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# Evaluation of cardiac autonomic dysfunction in patients with Type 2 DM

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**Abstract**

**Background:** Cardiovascular autonomic dysfunction is a common but often underdiagnosed complication of type 2 diabetes mellitus (T2DM) that contributes to increased cardiovascular morbidity and mortality.
Objective: To evaluate cardiac autonomic dysfunction in patients with T2DM and determine its association with clinical and metabolic characteristics.
**Materials and Methods:** This hospital-based cross-sectional study included 90 patients with T2DM. Clinical details, anthropometric measurements, and laboratory parameters, including glycated haemoglobin (HbA1c), were recorded. Cardiac autonomic function was assessed using Ewing's cardiovascular autonomic reflex tests. Cardiac autonomic neuropathy (CAN) was classified according to Ewing's criteria. Statistical analysis was performed using SPSS version 26.0, with $p < 0.05$ considered statistically significant.
**Results:** The mean age of the participants was 56.84 ± 10.92 years, and 61.1% were males. Cardiac autonomic dysfunction was present in 56.7% of patients, with 23.3% having early CAN, 22.2% definite CAN, and 11.1% severe CAN. Abnormal Valsalva ratio (36.7%) and deep breathing test (35.6%) were the most common abnormalities. Patients with CAN had significantly older age, longer duration of diabetes, higher HbA1c, higher BMI, and a greater prevalence of hypertension ($p < 0.05$). Duration of diabetes >10 years, HbA1c >8%, age >60 years, and hypertension were independent predictors of CAN.
**Conclusion:** Cardiac autonomic dysfunction is highly prevalent among patients with T2DM and is significantly associated with longer disease duration, poor glycaemic control, older age, and hypertension. Routine screening using cardiovascular autonomic reflex tests may facilitate early diagnosis and improve cardiovascular risk stratification.

**Keywords:** Type 2 diabetes mellitus; cardiovascular autonomic neuropathy; cardiac autonomic dysfunction; Ewing's cardiovascular reflex tests; HbA1c.

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## Introduction

Type 2 diabetes mellitus (T2DM) is one of the most prevalent non-communicable diseases worldwide and represents a major public health challenge because of its rapidly increasing incidence and long-term complications. According to the International Diabetes Federation (IDF) Diabetes Atlas 2025, approximately 589 million adults are living with diabetes globally, of whom nearly 90–95% have type 2 diabetes. India is among the countries with the highest diabetes burden, with more than 89 million affected adults, and this number is projected to increase substantially in the coming decades.[1] Persistent hyperglycaemia and insulin resistance lead to progressive metabolic, vascular, and neural damage, resulting in significant morbidity, premature mortality, and increased healthcare expenditure. In addition to well-recognised microvascular complications such as retinopathy, nephropathy, and peripheral neuropathy, diabetes is also associated with cardiovascular complications that substantially affect patient survival and quality of life.[2,3]Among the neurological complications of diabetes, cardiovascular autonomic neuropathy (CAN) is one of the most serious yet frequently underdiagnosed complications. CAN results from damage to the autonomic nerve fibres supplying the

heart and blood vessels, leading to impaired sympathetic and parasympathetic regulation of cardiovascular function. The Toronto Consensus Panel on Diabetic Neuropathy defines CAN as impairment of cardiovascular autonomic control in patients with established diabetes after excluding other causes of autonomic dysfunction.[4] Since autonomic impairment develops gradually and is often asymptomatic in its early stages, the condition frequently remains undetected until advanced disease develops. Clinically, CAN may manifest as resting tachycardia, orthostatic hypotension, exercise intolerance, silent myocardial ischaemia, prolonged QT interval, perioperative haemodynamic instability, cardiac arrhythmias, and an increased risk of sudden cardiac death.[2,4,5]The pathogenesis of cardiac autonomic dysfunction is complex and multifactorial. Chronic hyperglycaemia induces oxidative stress, activation of the polyol pathway, accumulation of advanced glycation end products (AGEs), endothelial dysfunction, mitochondrial injury, and chronic inflammation, resulting in neuronal ischemia, axonal degeneration, and demyelination of autonomic nerve fibres.[6,7] Parasympathetic dysfunction usually occurs first and is characterised by reduced heart rate variability, while sympathetic involvement develops with disease progression, leading to further impairment of cardiovascular regulation.[2,5]

The reported prevalence of CAN among patients with T2DM ranges from approximately 20% to more than 60%, depending on the duration of diabetes, glycaemic control, associated comorbidities, and diagnostic criteria used.[2,3,8] Increasing age, longer duration of diabetes, poor glycaemic control, hypertension, obesity, dyslipidaemia, diabetic nephropathy, retinopathy, and peripheral neuropathy are recognised risk factors for the development of autonomic dysfunction.[2,5,9] Importantly, several studies have demonstrated that CAN is an independent predictor of cardiovascular morbidity and mortality, with affected patients having significantly higher risks of silent myocardial infarction, heart failure, malignant arrhythmias, and all-cause mortality compared with diabetic patients without autonomic dysfunction.[2,3,5]Early detection of cardiac autonomic dysfunction is essential because timely intervention may delay disease progression and reduce cardiovascular complications. Cardiovascular autonomic reflex tests (CARTs), described by Ewing and Clarke, remain the standard bedside method for evaluating autonomic function and assess both parasympathetic and sympathetic activity through heart rate response to deep breathing, the Valsalva manoeuvre, standing (30:15 ratio), blood pressure response to standing, and sustained handgrip testing. Heart rate variability analysis and electrocardiographic parameters provide additional sensitive tools for identifying subclinical autonomic dysfunction before overt clinical manifestations become apparent.[4,5] The American Diabetes Association also recommends assessment of diabetic neuropathy, including autonomic involvement, particularly in patients with long-standing diabetes and those with microvascular complications.[10]Despite its significant prognostic implications, routine screening for cardiac autonomic dysfunction is still not universally practiced, particularly in resource-limited settings, resulting in delayed diagnosis and missed opportunities for early intervention.[2,4] Furthermore, data regarding the prevalence and determinants of cardiac autonomic dysfunction among Indian patients with type 2 diabetes remain limited. Therefore, the present study was undertaken to evaluate cardiac autonomic dysfunction in patients with type 2 diabetes mellitus and to determine its association with demographic characteristics, duration of diabetes, glycaemic control, and other clinical parameters.

**Methodology:**

This hospital-based observational cross-sectional study was conducted in the Department of General Medicine A total of 90 consecutive patients with diagnosed type 2 diabetes mellitus attending the outpatient and inpatient departments during the study period were enrolled after obtaining written informed consent.

**Inclusion Criteria**

- Patients aged 30–70 years.
- Diagnosed cases of type 2 diabetes mellitus (ADA criteria).
- Duration of diabetes ≥1 year.
- Willing to participate in the study.

**Exclusion Criteria**

Patients with type 1 diabetes, gestational diabetes, ischemic heart disease, heart failure, cardiac arrhythmias, uncontrolled hypertension, chronic kidney disease (stage IV/V), chronic liver disease, thyroid disorders, neurological diseases causing autonomic dysfunction, pregnancy, acute illness, or those receiving drugs affecting autonomic function were excluded.

**Data Collection**

Demographic details, medical history, duration of diabetes, smoking, alcohol intake, body mass index (BMI), blood pressure, and diabetic complications were recorded. Laboratory investigations included fasting blood glucose, postprandial blood glucose, glycated haemoglobin (HbA1c), serum creatinine, and lipid profile.

**Assessment of Cardiac Autonomic Function**

Cardiac autonomic function was assessed using Ewing's cardiovascular autonomic reflex tests (CARTs) under standard conditions, including:

- Heart rate response to deep breathing (E:I ratio)
- Heart rate response to standing (30:15 ratio)
- Valsalva manoeuvre
- Blood pressure response to standing
- Blood pressure response to sustained handgrip

Cardiac autonomic neuropathy was classified according to Ewing's criteria as normal, early, definite, or severe.

**Statistical Analysis**

Data were analysed using IBM SPSS Statistics version 26.0. Continuous variables were expressed as mean ± standard deviation (SD) and categorical variables as frequency and percentage. Comparisons were performed using the Student's t-test or Mann–Whitney U test for continuous variables and the Chi-square test or Fisher's exact test for categorical variables. Multivariable logistic regression analysis was performed to identify predictors of cardiac autonomic dysfunction. A p-value <0.05 was considered statistically significant.

**Results:**

A total of 90 patients with type 2 diabetes mellitus were included in the study. The mean age of the participants was 56.84 ± 10.92 years, with a median age of 57 years (IQR: 49–65 years) and an age range of 32–78 years. The majority belonged to the 46–60-year age group (43.3%), followed by those aged >60 years (36.7%), while 20.0% were aged 30–45 years. Males constituted 61.1% of the study population. The mean duration of diabetes was 9.12 ± 5.18 years, mean BMI was 27.82 ± 3.94 kg/m², and mean HbA1c was 8.46 ± 1.52%. Hypertension was the most common comorbidity, present in 46.7% of patients, followed by dyslipidaemia (40.0%), smoking (27.8%), and alcohol consumption (23.3%) (Table 1).Assessment of cardiac autonomic function using Ewing's cardiovascular autonomic reflex tests showed that the highest proportion of abnormal responses was observed with the Valsalva ratio (36.7%), followed by the heart rate response to deep breathing (35.6%), 30:15 ratio (33.3%), sustained handgrip test (28.9%), and blood pressure response to standing (23.3%). The distribution of normal, borderline, and abnormal autonomic reflex test responses is presented in (Table 2), while the comparative pattern of test abnormalities is illustrated in (Figure 1).

According to Ewing's classification, 39 (43.3%) patients had normal autonomic function, whereas 51 (56.7%) had cardiac autonomic dysfunction. Early CAN was identified in 21 (23.3%) patients, definite CAN in 20 (22.2%), and severe CAN in 10 (11.1%) patients (Table 3). The distribution of cardiac autonomic neuropathy severity is shown in (Figure 2).Patients with cardiac autonomic dysfunction were significantly older than those without dysfunction (60.21 ± 9.41 vs. 52.43 ± 11.22 years; p=0.001). They also had a longer duration of diabetes (11.82 ± 4.83 vs. 5.64 ± 3.21 years; p<0.001), higher HbA1c levels (9.12 ± 1.33% vs. 7.60 ± 1.21%; p<0.001), and higher BMI (28.61 ± 3.71 vs. 26.78 ± 3.84 kg/m²; p=0.029). Hypertension (60.8% vs. 28.2%; p=0.003) and dyslipidaemia (51.0% vs. 25.6%; p=0.017) were also significantly more common among patients with CAN (Table 4).On multivariable logistic regression analysis, duration of diabetes >10 years was the strongest independent predictor of cardiac autonomic dysfunction (adjusted OR 3.58; 95% CI: 1.69–7.58; p<0.001). Other significant predictors included HbA1c >8% (adjusted OR 2.91; 95% CI: 1.33–6.38; p=0.007), hypertension (adjusted OR 2.26; 95% CI: 1.02–5.01; p=0.044), and age >60 years (adjusted OR 2.14; 95% CI: 1.04–4.39; p=0.038). BMI ≥30 kg/m² was not a statistically significant predictor (adjusted OR 1.68; 95% CI: 0.76–3.74; p=0.201) (Table 5, Figure 3).

**Table 1. Baseline Demographic and Clinical Characteristics of the Study Population (n = 90)**

| **Variable** | **Value** |
|---|---|
| **Age (years)** | |
| Mean ± SD | **56.84 ± 10.92** |
| Median (IQR) | **57 (49–65)** |
| Range | **32–78** |
| **Age Group (years)** | n (%) |
| 30–45 | 18 (20.0) |
| 46–60 | 39 (43.3) |
| >60 | 33 (36.7) |
| **Sex** | |
| Male | 55 (61.1) |
| Female | 35 (38.9) |

| | |
|---|---|
| **Duration of Diabetes (years)** | **9.12 ± 5.18** |
| **BMI (kg/m²)** | **27.82 ± 3.94** |
| **HbA1c (%)** | **8.46 ± 1.52** |
| Hypertension | 42 (46.7) |
| Dyslipidaemia | 36 (40.0) |
| Smoking | 25 (27.8) |
| Alcohol consumption | 21 (23.3) |

**Table 2. Cardiovascular Autonomic Reflex Test Results (n = 90)**

| Test | Normal n (%) | Borderline n (%) | Abnormal n (%) |
|---|---|---|---|
| Deep breathing (E:I ratio) | 46 (51.1) | 12 (13.3) | 32 (35.6) |
| 30:15 ratio | 50 (55.6) | 10 (11.1) | 30 (33.3) |
| Valsalva ratio | 48 (53.3) | 9 (10.0) | 33 (36.7) |
| BP response to standing | 69 (76.7) | — | 21 (23.3) |
| Sustained handgrip test | 64 (71.1) | — | 26 (28.9) |

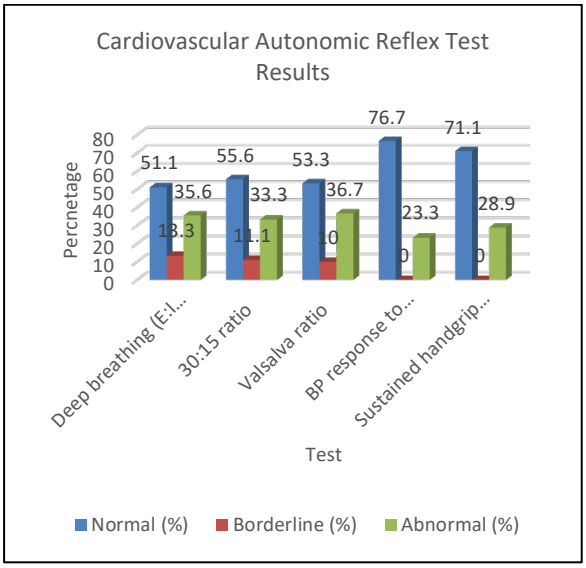


**Figure 1. Cardiovascular Autonomic Reflex Test Results (n = 90)**

**Table 3. Classification of Cardiac Autonomic Neuropathy (Ewing's Criteria)**

| Category | n (%) |
|---|---|
| Normal | 39 (43.3) |
| Early CAN | 21 (23.3) |
| Definite CAN | 20 (22.2) |
| Severe CAN | 10 (11.1) |

Overall prevalence of cardiac autonomic dysfunction = 51 (56.7%)

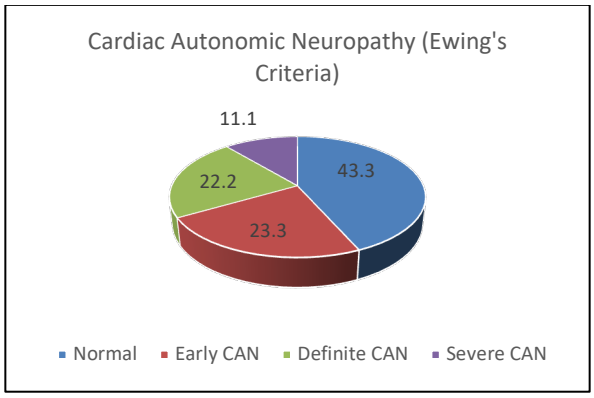


**Figure 2. Classification of Cardiac Autonomic Neuropathy (Ewing's Criteria)**

**Table 4. Comparison Between Patients With and Without Cardiac Autonomic Dysfunction**

| Variable | CAN Present (n=51) | CAN Absent (n=39) | p-value |
|---|---|---|---|
| Age (years) | 60.21 ± 9.41 | 52.43 ± 11.22 | **0.001** |
| Duration of diabetes (years) | 11.82 ± 4.83 | 5.64 ± 3.21 | **<0.001** |
| HbA1c (%) | 9.12 ± 1.33 | 7.60 ± 1.21 | **<0.001** |
| BMI (kg/m²) | 28.61 ± 3.71 | 26.78 ± 3.84 | **0.029** |
| Hypertension | 31 (60.8%) | 11 (28.2%) | **0.003** |

| | | | |
|---|---|---|---|
| Dyslipidaemia | 26 (51.0%) | 10 (25.6%) | **0.017** |

**Table 5. Multivariable Logistic Regression Analysis for Predictors of Cardiac Autonomic Dysfunction**

| Variable | Adjusted OR | 95% CI | p-value |
|---|---|---|---|
| Age >60 years | 2.14 | 1.04–4.39 | 0.038 |
| Duration of diabetes (>10 years) | 3.58 | 1.69–7.58 | <0.001 |
| HbA1c (>8%) | 2.91 | 1.33–6.38 | 0.007 |
| Hypertension | 2.26 | 1.02–5.01 | 0.044 |
| BMI ≥30 kg/m² | 1.68 | 0.76–3.74 | 0.201 |

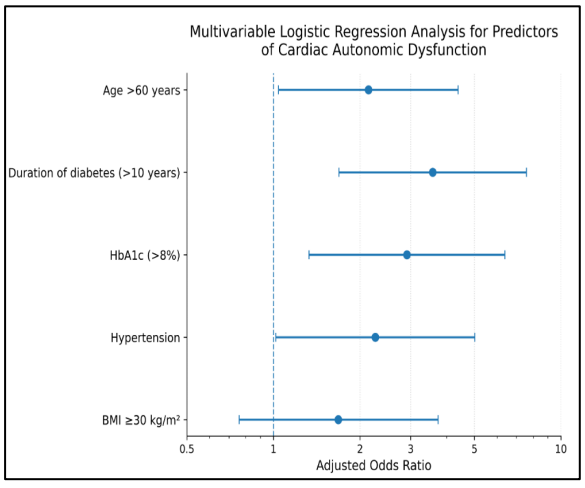


**Figure 3. Multivariable Logistic Regression Analysis for Predictors of Cardiac Autonomic Dysfunction**

## Discussion

In the present study, cardiac autonomic dysfunction (CAN) was detected in 51 (56.7%) of 90 patients with type 2 diabetes mellitus. According to Ewing's classification, 23.3% had early CAN, 22.2% had definite CAN, and 11.1% had severe CAN. These findings indicate that autonomic dysfunction is a common complication among patients with T2DM. Our findings are comparable to those of Ko et al. [11], who reported a baseline CAN prevalence of 55.7% among 1,458 patients with T2DM. Similarly, Valensi et al. [12], in a multicentre study of 396 diabetic patients, observed a CAN prevalence of 51%. Together, these studies support the high prevalence of autonomic dysfunction observed in our population.

Among the autonomic function tests, the Valsalva ratio showed the highest abnormality (36.7%), followed by the deep breathing test (35.6%), 30:15 ratio (33.3%), sustained handgrip (28.9%), and blood pressure response to standing (23.3%). These findings suggest predominant early parasympathetic involvement. Similarly, Valensi et al. [12] demonstrated that abnormalities in heart rate variability tests increased significantly with longer diabetes duration, while Verrotti et al. [13] reported reduced heart rate variability as one of the earliest manifestations of diabetic autonomic neuropathy.Patients with CAN in our study were significantly older (60.21 ± 9.41 vs. 52.43 ± 11.22 years; p=0.001), had a longer duration of diabetes (11.82 ± 4.83 vs. 5.64 ± 3.21 years; p<0.001), higher HbA1c (9.12 ± 1.33% vs. 7.60 ± 1.21%; p<0.001), higher BMI (28.61 ± 3.71 vs. 26.78 ± 3.84 kg/m²; p=0.029), and a greater prevalence of hypertension (60.8% vs. 28.2%; p=0.003) than those without CAN. These observations agree with Valensi et al. [12], who identified longer diabetes duration, obesity, and microvascular complications as significant determinants of CAN. Likewise, Verrotti et al. [13] reported that advancing age, prolonged diabetes duration, poor glycaemic control, hypertension, and obesity are major risk factors for autonomic neuropathy. Thomas [14] further explained that chronic hyperglycaemia induces oxidative stress and neuronal degeneration, leading to progressive autonomic nerve damage.In our study, duration of diabetes >10 years (adjusted OR 3.58; p<0.001), HbA1c >8% (adjusted OR 2.91; p=0.007), age >60 years (adjusted OR 2.14; p=0.038), and hypertension (adjusted OR 2.26; p=0.044) were independent predictors of CAN. Comparable findings were reported by Valensi et al. [12] and Ko et al. [11], who also found that increasing age, longer diabetes duration,

hypertension, and diabetic complications significantly increased the risk of autonomic dysfunction. Furthermore, Ko et al. [11] demonstrated that patients with CAN had a significantly higher risk of acute ischaemic stroke during 7 years of follow-up, with severe CAN increasing stroke risk by 2.7-fold.

The beneficial effect of intensive glycaemic control on autonomic function has been demonstrated by Pop-Busui et al. [15] in the DCCT/EDIC study, which showed that prior intensive insulin therapy significantly reduced the progression of cardiac autonomic neuropathy. Similarly, Buse et al. [16] emphasized aggressive management of glycaemia, blood pressure, lipids, and other cardiovascular risk factors for primary prevention of cardiovascular disease in diabetes. These observations are consistent with our finding that poor glycaemic control and hypertension were important predictors of CAN.

## Conclusion

Cardiac autonomic dysfunction was present in more than half of the patients with type 2 diabetes mellitus, indicating a high burden of subclinical cardiovascular autonomic impairment. Longer duration of diabetes, poor glycaemic control, older age, and hypertension were significant predictors of autonomic dysfunction. Routine screening using cardiovascular autonomic reflex tests may facilitate early diagnosis and timely intervention, thereby reducing future cardiovascular complications.

## Limitations

This study was conducted at a single tertiary care centre with a relatively small sample size of 90 patients, which may limit the generalizability of the findings. In addition, the cross-sectional design precluded assessment of temporal relationships and long-term cardiovascular outcomes.

## Ethical approval

Ethical approval for this study was obtained from the Institutional Ethics Committee prior to the commencement of the study. The study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki and applicable institutional guidelines.

## Informed Consent

Written informed consent was obtained from all participants prior to their enrolment in the study.

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## Conflict of Interest Declaration

The authors declare no conflict of interest.

## Data Availability Statement

All data generated or analysed during this study are available from the corresponding author upon reasonable request.

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