

Original Research Article

HEART RATE VARIABILITY AS AN EARLY MARKER OF AUTONOMIC NEUROPATHY IN TYPE 2 DIABETES MELLITUS: A STUDY FROM RAICHUR, KARNATAKA

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ABSTRACT

Background: Cardiac autonomic neuropathy (CAN) is a common but frequently underdiagnosed complication of type 2 diabetes mellitus (T2DM). Heart Rate Variability (HRV) is a non-invasive and sensitive tool that can detect subclinical autonomic dysfunction before overt clinical manifestations appear. The objective is to assess HRV parameters in patients with T2DM. To determine the prevalence of autonomic neuropathy using HRV. To correlate HRV indices with duration of diabetes, glycaemic control, and diabetic complications.

Materials and Methods: This hospital-based cross-sectional observational study included 150 patients with T2DM aged 30–70 years. Demographic details, clinical history, HbA1c, fasting blood sugar, and diabetic complications were recorded. Five-minute resting electrocardiograms were obtained to analyse time-domain and frequency-domain HRV parameters. Data were analyzed using SPSS version 26.0.

Results: The mean age was 55.4 ± 9.8 years, and 58.7% were males. Reduced SDNN was observed in 64.0% patients, reduced RMSSD in 58.7%, and decreased HF power in 61.3%. Cardiac autonomic neuropathy was detected in 68.7% of participants. Significant negative correlations were observed between HbA1c and SDNN ($r = -0.48, p < 0.001$) and between diabetes duration and RMSSD ($r = -0.44, p < 0.001$). Patients with diabetic retinopathy and nephropathy had significantly lower HRV values.

Conclusion: HRV is a valuable, non-invasive tool for early detection of cardiac autonomic neuropathy in T2DM. Poor glycaemic control and longer disease duration are strongly associated with reduced HRV.

Keywords: Type 2 diabetes mellitus; Heart rate variability; Cardiac autonomic neuropathy; HbA1c; Autonomic dysfunction.

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is one of the most common chronic metabolic disorders worldwide and is associated with significant morbidity and mortality due to its microvascular and macrovascular complications. The global burden of diabetes continues to rise, posing a major challenge to healthcare systems across both developed and developing countries.^[1,2]

Among the various complications of diabetes, diabetic autonomic neuropathy is a serious but often underdiagnosed condition that affects the autonomic nervous system. Cardiac autonomic neuropathy

(CAN), a subset of diabetic autonomic neuropathy, results from damage to the autonomic nerve fibers innervating the heart and blood vessels, leading to abnormalities in heart rate control and vascular dynamics.^[3,4]

The prevalence of cardiac autonomic neuropathy in patients with diabetes has been reported to range from 20% to 70%, depending on the duration of diabetes, glycaemic control, and methods used for diagnosis.^[5,6] Early stages of CAN are frequently asymptomatic; however, progression may lead to resting tachycardia, exercise intolerance, orthostatic hypotension, silent myocardial ischemia, and sudden cardiac death.^[7,8]

Heart Rate Variability (HRV) refers to the physiological beat-to-beat variation in consecutive RR intervals on electrocardiography and reflects the dynamic interplay between sympathetic and parasympathetic influences on the sinoatrial node.^[8] Reduced HRV is considered one of the earliest and most sensitive indicators of cardiac autonomic dysfunction and has significant prognostic implications.^[9,10]

HRV can be analyzed using time-domain parameters such as SDNN, RMSSD, and pNN50, and frequency-domain parameters including low-frequency (LF), high-frequency (HF), and LF/HF ratio. These parameters provide objective and quantitative information regarding autonomic balance and vagal tone.^[11]

Several studies have demonstrated that patients with type 2 diabetes mellitus exhibit significantly reduced HRV compared to healthy individuals. Poor glycaemic control, longer duration of diabetes, and the presence of diabetic complications such as retinopathy, nephropathy, and peripheral neuropathy are associated with greater impairment in autonomic function.^[12,13]

Because cardiac autonomic neuropathy remains clinically silent in its early stages, there is a need for simple, non-invasive, and reproducible methods for early detection. HRV analysis offers a practical and sensitive approach for identifying subclinical autonomic dysfunction, thereby facilitating timely intervention and improved cardiovascular outcomes.^[14,15]

The present study was undertaken to evaluate Heart Rate Variability as an early marker of autonomic neuropathy in patients with Type 2 Diabetes Mellitus and to determine its correlation with clinical and biochemical parameters such as duration of diabetes and HbA1c levels.

Aim: To evaluate Heart Rate Variability as an early marker of autonomic neuropathy in patients with Type 2 Diabetes Mellitus.

Objectives

Primary Objective

To assess heart rate variability parameters in patients with Type 2 Diabetes Mellitus.

Secondary Objectives

1. To determine the prevalence of cardiac autonomic neuropathy using HRV analysis.
2. To correlate HRV parameters with duration of diabetes.
3. To correlate HRV parameters with glycaemic control as measured by HbA1c.
4. To assess the association between HRV abnormalities and diabetic complications such as retinopathy, nephropathy, and neuropathy.

MATERIALS AND METHODS

Study Design: Hospital-based cross-sectional observational study.

Study Setting: Department of General Medicine, Navodaya Medical college hospital and research centre, Raichur, Karnataka, India.

Study Duration: 18 months.

Sample Size: A total of 150 patients with Type 2 Diabetes Mellitus.

Study Population: Adult patients diagnosed with Type 2 Diabetes Mellitus attending outpatient and inpatient services.

Inclusion Criteria

1. Patients aged 30 to 70 years.
2. Diagnosed cases of Type 2 Diabetes Mellitus according to American Diabetes Association criteria.
3. Duration of diabetes of at least one year.
4. Patients willing to provide informed written consent.

Exclusion Criteria

1. Type 1 Diabetes Mellitus.
2. Known ischemic heart disease.
3. Cardiac arrhythmias.
4. Pacemaker implantation.
5. Heart failure.
6. Thyroid disorders.
7. Chronic kidney disease stage IV and V.
8. Use of drugs affecting autonomic function such as beta-blockers.
9. Acute illness or infection.
10. Pregnancy.

Data Collection Procedure

A detailed history was obtained regarding age, sex, duration of diabetes, treatment details, and symptoms suggestive of autonomic dysfunction. Clinical examination included measurement of pulse rate, blood pressure, height, weight, and body mass index. Fundus examination, urine albumin estimation, and neuropathy assessment were performed to identify diabetic complications.

Laboratory Investigations

1. Fasting blood sugar.
2. Postprandial blood sugar.
3. HbA1c.
4. Serum creatinine.
5. Lipid profile.
6. Urine routine examination.
7. Urine albumin-creatinine ratio.

HRV Recording: A 5-minute resting electrocardiogram was recorded in the supine position after a 10-minute rest in a quiet room. Patients were advised to avoid caffeine, smoking, and strenuous exercise for at least 12 hours before the test.

HRV Parameters Assessed

Time Domain Parameters

1. SDNN (Standard Deviation of Normal-to-Normal Intervals)
2. RMSSD (Root Mean Square of Successive Differences)
3. pNN50 (Percentage of successive RR intervals differing by more than 50 ms)

Frequency Domain Parameters

1. Total Power
2. Low Frequency (LF)

3. High Frequency (HF)

4. LF/HF Ratio

Definition of Cardiac Autonomic Neuropathy:

Patients with two or more abnormal HRV parameters below age-adjusted reference values were considered to have cardiac autonomic neuropathy.

Statistical Analysis: Data were entered into Microsoft Excel and analyzed using IBM SPSS Statistics version 26.0. Continuous variables were

expressed as mean \pm standard deviation, and categorical variables as frequency and percentage. Independent t-test and ANOVA were used to compare means. Pearson correlation coefficient was used to assess relationships between HRV parameters and HbA1c and diabetes duration. Chi-square test was used for categorical data. A p-value < 0.05 was considered statistically significant.

RESULTS

Table 1: Age Distribution of Study Participants (n = 150)

| Age Group (years) | Frequency | Percentage (%) |
|-------------------|-----------|----------------|
| 30–40 | 18 | 12 |
| 41–50 | 34 | 22.7 |
| 51–60 | 56 | 37.3 |
| 61–70 | 42 | 28 |
| Total | 150 | 100 |

[Table 1] shows the age-wise distribution of the 150 study participants. The largest proportion of patients belonged to the 51–60 years age group, accounting for 56 participants (37.3%), followed by the 61–70 years age group with 42 participants (28.0%). Patients aged 41–50 years constituted 34 cases

(22.7%), while the youngest age group of 30–40 years included 18 participants (12.0%). These findings indicate that the majority of patients with Type 2 Diabetes Mellitus in the present study were middle-aged to elderly, with a predominance of individuals aged above 50 years.

Table 2: Gender Distribution

| Gender | Frequency | Percentage (%) |
|--------|-----------|----------------|
| Male | 88 | 58.7 |
| Female | 62 | 41.3 |
| Total | 150 | 100 |

[Table 2] depicts the gender distribution of the 150 study participants. Out of the total participants, 88 (58.7%) were males and 62 (41.3%) were females.

The findings indicate a male predominance in the study population, with males constituting more than half of the participants.

Table 3: Duration of Diabetes Mellitus

| Duration of Diabetes (years) | Frequency | Percentage (%) |
|------------------------------|-----------|----------------|
| 1–5 | 36 | 24 |
| 6–10 | 54 | 36 |
| 11–15 | 38 | 25.3 |
| >15 | 22 | 14.7 |
| Total | 150 | 100 |

[Table 3] shows the distribution of study participants according to the duration of Type 2 Diabetes Mellitus. The majority of patients, 54 (36.0%), had a duration of diabetes of 6–10 years, followed by 38 (25.3%) with a duration of 11–15 years. A total of 36 participants (24.0%) had diabetes for 1–5 years,

while 22 patients (14.7%) had diabetes for more than 15 years. These findings indicate that most participants had been living with diabetes for more than five years, suggesting a substantial risk for the development of chronic diabetic complications, including autonomic neuropathy.

Table 4: Glycaemic Control Based on HbA1c

| HbA1c Category | Frequency | Percentage (%) |
|-----------------------------|-----------|----------------|
| <7.0% (Good control) | 32 | 21.3 |
| 7.0–8.9% (Moderate control) | 58 | 38.7 |
| $\geq 9.0\%$ (Poor control) | 60 | 40 |
| Total | 150 | 100 |

[Table 4] presents the distribution of study participants according to glycaemic control based on HbA1c levels. Poor glycaemic control (HbA1c $\geq 9.0\%$) was observed in 60 participants (40.0%), making it the most common category. Moderate glycaemic control (HbA1c 7.0–8.9%) was seen in 58 participants (38.7%), while only 32 participants

(21.3%) had good glycaemic control with HbA1c levels below 7.0%. These findings indicate that the majority of patients had suboptimal glycaemic control, which is an important risk factor for the development and progression of diabetic autonomic neuropathy.

Table 5: Prevalence of Diabetic Complications

| Complication | Present n (%) | Absent n (%) |
|-----------------------|---------------|--------------|
| Retinopathy | 48 (32.0) | 102 (68.0) |
| Nephropathy | 36 (24.0) | 114 (76.0) |
| Peripheral Neuropathy | 52 (34.7) | 98 (65.3) |

[Table 5] shows the prevalence of diabetic complications among the 150 study participants. Peripheral neuropathy was the most common complication, present in 52 patients (34.7%), followed by diabetic retinopathy in 48 patients (32.0%) and diabetic nephropathy in 36 patients (24.0%). The remaining participants did not have

these complications, with 98 (65.3%) free of peripheral neuropathy, 102 (68.0%) free of retinopathy, and 114 (76.0%) free of nephropathy. These findings indicate that microvascular complications were common in the study population and may be associated with an increased risk of cardiac autonomic dysfunction.

Table 6: Mean HRV Time-Domain Parameters

| Parameter | Mean ± SD | Reference Interpretation |
|------------|-------------|--------------------------|
| SDNN (ms) | 31.8 ± 12.6 | Reduced |
| RMSSD (ms) | 20.4 ± 10.2 | Reduced |
| pNN50 (%) | 4.8 ± 3.6 | Reduced |

[Table 6] presents the mean values of time-domain heart rate variability (HRV) parameters among the study participants. The mean SDNN was 31.8 ± 12.6 ms, the mean RMSSD was 20.4 ± 10.2 ms, and the mean pNN50 was 4.8 ± 3.6%. All three parameters were reduced when compared with standard

reference values, indicating diminished beat-to-beat variability and impaired parasympathetic activity. These findings suggest the presence of significant autonomic dysfunction in patients with Type 2 Diabetes Mellitus and support the utility of HRV as an early marker of cardiac autonomic neuropathy.

Table 7: Mean HRV Frequency-Domain Parameters

| Parameter | Mean ± SD |
|--------------------------------|-------------|
| Total Power (ms ²) | 842 ± 356 |
| LF Power (ms ²) | 332 ± 148 |
| HF Power (ms ²) | 198 ± 96 |
| LF/HF Ratio | 2.42 ± 0.88 |

[Table 7] presents the frequency-domain heart rate variability (HRV) parameters among the study participants. The mean total power was 842 ± 356 ms², indicating an overall reduction in autonomic modulation. The mean low-frequency (LF) power was 332 ± 148 ms², while the mean high-frequency (HF) power was 198 ± 96 ms². The relatively lower

HF power reflects reduced parasympathetic (vagal) activity. The mean LF/HF ratio was 2.42 ± 0.88, suggesting a shift toward sympathetic predominance and an imbalance in sympathovagal regulation. These findings further support the presence of cardiac autonomic dysfunction in patients with Type 2 Diabetes Mellitus.

Table 8: Prevalence of Abnormal HRV Parameters

| HRV Parameter | Abnormal n | Percentage (%) |
|---------------|------------|----------------|
| SDNN | 96 | 64 |
| RMSSD | 88 | 58.7 |
| pNN50 | 82 | 54.7 |
| HF Power | 92 | 61.3 |

[Table 8] shows the prevalence of abnormal heart rate variability (HRV) parameters among the 150 study participants. Reduced SDNN was the most common abnormality, observed in 96 patients (64.0%), followed by decreased HF power in 92 patients (61.3%). Reduced RMSSD was present in 88 patients

(58.7%), while abnormal pNN50 was noted in 82 patients (54.7%). These findings indicate that a substantial proportion of patients with Type 2 Diabetes Mellitus had impaired HRV parameters, reflecting early cardiac autonomic dysfunction, particularly involving parasympathetic activity.

Table 9: Prevalence of Cardiac Autonomic Neuropathy

| Cardiac Autonomic Neuropathy | Frequency | Percentage (%) |
|------------------------------|-----------|----------------|
| Present | 103 | 68.7 |
| Absent | 47 | 31.3 |
| Total | 150 | 100 |

[Table 9] shows the prevalence of cardiac autonomic neuropathy among the study participants based on

heart rate variability analysis. Cardiac autonomic neuropathy was detected in 103 out of 150 patients,

accounting for 68.7% of the study population, while 47 patients (31.3%) did not demonstrate evidence of autonomic neuropathy. These findings indicate that more than two-thirds of patients with Type 2

Diabetes Mellitus had evidence of cardiac autonomic dysfunction, highlighting the high burden of subclinical autonomic neuropathy in this population.

Table 10: Correlation of HRV Parameters with HbA1c and Duration of Diabetes

| Variable | SDNN (r) | RMSSD (r) | p-value |
|----------------------|----------|-----------|---------|
| HbA1c | -0.48 | -0.42 | <0.001 |
| Duration of Diabetes | -0.46 | -0.44 | <0.001 |

[Table 10] illustrates the correlation between heart rate variability (HRV) parameters and key clinical variables. HbA1c showed a significant negative correlation with SDNN ($r = -0.48$) and RMSSD ($r = -0.42$), indicating that poorer glycaemic control was associated with lower HRV values and greater autonomic dysfunction. Similarly, duration of diabetes demonstrated a significant negative correlation with SDNN ($r = -0.46$) and RMSSD ($r =$

-0.44), suggesting that longer duration of disease was associated with progressive impairment of autonomic function. All correlations were statistically highly significant ($p < 0.001$). These findings emphasize that both poor glycaemic control and prolonged diabetes are important determinants of reduced heart rate variability and cardiac autonomic neuropathy in patients with Type 2 Diabetes Mellitus.

Table 11: Comparison of SDNN in Patients with and Without Diabetic Complications

| Complication | Present (Mean \pm SD) | Absent (Mean \pm SD) | p-value |
|-----------------------|-------------------------|------------------------|---------|
| Retinopathy | 24.8 \pm 8.2 | 35.1 \pm 12.4 | <0.001 |
| Nephropathy | 23.9 \pm 7.8 | 34.3 \pm 11.9 | <0.001 |
| Peripheral Neuropathy | 25.6 \pm 8.6 | 35.0 \pm 12.1 | <0.001 |

[Table 11] compares the mean SDNN values between patients with and without diabetic complications. Patients with diabetic retinopathy had a significantly lower mean SDNN (24.8 ± 8.2 ms) compared to those without retinopathy (35.1 ± 12.4 ms). Similarly, participants with nephropathy showed a lower mean SDNN (23.9 ± 7.8 ms) than those without nephropathy (34.3 ± 11.9 ms). Patients with peripheral neuropathy also had reduced SDNN values (25.6 ± 8.6 ms) compared to participants without neuropathy (35.0 ± 12.1 ms). All differences were statistically highly significant ($p < 0.001$). These findings indicate that the presence of diabetic microvascular complications is strongly associated with greater impairment in heart rate variability and more severe cardiac autonomic dysfunction.

DISCUSSION

In the present study, the mean age of the participants was 55.4 ± 9.8 years, with the majority of patients (37.3%) belonging to the 51–60 years age group, followed by 28.0% in the 61–70 years age group. This indicates that Type 2 Diabetes Mellitus and associated autonomic dysfunction were predominantly observed in middle-aged and elderly individuals. [Table 1]

These findings are comparable to those reported by Benichou et al¹⁰, who observed that reduced heart rate variability and cardiac autonomic dysfunction were more common in older adults with Type 2 Diabetes Mellitus. Vinik and Casellini¹² also noted that advancing age is an important determinant of diabetic autonomic neuropathy due to age-related decline in parasympathetic activity. Freeman et al,¹³ similarly reported that autonomic dysfunction becomes

increasingly prevalent with advancing age and longer disease duration.

Thus, the age distribution in the present study is consistent with previous literature showing that cardiac autonomic neuropathy is more frequently detected in patients above 50 years of age.

In the present study, males constituted 58.7% of the study population, while females accounted for 41.3%, indicating a slight male predominance. [Table 2]

Similar observations were reported by Ziegler et al,¹⁵ who found a higher proportion of male participants in studies evaluating cardiovascular autonomic dysfunction in diabetes. Benichou et al,¹⁰ in their systematic review and meta-analysis, included studies where male participants predominated, reflecting the higher prevalence of Type 2 Diabetes Mellitus and cardiovascular risk factors among men in many populations.

Vinik et al and Pop-Busui et al reported that although cardiac autonomic neuropathy can affect both sexes, men often exhibit a higher burden of cardiovascular risk factors that may predispose them to earlier autonomic dysfunction.^{3,4}

Therefore, the gender distribution in the present study is in agreement with previous studies demonstrating a modest male predominance among patients with Type 2 Diabetes Mellitus undergoing evaluation for cardiac autonomic neuropathy.

In the present study, the mean time-domain heart rate variability (HRV) parameters were markedly reduced, with SDNN of 31.8 ± 12.6 ms, RMSSD of 20.4 ± 10.2 ms, and pNN50 of $4.8 \pm 3.6\%$. These findings indicate significant impairment of parasympathetic activity and reduced overall

autonomic modulation in patients with Type 2 Diabetes Mellitus. [Table 6]

These observations are consistent with the findings of Benichou et al,^[10] who, in a systematic review and meta-analysis, reported significantly lower SDNN, RMSSD, and pNN50 values in patients with Type 2 Diabetes Mellitus compared with healthy controls. The study concluded that reduced HRV is a sensitive marker of early cardiac autonomic neuropathy.

Bernardi et al,^[14] also demonstrated substantially reduced parasympathetic indices, particularly RMSSD and pNN50, in diabetic patients, indicating impaired vagal modulation of heart rate. Similarly, Ziegler et al,^[15] found that SDNN and other time-domain parameters were significantly lower in diabetic individuals with autonomic dysfunction compared with those without neuropathy.

Vinik and Casellini,^[12] reported that reduced SDNN and RMSSD are among the earliest abnormalities detected in diabetic autonomic neuropathy and correlate closely with disease duration and glycaemic control. Freeman et al,^[13] further emphasized that lower HRV parameters are associated with increased cardiovascular risk and mortality in diabetic patients. Thus, the findings of the present study are in close agreement with previous literature and confirm that time-domain HRV parameters, particularly SDNN and RMSSD, are significantly reduced in patients with Type 2 Diabetes Mellitus and can serve as reliable early markers of cardiac autonomic neuropathy.

In the present study, reduced SDNN was the most common abnormal heart rate variability (HRV) parameter, observed in 96 patients (64.0%), followed by decreased HF power in 92 patients (61.3%). Reduced RMSSD was present in 88 patients (58.7%), while abnormal pNN50 was noted in 82 patients (54.7%). These findings indicate that a substantial proportion of patients with Type 2 Diabetes Mellitus had impaired HRV parameters, reflecting early parasympathetic dysfunction and reduced overall autonomic modulation. [Table 8]

These findings are comparable to those reported by Benichou et al¹⁰, who demonstrated that SDNN and RMSSD are consistently reduced in a large proportion of patients with Type 2 Diabetes Mellitus, even before the appearance of overt symptoms of autonomic neuropathy. Ziegler et al,^[15] similarly observed that abnormalities in SDNN and spectral HRV parameters were among the earliest indicators of cardiovascular autonomic dysfunction in diabetic patients. Bernardi et al,^[14] also reported reduced HF power and vagally mediated indices in diabetic individuals, highlighting early parasympathetic impairment.

In the present study, cardiac autonomic neuropathy (CAN), defined by the presence of two or more abnormal HRV parameters, was detected in 103 out of 150 patients (68.7%). This high prevalence suggests that subclinical autonomic dysfunction is common among patients with Type 2 Diabetes Mellitus. [Table 9]

The prevalence observed in the present study is consistent with reports by Spallone et al⁵, who noted that the prevalence of CAN in diabetic patients ranges from 20% to 70% depending on disease duration, glycaemic control, and diagnostic criteria. Vinik et al,^[3] and Maser and Lenhard,^[9] also documented that CAN is highly prevalent in patients with long-standing diabetes and poor metabolic control. Pop-Busui et al,^[4] emphasized that many cases remain asymptomatic and can only be identified through objective tests such as HRV analysis.

Overall Interpretation

The high frequency of abnormal HRV parameters [Table 8] and the corresponding prevalence of cardiac autonomic neuropathy [Table 9] in the present study are in close agreement with previously published literature. These findings confirm that HRV analysis is a sensitive and practical method for detecting early cardiac autonomic dysfunction in patients with Type 2 Diabetes Mellitus, particularly in those with poor glycaemic control and longer disease duration.

CONCLUSION

HRV is a valuable, non-invasive tool for early detection of cardiac autonomic neuropathy in T2DM. Poor glycaemic control and longer disease duration are strongly associated with reduced HRV.

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