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Original Research Article

FREQUENCY OF CARDIAC AUTONOMIC NEUROPATHY IN TYPE 2 DIABETES MELLITUS PATIENTS PRESENTING TO KHYBER TEACHING HOSPITAL PESHAWAR

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Abstract: *This study aimed to determine the frequency of cardiac autonomic neuropathy in patients with type 2 diabetes. A cross-sectional study was conducted at the Department of Medicine, Khyber Teaching Hospital Peshawar, Pakistan, from June 2022 to June 2023. The study included 285 individuals aged 40-60 diagnosed with type 2 diabetes for at least 5 to 10 years. The study aimed to evaluate the frequency of cardiac autonomic neuropathy in type 2 diabetics. Chi-square was applied for statistical analysis with a significance level of p≤0.05. Of 285 type 2 diabetic patients, 199 (69.82%) were male, and 86 (30.18%) were female. 26.31% of the participants were diagnosed with cardiac autonomic neuropathy, of which 26.67% were male and 73.33% were female. This difference was statistically significant. 37.35% of the patients with cardiac autonomic neuropathy were smokers, while 62.65% were non-smokers. All the patients with CAN were either overweight or obese. This study found that prolonged diabetes is directly related to the development of cardiac autonomic neuropathy, and there was a statistically significant association between diabetes and gender, as well as smoking.*

Keywords: Cardiac Autonomic Neuropathy, Type 2 Diabetes Mellitus, Cardiac Autonomic Dysfunction

Introduction

Diabetes Mellitus (DM) is a widespread endocrine condition characterized by abnormal elevation of glucose levels in the blood (John APP et al., 2022). The number of diabetic patients increases rapidly; by 2045, it is estimated that it will rise to 693 million globally (Ogurtsova K et al., 2017). Developing countries are the main hub of diabetic patients, and the number of these patients increases at a rate of 69% compared to developed nations, where the rate of increase is 20% (Akhtar S et al., 2019; Hu FB., 2011). Pakistan, a developing nation, is also facing a high rise in the diabetic population (Meo S.A et al., 2016; Aamir A. et al., 2019). The heart, kidneys, vasculature, and eyes can all be affected by type 2 diabetes (John APP et al., 2022). A common but underreported consequence of type 2 diabetes (T2D) is cardiac autonomic dysfunction, which is linked to arrhythmia, myocardial infarction, and sudden death. Increased heart rate, intolerance to exercise, hypotension due to positional changes, and asymptomatic myocardial ischemia signify cardiac autonomic dysfunction. Reduced heart rate variability (HRV) is one of the early presentations of cardiac autonomic dysfunction, with parasympathetic loss preceding sympathetic impairment (Dhumad MM et al., 2021). According to published research, the prevalence of CAN in type 2 diabetes (T2DM) ranges from 25% to 75% (Shah AS., 2019). Cardiac autonomic neuropathy can be clinically visible or subclinical, and it is characterized by functional and reversible neural changes; hence, it is a potentially curable illness if timely intervention is offered. Only an autonomic nerve function test might detect the subclinical stage of Cardiac Autonomic Neuropathy (CAN). In a recent statement by the American Diabetes Association, HRV was indicated as one of the diagnostic tests for Cardiac Autonomic Neuropathy. HRV has been described as a highly accurate, non-invasive, and typically reproducible measuring tool; hence, it might be utilized as a diagnostic for Cardiac Autonomic Neuropathy (Bissinger A. et al., 2017; Phurpa et al., 2017). Detection at an early stage of Cardiac autonomic neuropathy is critical because it is reversible and, in particular, susceptible to lifestyle changes. Cardiac autonomic neuropathy therapy includes multifactorial targeted risk factor interventions such as optimizing glycemic control, dyslipidemia, and hypertension (Williams S et al., 2022). Because cardiac autonomic dysfunction or neuropathy is a major predictor of cardiovascular events and mortality, it must be treated as soon as feasible (Phurpa et al., 2017; Williams et al., 2019). This study was conducted to know the incidence of cardiac autonomic dysfunction or neuropathy in patients with type 2 diabetes mellitus presenting to Khyber Teaching Hospital Peshawar, as no such study has been conducted in our local population.

Methodology

This prospective study was conducted at the Department of Medicine, Khyber Teaching Hospital Peshawar, Pakistan, from June 2022 to June 2023. The same hospital's ethics board granted ethical approval. After receiving written informed permission, 285 patients of both genders aged 40-60 years with at least 5 to 10 years of type 2 diabetes mellitus were recruited from the Outpatient Department. All of these individuals received solely oral antidiabetic medications in addition to lifestyle changes. Patients with

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diabetes retinopathy, any cardiac disease, hypertension, epilepsy, psychiatric disorders, migraine, respiratory disorders, endocrine abnormality other than diabetes, using medications that affect the nervous system, and athletes were excluded. The participants were all admitted to the medical unit. Patients were instructed to fast for 12 hours. Cardiac autonomic functioning was assessed using an electrocardiography (ECG) patient monitors utilising three conventional Ewing non-invasive tests (Chowdhury M et al., 2021). The tests were conducted early in the morning. Cardiac autonomic neuropathy was confirmed if any of the following test results were found abnormal:

(a) Heart rate (HR) response to a deep breathing test: ECG leads were attached to the patient under examination. The patient was instructed to breathe for 2 minutes in a normal style while lying supine, followed by 6 deep breaths for a minute. E: I ratio (exhalation to inspiration ratio) was calculated as E: I ratio = mean value of the longest R-R interval during expiration/mean value of the shortest R-R interval during inspiration. Heart rate difference ≥15 beats/min was normal; 11–14 beats/min was borderline, while ≤10 beats/min was abnormal.

(b) Immediate heart rate (HR) response to standing: ECG leads were attached to the patient under examination. The patient sat quietly for 3 minutes, followed by standing, remaining calm and motionless. The 30:15 ratio was derived by dividing the maximum R-R interval at the 15th beat and the minimum interval at the 30th after standing. A ratio ≥1.04 was termed normal; 1.01–1.03 was termed borderline, and ≤1.00 was termed abnormal.

(c) Blood pressure (BP) response to standing: The patient's blood pressure was noted while lying down quietly and again when standing up 1-2 minutes later. The difference between BP (systolic and diastolic BP) resting and BP (systolic and diastolic BP) standing was recorded as the postural drop in BP after 2 minutes. A drop in SBP by ≤10 mmHg in response to standing was considered normal, whereas a fall in SBP of ≥30 mmHg was considered abnormal.

BMIs ranging from 18.5 to 24.9 were considered normal weight, BMIs ranging from 25 to 29.9 were considered overweight, and BMIs of 30 or more were deemed obese.

The data was analyzed in SPSS version 23. Means ± standard deviation were calculated for continuous variables, while frequencies and percentages were calculated for qualitative variables. The chi-square test was applied with ≤0.05 significance of p-value.

Results

The demographic characteristics of the study population include gender distribution, age distribution, BMI, and smoking status. Most patients were male (69.82%), and most fell within 40 to 60 years. The average BMI was 35±7.63, with a significant percentage of non-smokers (81.05%) (Table, Figure 1).

Table 2 provides information on Cardiac Autonomic Neuropathy (CAN) diagnosis and its related factors. 26.31% of patients were diagnosed with CAN, with a significant gender difference, with a higher prevalence among females (73.33%). Smoking was significantly associated with CAN, with a higher proportion of smokers among CAN patients (37.35%). All CAN patients were overweight or obese, and only a small percentage had a normal BMI. Additionally, the duration of diabetes showed a direct relationship with the development of CAN.

These tables offer a clear overview of the study's findings related to the study population and the factors associated with Cardiac Autonomic Neuropathy.

Table 1: Demographic Profile of Study Population

Variable	Value
Total patients	285
Male gender	199 (69.82%)
Female gender	86 (30.18%)
Age Distribution	
- 40 to 49 years	131 (46%)
- 50 to 60 years	154 (54%)
BMI (Body Mass Index)	35±7.63
Smoking Status	
- Smokers	54 (18.95%)
- Non-smokers	231 (81.05%)

Table 2: Cardiac Autonomic Neuropathy (CAN) Diagnosis and Related Factors

Variable	Value
Total CAN patients	75 (26.31%)
Gender Distribution among CAN Patients	
- Male	20 (26.67%)
- Female	55 (73.33%)
Smoking Status among CAN Patients	
- Smokers	28 (37.35%)
- Non-smokers	47 (62.65%)
BMI Distribution among CAN Patients	
- Overweight	25.33%
- Obese	69.33%
- Normal BMI	5.34%

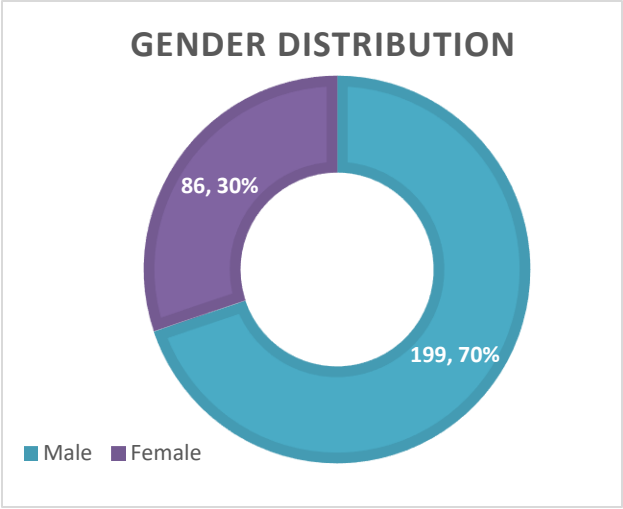

Figure 1. Gender-wise distribution of the study population

Discussion

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CAN etiology is multifaceted and complicated. The activation of the polyol pathway by hyperglycemia causes direct neuronal injury and the activation of protein kinase C, resulting in vasoconstriction and reduced neuronal blood flow. Other processes at work include increased oxidative stress, increased free radical formation, nitric oxide production failure, immunological mechanisms, and neurotrophic growth factor insufficiency. The accumulation of advanced glycosylation end products in neuronal blood vessels causes hypoxia and changes in nerve function (Pathak et al., 2017; Menon AS et al., 2017). The first indicator of a CAN diagnosis is a decrease in HRV. A balance between sympathetic and parasympathetic activity in response to a baseline metabolic rate regulates the heterogeneity with each heartbeat. The HRV in healthy people is very high. The intensity and duration of T2DM are connected to a decrease in HRV (Bhuyan AK et al., 2019).

The autonomic nerve system is one of the body's principal homeostatic regulation systems. Parasympathetic activity diminishes, whereas sympathetic activity rises in most clinical situations (Breder ISS et al., 2019). The presence of CAN is closely linked to increased mortality and morbidity, including stroke, coronary artery disease, and silent myocardial ischemia. This is supported by the findings of the European Epidemiology and Prevention of Diabetes (EURODIAB) research and the Action to Control Cardiovascular Risk in Diabetes (ACCORD) experiment (Liao D et al., 1998; Pop-Busui R et al., 2010). The American Diabetes Association (ADA) has suggested that all patients with type 2 diabetes be evaluated for diabetic neuropathy beginning at diagnosis for early identification and quick management of CAN (21. Witte DR et al., 2005). CAN treatment consists of symptomatic care and effective medicines to delay or reverse the disease's course. Therapy options include lifestyle changes, strict glucose management, antioxidants, and orthostatic hypotension therapy (American Diabetes Association., 2018).

Male patients outweigh female patients in our study, which is consistent with the findings of Birajdar SV et al. and Bhuyan AK et al. (Bhuyan AK et al., 2019; Birajdar SV et al., 2017). The mean age of our study's patients was 50.412 years, similar to the 53.3 10.37 years recorded by Bhuyan AK et al. (Bhuyan AK et al., 2019). The current study found that T2DM patients had lower parasympathetic and sympathetic activity. T2DM may impair the heart's sympathetic and parasympathetic fibers, resulting in cardiac autonomic neuropathy. The current investigation confirmed the presence of CAN in 26.31% of T2DM patients. In other investigations, Moţăţăianu A et al. and Pan I et al. found that 39.1% and 62.6% of T2DM patients had CAN, respectively (Moţăţăianu A et al., 2018; Pan I et al., 2019). This might be due to differences in sample sizes and participant ages in various research. The duration of diabetes was found to be directly associated with the development of cardiac autonomic neuropathy. Birajdar SV et al. made similar observations (Birajdar SV et al., 2019).

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Conclusion

There is a statistically significant association between diabetic cardiac autonomic neuropathy and gender as well as smoking. In addition to glycemic control and management of other complications in type 2 diabetes mellitus, we should also prioritize these variables.

Declarations

Data Availability statement
All data generated or analyzed during the study are included in the manuscript.
Ethics approval and consent to participate.
Approved by the department Concerned.
Consent for publication
Approved
Funding
Not applicable

Conflict of interest

The authors declared an absence of conflict of interest.

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