



## **FREQUENCY AND DIAGNOSTIC APPROACHES OF CARDIAC AUTONOMIC NEUROPATHY AMONG INDIVIDUALS WITH DIABETES IN A TERTIARY CARE CENTER**

**DR.K.P. SELVARAJAN CHETTIYAR  
DR. KA. SUGANTHAN NITHISH**

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**1.PROFESSOR, DEPARTMENT OF GENERAL MEDICINE, SREE MOOKAMBIKA INSTITUTE OF MEDICAL SCIENCES, KULASEKHARAM, TAMILNADU, INDIA**

**2.JUNIOR RESIDENT, DEPARTMENT OF GENERAL MEDICINE, SREE MOOKAMBIKA INSTITUTE OF MEDICAL SCIENCES, KULASEKHARAM, TAMILNADU, INDIA.**

**CORRESPONDING AUTHOR**

**DR. KA. SUGANTHAN NITHISH**

**JUNIOR RESIDENT, DEPARTMENT OF GENERAL MEDICINE, SREE MOOKAMBIKA INSTITUTE OF MEDICAL SCIENCES, KULASEKHARAM, TAMILNADU, INDIA.**

### **ABSTRACT:**

Background: Cardiovascular autonomic neuropathy (CAN) represents a significant yet frequently under-diagnosed complication of diabetes mellitus (DM), arising from impaired autonomic regulation of the cardiovascular system, excluding other etiologies. Early detection of CAN is crucial, as prompt interventions targeting lifestyle modification, glycemic control, and cardiovascular risk reduction may decelerate or potentially reverse disease progression. Materials and Methods: This cross-sectional study encompassed 60 consecutive patients with diabetes mellitus, diagnosed in accordance with the American Diabetes Association (ADA) criteria. CAN was assessed utilizing Ewing’s battery of five standard bedside autonomic function tests, which evaluate both sympathetic and parasympathetic activity. Results: CAN was identified in 53 patients (88.3%). Of these, 38.3% exhibited early CAN, 38.3% had definite CAN, and 7% presented with severe CAN. The most prevalent abnormal autonomic test was the expiration–inspiration (E:I) ratio, indicative of parasympathetic dysfunction, observed in 75% of patients. QTc interval prolongation on ECG demonstrated high specificity for diagnosing and grading CAN severity, although sensitivity was comparatively low. Conclusion: CAN is highly prevalent among individuals with diabetes mellitus and is associated with an elevated risk of mortality. Routine screening for CAN at the time of diabetes diagnosis and periodic follow-up, as advocated by the ADA, is imperative. Early glycemic optimization and lifestyle interventions may aid in preventing CAN-related cardiovascular complications. Keywords: Cardiac autonomic neuropathy, Diabetes mellitus, Ewing’s battery, QTc interval

### **Introduction:**

Diabetes mellitus has emerged as a significant global public health challenge in the modern era. Between 1980 and 2000, the global prevalence of diabetes among adults aged over 18 years increased markedly from 4.7% to 8.5%, reflecting a rapid epidemiological transition driven by urbanization, lifestyle changes, and increasing life expectancy.<sup>1</sup> In India, the burden is particularly alarming, with an estimated 8.7% of individuals aged 20–70 years affected by diabetes, positioning the country as one of the largest contributors to the global diabetes population.<sup>2</sup> This escalating prevalence has earned India the distinction of being termed the “diabetes capital of the world,” underscoring the urgent need to address diabetes-related complications. Cardiovascular complications are the leading cause of morbidity and mortality in



patients with diabetes mellitus. These complications can be broadly categorized into three major entities: diabetic cardiomyopathy, atherosclerotic coronary artery disease, and cardiac autonomic neuropathy (CAN).<sup>3</sup>

Among these, CAN remains one of the most under-recognized yet clinically significant complications. CAN is defined as the impairment of autonomic regulation of the cardiovascular system in individuals with diabetes, after exclusion of other potential causes of autonomic dysfunction. The underlying pathophysiology of CAN is complex and multifactorial, involving chronic hyperglycemia-induced oxidative stress, microvascular ischemia, inflammation, and neuronal damage. One of the major challenges in managing CAN is its insidious onset. In the early stages, CAN is often asymptomatic and may go undetected until advanced disease develops. Clinical manifestations typically appear late and may include resting tachycardia, exercise intolerance, orthostatic hypotension, and silent myocardial ischemia. Early identification of CAN is therefore of paramount importance, as prompt intervention through intensive lifestyle modification, optimal glycemic control, and aggressive management of cardiovascular risk factors has the potential to delay disease progression and, in some cases, partially reverse autonomic dysfunction.<sup>4</sup>

Cardiovascular reflex testing is key for early detection of CAN and gives important future health information.<sup>5</sup> Problems with the autonomic nervous system can lead to many issues like fast heartbeat, constant heart rate, dizziness when standing, high blood pressure when lying down, less ability to exercise, and more heart problems during surgery. The vagus nerve, the longest autonomic nerve, is responsible for about 75% of parasympathetic activity. Since autonomic neuropathy first affects the longest nerves, parasympathetic problems are usually the first sign in diabetic patients. Early CAN often shows as a loss of parasympathetic function with more sympathetic activity. Despite its importance, there is little data on how common CAN is among diabetic patients in India, especially in the west. Few local studies and different ways of diagnosing make it hard to know how common this problem is. This study was done to find out how often cardiac autonomic neuropathy occurs and to look at risk factors in type 2 diabetes patients in the study group. This knowledge can help with early screening and targeted treatments to lower heart-related health issues and deaths in diabetic patients.

## AIM AND OBJECTIVE OF THE STUDY

### Aim

To assess the prevalence of cardiac autonomic neuropathy (CAN) in patients with type 2 diabetes mellitus and to evaluate its association with clinical and metabolic risk factors.

### Objectives

1. To determine the frequency and severity of cardiac autonomic neuropathy in patients with type 2 diabetes mellitus using Ewing's battery of autonomic function tests.
2. To assess the pattern of autonomic dysfunction (parasympathetic and sympathetic involvement) in diabetic patients.

## MATERIALS AND METHODS

This prospective observational study was carried out in a tertiary care hospital over an 18-month period and included 60 patients with diabetes mellitus. Both type 1 and type 2 diabetic patients diagnosed according to American Diabetes Association (ADA) criteria were recruited. Patients with disorders affecting the autonomic nervous system—such as significant cardiac, pulmonary, renal, malignant, or



thyroid diseases—were excluded. Those receiving medications known to influence autonomic function (beta-blockers, sympathomimetics, vasodilators, diuretics, or anti-arrhythmic drugs), patients with pre-existing structural heart disease, and individuals who were uncooperative or physically unable to participate were also excluded.

Baseline demographic details including age, sex, occupation, religion, and place of residence were documented. A detailed medical history was obtained, covering the duration of diabetes, treatment modalities (oral hypoglycemic agents or insulin), presenting symptoms, and vital signs. All participants underwent comprehensive general, cardiovascular, and neurological examinations. Routine laboratory investigations included complete blood count, renal and liver function tests, serum electrolytes, fasting and random blood glucose levels, urine protein estimation by dipstick, estimation of glomerular filtration rate (eGFR) using the MDRD formula, and electrocardiography with measurement of the corrected QT interval. Additional assessments included fundoscopy for diabetic retinopathy, urine protein-to-creatinine ratio, glycated hemoglobin (HbA1c), and fasting lipid profile.

Cardiac autonomic neuropathy (CAN) was evaluated using Ewing's battery of five standardized autonomic function tests. Parasympathetic activity was assessed through resting heart rate, heart rate variability during deep breathing (E:I ratio), and the Valsalva maneuver, while sympathetic function was examined using blood pressure responses to standing and sustained handgrip. A cumulative CAN score was calculated based on these tests and classified as absent, early, definite, or severe, enabling grading of autonomic dysfunction and assessment of its severity in diabetic patients.

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS). Quantitative data were expressed as mean  $\pm$  standard deviation, while categorical variables were expressed as frequencies and percentages. Independent t-tests were used to compare continuous variables after verifying normal distribution. Chi-square tests were applied to analyze differences between categorical variables. Logistic regression models were used to adjust for age and estimate the independent effects of hypertension, ischemic heart disease, and diabetes mellitus. A p-value of less than 0.05 was considered statistically significant.

## Results:

This study enrolled 60 patients with diabetes mellitus aged between 13 and 75 years, with a mean age of  $46.4 \pm 14.34$  years; 44 were males and 16 were females. The average duration of diabetes was  $72.60 \pm 22$  months (range: 6 months to 25 years). Patients were categorized into two groups: those with cardiac autonomic neuropathy (CAN) and those without CAN.

Patients with CAN were significantly older ( $p = 0.013$ ), had a longer duration of diabetes ( $78.3$  vs  $29.14$  months;  $p < 0.001$ ), and showed higher fasting blood sugar ( $p = 0.035$ ) and HbA1c levels ( $p = 0.043$ ) compared to those without CAN. Microvascular complications such as nephropathy ( $p = 0.035$ ), retinopathy ( $p = 0.01$ ), and peripheral neuropathy ( $p = 0.036$ ) were more common in CAN-positive patients. QTc interval prolongation was also significantly greater in patients with CAN, particularly in severe cases ( $443.86$  ms vs  $407.71$  ms).

No significant differences were noted between the groups regarding gender, body mass index, blood pressure, lipid profile, or serum creatinine. Easy fatigability was the most common symptom (53%), followed by giddiness (30%) and light-headedness (16%). Overall, CAN was detected in 88.3% of



patients, with 38.3% each having early and definite CAN, and 7% having severe CAN. Abnormal autonomic test findings were frequent, particularly reduced E:I ratio (75%), abnormal Valsalva ratio (73.3%), and impaired blood pressure response to handgrip (60%).

## Discussion

In the tapestry of our study, the prevalence of CAN wove itself into a striking 88.3%, a figure that dances slightly above the findings of Birajdar et al. (58%) and Mehta et al. (57.5%). The most frequently observed autonomic function test anomaly was an abnormal E:I ratio, casting its shadow over 75% of patients. Bhuyan et al. painted a similar picture with a 70% prevalence of CAN, where the most common anomaly was an abnormal E:I difference in 56% of patients, echoing our own findings. In contrast, Birajdar et al. discovered that 58% of participants bore the mark of CAN, with an abnormal 30:15 ratio being the most common anomaly in 38% of cases. The higher prevalence of CAN in our study can be attributed to the inclusion of individuals with long-term diabetes, averaging a duration of 72 months. Moreover, the majority of patients at our center, often uneducated, delay seeking medical advice and are diagnosed with DM only after symptoms manifest, particularly in the suburban population we serve.

These patients frequently present with diabetes-related complications. In our sample, a longer disease duration emerged as a significant predictor of CAN ( $p < 0.001$ ). However, Chaya Ahire et al. also noted that early CAN often appeared in patients with a shorter disease duration, suggesting that CAN screening should be conducted for all newly diagnosed type 2 DM patients. Our research further illuminated that individuals with less than a decade of diabetes exhibited early CAN, while those with over ten years of diabetes faced heightened CAN risks in both type 1 and type 2 DM groups. Although the study was cross-sectional, we identified a statistically significant link between advancing age and CAN in both Type 1 and Type 2 DM within our sample, harmonizing with findings from other studies. Uncontrolled fasting and postprandial blood sugars (PPBS), along with elevated HbA1c levels, were significantly correlated with CAN in our research.

This is likely due to the increased risk of advanced glycation end products accumulating in cases of uncontrolled blood sugar. Diabetic microangiopathic complications share a similar pathogenesis, closely intertwining them. Our study found that CAN was linked to other microvascular complications, including peripheral neuropathy, nephropathy, and retinopathy. Specifically, nephropathy was present in 79% of patients, neuropathy in 56%, and retinopathy in 58%. Another notable finding was the association between QT prolongation and CAN severity. Patients with definite and severe CAN had an average QTc exceeding 440 milliseconds, compared to those with early CAN. Our study diverged from previous ones by including patients from all DM categories (type 1 and type 2). It is also the first to include patients who had been infected with or recently recovered from COVID-19, although the COVID cohort was too small for definitive conclusions. Furthermore, our study established a link between QTc and CAN severity, suggesting its potential as a bedside diagnostic tool.

## Conclusion:

Cardiac autonomic neuropathy (CAN) is an often underrecognized microvascular complication of diabetes mellitus, with a high prevalence of 88.3% observed in this study. The results indicate predominant parasympathetic involvement, evidenced by abnormal autonomic function tests. An altered expiration-to-inspiration (E:I) ratio was the most frequent abnormality, seen in 75% of patients. Longer duration of diabetes, advancing age, and coexisting microvascular complications were key predictors of CAN. QTc interval prolongation on ECG showed good specificity for identifying CAN severity, though sensitivity was limited. Given its strong association with increased mortality, routine screening for CAN is essential. Screening should be performed at the time of diabetes diagnosis and



repeated annually as per ADA recommendations. Early glycemc control and lifestyle modification remain central to preventing CAN and its complications.

**Conflict of interest statement:**

There is no conflict of interest among the authors.

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