ORIGINAL ARTICLE

PREVALENCE OF CARDIAC AUTONOMIC NEUROPATHY AMONG TYPE 2 DIABETICS AT A TERTIARY CARE CENTRE

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Background: In the context of Type 2 diabetes mellitus (T2DM), the frequency of cardiac autonomic neuropathy has become a subject of intensive research. Understanding the prevalence and associated risk factors is pivotal for early detection, intervention, and improved patient outcomes. The objective of this study was to assess the prevalence of cardiac autonomic neuropathy in individuals with type 2 diabetes mellitus at a Hayatabad Medical Complex Peshawar. **Methods:** This cross-sectional study was conducted at Department of Medicine, Hayatabad Medical Complex, Peshawar, from 16th Nov 2022 to 16 May 2023 on patients presenting with type 2 diabetes in the age group 20–75 years. Pregnant women, patients with end-stage renal disease and neurological abnormalities were excluded. The frequency of cardiac autonomic neuropathy (CAN) was determined. **Results:** There was a total of 260 patients presenting with type 2 Diabetes mellitus during the study period. The mean age of the patients was 50.36±15.56 years. The frequency of cardiac autonomic neuropathy was 92 (35.4%), 62 were male and 30 were female. **Conclusion:** Cardiac autonomic neuropathy is a common micro-vascular complication in T2DM with duration of diabetes, age, and other microvascular complications being the significant contributors to its pathogenesis and severity.

Keywords: Type 2 Diabetes Mellitus, Cardiac autonomic neuropathy, Microvascular complications

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INTRODUCTION

Over the past few years, there has been a steady and progressive rise in the prevalence of diabetes worldwide.[1] According to the International Diabetes Federation, in 2022, 26.7% of adults in Pakistan were affected by diabetes making the total number of cases approximately 33,000,000.[1] Cardiac autonomic neuropathy (CAN) is often an underdiagnosed complication of diabetes mellitus (DM) and is associated with increased mortality and morbidity. The aetiology of CAN is intricate and involves multiple factors. CAN is asymptomatic at first and only shows symptoms in the advanced stages of the disease. It is crucial to identify people with CAN early because starting aggressive therapies focusing on lifestyle, glycaemic control, and cardiovascular risk factors can help slow down the progression of CAN and potentially reverse it if detected soon after it begins.[2]

Nevertheless, individuals with diabetes consistently exhibit these well-established risk factors for cardiovascular disease (CVD) to a greater extent than those without diabetes. The conditions encompass obesity, hypertension, and dyslipidemia.[3] Cardiac autonomic neuropathy refers to a neuropathy of the cardiovascular autonomic system that occurs in the presence of diabetes, when no other causes are present. Implementing lifestyle changes, maintaining optimal glycaemic control, and effectively managing other existing health conditions might lead to improvement and may minimise the advancement of CAN.[4]

CAN is a prevalent yet subtle consequence of diabetes, distinguished by symptoms such as reduced ability to tolerate exercise, abnormally high resting heart rate, and low blood pressure upon standing.[5,6] The Detection of Ischemia in Asymptomatic Diabetics research showed that CAN is an autonomous predictor of silent myocardial ischemia in patients with T2DM.[7]

The investigation of the prevalence of CAN has been a focal point of research in the context of T2DM. Gaining knowledge about the frequency and related aspects is crucial for promptly identifying, intervening, and enhancing the results for patients. This study seeks to examine the existing literature to clarify how often CAN occurs in persons with T2DM, providing insight into the complex connection between diabetes and autonomic dysfunction. By conducting a thorough examination of the existing evidence, our aim is to enhance the overall comprehension of intricate relationship between diabetes and cardiovascular problems. This will provide valuable insights for clinical management and guide future research in this field.

MATERIAL AND METHODS

This descriptive study was carried out in the Department of Medicine, Hayatabad Medical Complex, Peshawar, from 16 Nov 2022 to 16 May 2023. The sample size

was determined to be 260 using the calculator.net software.[8] This calculation was based on a CAN rate of 42%[9] in T2DM patients, 95% confidence level, and a 6% margin of error. The sample method employed was non-probability sequential sampling. All individuals diagnosed with T2DM, with history of diabetes for over 5 years, and age 20–75 years were included in the study. Patients who were pregnant, had end-stage renal illness, or had neurological difficulties were excluded.

After explanation of the various manoeuvres and obtaining informed written consent, the patients underwent testing to assess their resting heart rate (RHR). In addition, their heart rate reaction to standing from recumbent position was assessed. This was done by measuring the R-R interval on the electrocardiogram (ECG) at beats 15 and 30 after the transition from a lying down position to standing. The patient underwent orthostatic hypotension assessment involving measuring blood pressure while in a supine posture followed by instructing the patient to stand up. The blood pressure was reassessed after a 2-minute period of standing. A typical reaction was a decrease in systolic blood pressure (SBP) of <10 mmHg, a borderline response was a decrease of 10–29 mmHg, and an abnormal response was a decrease of >30 mmHg.

The data was entered and analysed using SPSS-23. Calculations were performed to determine the mean and standard deviation of numerical variables such as age, BMI, height, and weight. Categorical data, such as gender, CAN, hypertension, and smoking status, were analysed to determine frequencies and percentages. CAN participants were categorised according to age, BMI, gender, hypertension, and smoking status in order to examine the effect modifiers. A post-stratification Chi-square test was conducted and $p \leq 0.05$ was considered as statistically significant.

RESULTS

This study was conducted on a sample of 260 participants who had T2DM. The age of the patients was 50.36±15.56 years. There were 152 (58.2%) male and 108 (41.5%) female patients. The mean BMI was 28.96±2.51 Kg/m^2. The prevalence of cardiac autonomic neuropathy was 92 (35.4%) of the total.

Majority (41.3%) of the cases of CAN fell in age group 61–75 years. There was a male predominance (67.4%, $p<0.05$), and no significant association with hypertension and smoking. (Table 1–4).

Table-1: Stratification of cardiac autonomic neuropathy with age [n (%)]

CAN	Age distribution (Years)				Total	*p*
	20 –35	36–50	51–60	61–75		
Yes	17 (18.5)	24 (26.1)	13 (14.1)	38 (41.3)	92 (100)	0.41
No	36 (21.4)	50 (29.8)	30 (17.9)	52 (31.0)	168 (100)	

Table-2: Stratification of cardiac autonomic neuropathy with gender [n (%)]

CAN	Male	Female	Total	*p*
Yes	62 (67.4)	30 (32.6)	92 (100.0)	0.03
No	90 (53.6)	78 (46.4)	168 (100.0)	

Table-3: Stratification of cardiac autonomic neuropathy with hypertension [n (%)]

CAN	Hypertension		Total	*p*
	Yes	No		
Yes	32 (34.8)	60 (65.2)	92 (100.0)	0.27
No	70 (41.7)	98 (58.3)	168 (100.0)	

Table-4: Stratification of cardiac autonomic neuropathy with smoking status [n (%)]

CAN	Smoker	Non-smoker	Total	*p*
Yes	22 (23.9)	70 (76.1)	92 (100.0)	0.89
No	39 (23.2)	129 (76.8)	168 (100.0)	

DISCUSSION

The prevalence of cardiac autonomic neuropathy in individuals with T2DM shows considerable variation. Studies have shown variation in prevalence of early and definite CAN.[10] Significant risk factors for the development of CAN in T2DM include higher HbA1c, weight, BMI and tryglycerides.[11]

It has been shown that CAN is a debilitating ailment primarily found in individuals with long-standing T2DM, but it can also manifest earlier, even prior to the diagnosis of diabetes.[12] Under diagnosis of CAN is likely to be due to absence of a globally acknowledged standardised diagnostic approach. This study was conducted with the objective of determining the prevalence and identifying the risk factors of CAN among individuals in the local area having T2DM.

The majority of patients were in the age range over 50 years, and most of the participants were male. The incidence of CAN among individuals with T2DM was 35.4%, which closely aligns with another study[9] that found a prevalence of 42% for CAN. In a research conducted on the Egyptian population[13], the incidence of CAN was found to be 60%; they had a smaller sample size compared to ours. However, our study was limited by the fact that we haven't categorised CAN based on severity, specifically into early, definite, and severe CAN. In a study conducted by Qi Pan[14] in China a large sample of 2,048 patients were used which included both type 1 and type 2 diabetics. The prevalence of CAN in that study was 62.6% with significant difference in comparison to patients without CAN in terms of age, education, childbearing history and medical payments. Prevalence of CAN varies widely and with a large sample the prevalence has increased. The study by Qi Pan[14] also included type 1 diabetics but their sample was small, although the prevalence remained almost the same.

The substantial disparity in the frequency of CAN can be attributed to lack of uniformity in the

diagnostic criteria and notable variations in the characteristics of the studied populations, particularly with regards to risk factors for CAN such as age, sex, and duration of diabetes mellitus, among others.

Our study found that among risk variables for CAN in type 2 diabetes patients, only gender was substantially associated with CAN. There was no observed relationship between age, smoking status, and hypertension. The study conducted by Shahlash MM[13] demonstrated a substantial correlation between CAN and factors such as age, length of disease, HbA1c, creatinine, total cholesterol, and LDL.

Nevertheless, some other studies contradicted our findings about the risk variables. A study conducted by Maryam *et al*[15] showed no association of gender with prevalence of CAN. That study was dominated by 65% female patients. We observed male predominance and significant gender association in our subjects. Our study has a small sample based on prevalence of 42%. The range of prevalence in the study by Maryam *et al* was 31 to 73% because they calculated prevalence for different manifestation of CAN separately while we calculated all manifestation as one. This is a limitation of our study.

CONCLUSION

The prevalence of CAN in individuals with T2DM is a noteworthy issue because of its incapacitating characteristics and prospective consequences on cardiovascular well-being. Prevalence of CAN exhibits significant variation among T2DM patients, with risk variables such as age, duration of diabetes, and other microvascular complications. Further large scale studies should be conducted to determine the individual manifestations of CAN in patients with T2DM.

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IQ: Study concept and design, Discussion
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