence of CAN among type-II Diabetes as 35%²³. Gupta and Gupta in 2017²⁴ found that CAN was present in 54 patients (54%) out of 100 patients. Barthwal et al. in 1997²⁵ reported prevalence of cardiac dysautonomia as 36.2% in Indian diabetic patients whereas Mathur and Gupta in 2006²⁶ reported prevalence of CAN as 58%.

Our study reported increasing age as a risk factor for CAN. Similarly, Pappachan J et al.²⁷ & Refaie W et al.²⁸ in their studies reported increasing age as a risk factor for the development of CAN among diabetes patients.

Our study found that the male gender is more associated with CAN. This is in contrast with the study done by Sukl et al.²⁹ which reported that female gender is the risk factor for developing CAN.

Our study reported that poor glycaemic control is a risk factor for CAN. Similarly, Haji Khan Khoharo et al. reported that the prevalence of CAN is associated with poor glycaemic control³⁰.

Our study reported an increased duration of diabetes as a risk factor for CAN. Similarly, Ahire et al.³¹ reported that CAN is associated with an increased duration of diabetes & David CL et al.³² also reported an increase in CAN prevalence as the duration of diabetes is increased.

Our study reported that dyslipidemia is a risk factor for CAN. Similarly, Anca Moususianu et al. in their study reported that elevated triglyceride and cholesterol levels are associated with the prevalence of CAN³³

Our study reported that obesity is a risk factor for CAN. Similarly, R. H. Straub et al.³⁴ & B. Bergstrom³⁵ in their study observed that the prevalence of CAN is associated with obesity.

Our study reported Hypertension as a risk factor for CAN. Similarly, Vincenza Spallone et al.³⁶ in their study found that the prevalence of CAN among diabetic patients is associated with an increase in Blood Pressure.

Our study reported smoking as a risk factor for CAN. Similarly Shai I et al.³⁷ reported that there is an increased prevalence of Cardiac Autonomic Dysfunction in individuals with smoking.

CONCLUSION

The prevalence of CAN in our study was found to be 34% and it is high. So these simple bedside tests are helping in diagnosing the disease which enables to prevent its progression by appropriate interventions and it is concluded that risk factors are associated with the prevalence of CAN among type-II diabetes and therefore it highlights the importance of addressing not only glycaemic control but also modifiable risk factors like hypertension, dyslipidemia, smoking as a preventive strategy against CAN. So it is essential that risk factors associated with the progression and development of CAN be detected and treated at an early stage to further reduce morbidity and mortality.

In our study, the limitation of the study was the sample size which was not large enough to represent the whole population. so studies that include more subjects are required to confirm the findings of our study.

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Author contribution:

1. Dr. N.S. Muthiah has given suggestions in doing the journal.
2. Dr. M.V. Sailaja has done the review of the literature
3. Dr. K. Prabhu helped in doing statistics
4. B.V. Surendra written the article

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