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FREQUENCY AND PATTERN OF CARDIAC AUTONOMIC NEUROPATHY IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

Touqeer[*1], Abeer Memon[2], Muhammad Aqib[3], Minnal Tahir[4], Imtiaz Hussain[5], Saima Irshad[6]

*[*1,4,6]FCPS Resident Medicine, Liaquat University of Medical and Health Sciences, Jamshoro*
[2]Senior Registrar Medicine, Liaquat University of Medical and Health Sciences, Jamshoro
[3]MD Resident Cardiology, Liaquat University of Medical and Health Sciences, Jamshoro
[5]FCPS Resident Infectious Disease, Liaquat University of Medical and Health Sciences, Jamshoro

[*1]touqeerqureshi2376235@gmail.com

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Corresponding Author: * Touqeer

Abstract

Objective: *To determine the "frequency and pattern of cardiac autonomic neuropathy in patients with type 2 diabetes mellitus visiting at tertiary care hospital".*

Study Design: *Cross-sectional study*

Place and Duration of Study: *This study was conducted at the Department of Medicine, Liaquat University of Medical and Health Sciences, Jamshoro, over a period of six months.*

Materials and Methods: *A total of 100 patients of either gender with type 2 diabetes mellitus for ≥ 2 years having age ≥18 years were included. Cardiac Autonomic Neuropathy was determined (as resting heart rate is ≥100 beats/min and/or presence of arrhythmia, was detected clinically by checking pulse and upon ECG showed irregular pulse and absent p-waves) and its pattern were assessed.*

Results: *Total 100 patients were included. The mean age was 44.8 ± 9.8 years with mean duration of the T2DM was 8.4 ± 5.4 years. Most of the patients were male 35 (35%) and 65 (65%) were female. Cardiac Autonomic Neuropathy was found in 40 (40%) of the Patients with Type-2 Diabetes Mellitus. Regarding the patterns of the CAN, constipation found in 50 (50%), gastroparasis in 44 (44%), hypertension in 40 (40%), diarrhea in 39 (39%) and erectile dysfunction in 12 (12%) patients with T2DM.*

Conclusion: *The study concludes that frequency of cardiac autonomic neuropathy is quite high (40%) in T2DM patients.*

INTRODUCTION

Compared to high-income countries (HICs), the prevalence of diabetes is substantially greater in low- and middle-income countries (LMICs).[1] One LMICs are home to almost 80% of the world's diabetic population, and this number is expected to rise. Urbanisation, population ageing, a decline in physical activity, and rising rates of overweight and obesity are some of the main causes of this increase.[2] An underdiagnosed consequence of diabetes mellitus (DM) that is linked to higher mortality and morbidity is cardiac autonomic neuropathy (CAN).[3] Multiple variables contribute to the complex aetiology of CAN. Initially asymptomatic, CAN only exhibits symptoms when the illness has progressed. Because aggressive therapy that focus on lifestyle, glycaemic management, and cardiovascular risk factors can help slow down the course of CAN and perhaps cure it if discovered early, it is essential to identify individuals with CAN as soon as possible.[4] In type 2 diabetes, the prevalence of CAN ranges

from 31 to 73%, and the yearly incidence has been estimated to be 2%.[5]

However, these recognised risk factors for cardiovascular disease (CVD) are continuously more prevalent in people with diabetes than in people without the condition. These conditions include dyslipidaemia, hypertension, and obesity.[6] The term "cardiac autonomic neuropathy" describes a neuropathy of the cardiovascular autonomic system in the presence of diabetes and absence of other causes. Making lifestyle adjustments, preserving ideal glycaemic control, and skilfully managing any underlying medical diseases might improve and slow the progression of CAN[7]. CAN is a common but subtle side effect of diabetes that is characterised by symptoms including low blood pressure when standing, an unusually high resting heart rate, and a diminished capacity to withstand exercise.[8] CAN is an independent predictor of silent myocardial ischaemia in individuals with type 2 diabetes, according to the Detection of Ischaemia in Asymptomatic Diabetics study.[9,10]

In the context of type 2 diabetes, research has focused on analysing the prevalence of CAN. Understanding the frequency and associated factors is essential for quickly recognising, addressing, and improving patient outcomes. Determining the prevalence and pattern of cardiac autonomic neuropathy in patients with type 2 diabetes mellitus who are seen at a tertiary care hospital is the goal of the current investigation. The findings of this study will be useful in developing timely management methods, which will lower the burden of disease and associated death.

METHODOLOGY:

This cross-sectional study was carried out over a period of six months after approval of research protocol from the Ethical review committee of the hospital. A total of 100 patients of either gender with type 2 diabetes mellitus for > 2 years presenting having age >18 years and were willing to provide written informed consent were included.

"Patients with chronic kidney disease (eGFR< 60ml/min), chronic liver disease (ALT> 2 times normal), congestive cardiac failure (Echo showing E.F<50%), neurological diseases, gastrointestinal diseases, thyroid diseases and anemia (Hb <11g%), assessed by history and clinically were excluded". "Patients with diabetic retinopathy were also excluded because valsalva maneuver aggravates the condition. The sample size was calculated by taking the prevalence of cardiac autonomic neuropathy in patients with type 2 diabetes mellitus i.e. P = 30% [(10)], margin of error d = 9%, confidence interval = 95%, then calculated sample was 100".

Demographic data in terms of age, gender, height, weight, BMI, duration of diabetes mellitus, past medical history and family history was obtained. Detail history and general physical examination (temperature, pulse rate, blood pressure in supine and standing position, resting tachycardia in response to supine and standing position) was taken. ECG was done for each patient. The following investigations were done for each patients i.e. RBS, HbA1c, CBC, urine analysis and lipid profile. Venous blood sample was collected using a 10ml syringe and sent to the laboratory. Patients were assessed for the outcome variable i.e. CAN and pattern of autonomic neuropathy such as diarrhea, constipation, gastroparasis, hypertension and erectile dysfunction. SPSS-26 was used for data analysis. Mean + SD was calculated for quantitative data, whereas, frequency and percentages were computed for qualitative data. Chi-square/Fisher exact test was used to compare the frequency of CAN with respect to baseline data. A "p-value < 0.05 was considered as significant".

RESULTS:

Total 100 patients were included. The mean age was 44.8 + 9.8 years with mean duration of the T2DM was 8.4 + 5.4 years. Most of the patients were male 35 (35%) and 65 (65%) were female. 78 (78%) of the patients had h/o drug and only 14 (14%) had family h/o CAN (**Table - 1**).

Table # 1:
Descriptive Data of the Patients

Characteristics	Mean + SD/ n(%)
Age (Years)	44.8 + 9.8

BMI (kg/m^2)	30.6 + 2.73
Duration of T2DM (years)	8.4 + 5.4
Gender • Male • Female	 35 (35%) 65 (65%)
History of Drug • Yes • No	 78 (78%) 22 (22%)
Family history • **Yes** • **No**	 14 (14%) 86 (86%)

Cardiac Autonomic Neuropathy was found in 40 (40%) of the Patients with Type-2 Diabetes Mellitus. Regarding the patterns of the CAN, constipation found in 50 (50%), gastroparasis in 44 (44%), hypertension in 40 (40%), diarrhea in 39 (39%) and erectile dysfunction in 12 (12%) patients with T2DM **(Table - 2)**. The frequency CAN in T2DM patients was compared with respect to the baseline data, age, duration of T2DM, gender and family h/o CAN were found to significantly associated with the occurrence of Can, as the p-value < 0.05 **(Table - 3)**.

Table # 2:
Frequency and Pattern of Cardiac Autonomic Neuropathy in Patients with Type-2 Diabetes Mellitus

Cardiac Autonomic Neuropathy	**n (%)**
Yes	40 (40%)
No	60 (60%)
Patterns	
Diarrhea Yes No	 39 (39%) 61 (61%)
Constipation Yes No	 50(50%) 50 (50%)
Gastroparasis Yes No	 44 (44%) 56 (56%)
Hypertension Yes No	 40 (40%) 60 (87%)
Erectile dysfunction Yes No	 12 (12%) 88 (88%)

Table # 3:
Comparison of frequency of Cardiac Autonomic Neuropathy in Patients with Type-2 Diabetes Mellitus

Variables	**Cardiac Autonomic Neuropathy**		**P-value**
	Yes (n = 40)	**No (n = 60)**	
Age (Years)			

< 40 >40	4 36	28 32	0.00
Duration of DM < 5 >5	 10 30	 28 32	 0.036
BMI (kg/m^2) Obese Normal	 27 13	 41 19	 0.550
Gender Male Female	 05 35	 30 30	 0.00
History of drug Yes No	 34 06	 16 44	 0.220
Family h/o CAN Yes No	 14 26	 00 60	 0.000

DISCUSSION:

In those with type 2 diabetes, the incidence of cardiac autonomic neuropathy varies greatly. The prevalence of CAN varies among T2DM patients, according to studies.10 Higher HbA1c, weight, BMI, and tryglycerides are important risk factors for the development of CAN in people with type 2 diabetes.[11] According to research, CAN is a crippling condition that typically affects people with long-standing type 2 diabetes, however it can sometimes appear early, even before diabetes is diagnosed.[12] The lack of a widely accepted, standardised diagnostic method is probably the cause of underdiagnosis of CAN. The purpose of this study was to ascertain the prevalence and identify patterns of CAN among local T2DM patients.

Forty (40%) of the T2DM patients in the current research reported cardiac autonomic neuropathy. Our findings are consistent with those of a recent study that indicated that 54% of people had cardiac autonomic neuropathy.[13] A research conducted in 2017 revealed that 30% of people with type II diabetes have CAN.[14] In a research on the prevalence of autonomic neuropathy in individuals with poorly managed diabetes, M. Safi et al. discovered that 43% of patients had CAN. In a research on the prevalence of autonomic neuropathy in individuals with poorly managed diabetes, M. Safi et al. discovered that 43% of patients had CAN.[15]According to a different research, every patient had CAN.16 The results of the current study were different from those of the studies conducted by Dyck et al. and Neil et al., which found that only 7% of their patients had evidence of CAN, and Bhatia et al., which found that only 29% of their patients had this complication.[17-19]This broad estimate of CAN prevalence rates is probably caused by our patients' delayed presentations, poor glycaemic management, and extended duration of diabetes mellitus. However, the lack of a severity-based classification of CAN—that is, early, definite, and severe CAN—limited our investigation. Both type 1 and type 2 diabetics were among the 2,048 individuals in a large sample utilised in a research by Qi Pan in China.[20]In that research, 62.6% of patients had CAN, and their age, education, history of childbearing, and medical payments differed significantly from those of patients without CAN. The frequency of CAN varies greatly, and it has grown with a larger sample size. Type 1 diabetics were also included in Qi Pan's study,

although their sample size was limited, even though the prevalence was relatively constant.[20]

The gastrointestinal tract, constipation, diarrhoea, and hypertension were found to be the most involved CAN patterns in the current study. These findings were similar to those in the literature mentioned and to those reported by Maleki et al.[21], but they were different from those reported by Vinik and Erbas and Maser et al.[22]The longer duration of diabetes mellitus and inadequate glycaemic management are the reasons for the resemblance to the outcome reported by Maleki and his colleagues.[21] Their study was conducted in a cohort of more well-controlled diabetes patients with a certain length of DM and in a particular age range, which is why it differs from what Maser and his colleague reported. Patients with diabetes frequently experience erectile dysfunction (ED), which is frequently the sole sign of CAN. Due to patients' shame and doctors' unwillingness to address sexual things with them, it appears that ED is significantly more widespread in our culture than the recorded estimates. Retention and other bladder dysfunctions are quite uncommon. Additional research was required to identify the underlying reasons, which included dietary, environmental, and genetic aspects.

This study discovered that among the risk factors for CAN in individuals with type 2 diabetes, CAN was significantly correlated with gender, duration of disease, and family history of CAN. No correlation between age, BMI, and h/o drug was found. Shahlash MM's study showed a strong relationship between CAN and variables such age, illness duration, HbA1c, creatinine, total cholesterol, and LDL.[3] However, our findings on the risk factors were disputed by few other researches. There was no correlation between the frequency of CAN and gender, according to a research by Maryam et al.[24] the majority of patients in the study 65% were female. In our individuals, we found a substantial gender connection and a male preponderance. Based on a 40% prevalence rate, our study's sample size is tiny. Because Maryam et al. estimated prevalence for each CAN symptom separately, whereas we computed prevalence for all manifestations together, the range of prevalence in their study was 31 to 73%. This is a limitation of our study.

For diabetics, autonomic dysfunction is a common and dangerous consequence. Clinical signs of autonomic dysfunction can lead to fatal consequences, interfere with everyday activities (like exercise), and create distressing symptoms (like syncope). Recommendations for the use of non-invasive tests that have proven beneficial are justified since the patient's history and physical examination are insufficient for identifying early signs of autonomic nerve dysfunction. When weighed against the devastating outcomes associated with advanced cardiovascular, cerebrovascular, and renal problems, the economic impact of the suggestion to perform autonomic function testing is negligible.

CONCLUSION:

The study comes to the conclusion that due of its incapacitating features and potential effects on cardiovascular health, cardiac autonomic neuropathy is rather common (40%) in T2DM patients. Among patients with type 2 diabetes, the prevalence of CAN varies significantly depending on risk factors such age and the length of diabetes, among others. To identify the unique CAN symptoms in T2DM patients, further extensive research should be carried out.

"Conflict of interest: Nothing to declare

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Patients' consent: Written informed consent was provided by the patients.

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