e-ISSN: 0976-822X, p-ISSN:2961-6042

Available online on http://www.ijcpr.com/

International Journal of Current Pharmaceutical Review and Research 2026; 18(5); 1768-1775

Original Research Article

The Association Between Time Domain Analysis of Heart Rate Variability with Glycated Haemoglobin and Duration of Type 2 Diabetes Mellitus: A Cross-Sectional Study

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Received: 22-03-2026 / Revised: 24-04-2026 / Accepted: 28-05-2026

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Conflict of interest: Nil

Abstract:

Background: Type 2 Diabetes Mellitus (T2DM) is a chronic metabolic disorder associated with progressive microvascular and macrovascular complications. Cardiac autonomic neuropathy (CAN) is one of the serious but often underdiagnosed complications of diabetes mellitus and is associated with increased cardiovascular morbidity and mortality. Heart rate variability (HRV) is a non-invasive tool used to evaluate autonomic nervous system function. Time domain analysis of HRV has emerged as a reliable method for detecting autonomic dysfunction in diabetic patients. Poor glycaemic control and prolonged duration of diabetes are considered major contributors to autonomic imbalance and reduced HRV.

Aim: To evaluate the association between time domain parameters of heart rate variability with glycated haemoglobin (HbA1c) levels and duration of Type 2 Diabetes Mellitus.

Materials and Methods: This hospital-based cross-sectional observational study was conducted in the Department of Pharmacology in collaboration with the Department of Medicine at Darbhanga Medical College & Hospital, Laheriasarai, Bihar, from April 2025 to September 2025. A total of 100 diagnosed cases of Type 2 Diabetes Mellitus aged between 30 and 70 years were included in the study. HRV analysis was performed using a 5-minute resting electrocardiogram recording. Time domain parameters including SDNN, RMSSD, NN50, and pNN50 were assessed. HbA1c levels and duration of diabetes were recorded for all participants. Statistical analysis was performed using Pearson's correlation coefficient, independent t-test, and ANOVA.

Results: The mean age of study participants was 54.18±9.62 years. Mean HbA1c level was 8.14±1.52%. Significant negative correlation was observed between HbA1c and SDNN ($r=-0.52$, $p<0.001$), RMSSD ($r=-0.47$, $p<0.001$), NN50 ($r=-0.41$, $p=0.002$), and pNN50 ($r=-0.39$, $p=0.004$). Duration of diabetes also demonstrated significant inverse association with HRV parameters. Patients with diabetes duration >10 years had significantly lower mean SDNN and RMSSD values compared to patients with duration <5 years ($p<0.001$).

Conclusion: Poor glycaemic control and longer duration of Type 2 Diabetes Mellitus are significantly associated with reduced heart rate variability, indicating progressive cardiac autonomic dysfunction. Time domain HRV analysis may serve as a valuable non-invasive tool for early detection of autonomic neuropathy in diabetic patients.

Keywords: Type 2 Diabetes Mellitus; Heart Rate Variability; HbA1c; Cardiac Autonomic Neuropathy; Time Domain Analysis; SDNN.

DOI: 10.25258/ijcpr.18.5.282

Introduction

Type 2 Diabetes Mellitus (T2DM) is one of the most prevalent chronic metabolic disorders worldwide and has become a major public health challenge due to its rapidly increasing incidence and associated complications. According to the International Diabetes Federation, the global burden of diabetes is rising steadily, particularly in developing countries such as India, which is often referred to as the "diabetes capital of the world." The chronic hyperglycaemic state of diabetes leads to structural and functional abnormalities affecting multiple organ systems, including cardiovascular, renal, neurological, and retinal systems.[1]

Among the various complications associated with diabetes mellitus, diabetic autonomic neuropathy is considered one of the most serious yet frequently

underdiagnosed complications. Cardiac autonomic neuropathy (CAN) results from damage to autonomic nerve fibers innervating the heart and blood vessels, leading to abnormalities in heart rate control and vascular dynamics.[2] CAN has been associated with exercise intolerance, resting tachycardia, orthostatic hypotension, silent myocardial ischemia, arrhythmias, and increased risk of sudden cardiac death.

Heart rate variability (HRV) refers to beat-to-beat variation in the cardiac cycle and reflects autonomic regulation of the cardiovascular system.[3] It is considered a sensitive marker of sympathovagal balance and autonomic nervous system activity. Reduced HRV is regarded as an early indicator of autonomic dysfunction and has been associated with increased cardiovascular morbidity and mortality.

The autonomic nervous system maintains cardiovascular homeostasis through coordinated sympathetic and parasympathetic influences on the sinoatrial node. In healthy individuals, there is a dynamic fluctuation in heart rate in response to physiological demands. However, in diabetic patients, chronic hyperglycaemia and metabolic disturbances lead to neuronal ischemia, oxidative stress, and demyelination, resulting in autonomic imbalance and reduced vagal tone.[4]

Time domain analysis is one of the simplest and most commonly used methods for HRV assessment. It involves statistical analysis of RR intervals obtained from electrocardiographic recordings. Important time domain parameters include SDNN (standard deviation of normal-to-normal intervals), RMSSD (root mean square of successive differences), NN50 (number of adjacent NN intervals differing by more than 50 ms), and pNN50 (percentage of adjacent NN intervals differing by more than 50 ms).[5] These parameters primarily reflect parasympathetic modulation and overall autonomic activity.

Glycated haemoglobin (HbA1c) is a widely accepted marker for long-term glycaemic control and reflects average blood glucose levels over the previous 2–3 months.[6] Poor glycaemic control has been implicated in the development and progression of diabetic neuropathy and cardiovascular complications. Several studies have reported inverse associations between HbA1c levels and HRV indices, suggesting that chronic hyperglycaemia contributes significantly to autonomic dysfunction.

Duration of diabetes is another important determinant of diabetic complications. Prolonged exposure to hyperglycaemia may lead to progressive neuronal damage and worsening autonomic dysfunction.[7] Patients with longer duration of diabetes have been shown to exhibit significantly reduced HRV parameters compared to recently diagnosed individuals.

Early detection of cardiac autonomic dysfunction is essential because intervention at an early stage may help reduce cardiovascular complications and improve quality of life.[8] HRV analysis provides a simple, non-invasive, reproducible, and cost-effective method for evaluating autonomic function in diabetic patients.

Although several studies have evaluated HRV changes in diabetic patients, limited data are available from eastern India regarding the relationship between time domain HRV parameters, glycaemic control, and duration of diabetes. Therefore, the present study was undertaken to assess the association between time domain analysis of heart rate variability with glycated haemoglobin levels and duration of Type 2 Diabetes Mellitus in patients attending a tertiary care hospital in Bihar.

Materials and Methods

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

Study Place: Department of Pharmacology in collaboration with the Department of Medicine, Darbhanga Medical College & Hospital, Laheriasarai, Bihar.

Study Duration: Six months (April 2025 to September 2025).

Sample Size: A total of 100 patients with Type 2 Diabetes Mellitus were included in the study.

Study Population: Diagnosed cases of Type 2 Diabetes Mellitus attending the Medicine outpatient department and inpatient wards.

Inclusion Criteria

1. Patients diagnosed with Type 2 Diabetes Mellitus.
2. Age between 30 and 70 years.
3. Patients willing to participate in the study.
4. Patients providing informed written consent.

Exclusion Criteria

1. Type 1 Diabetes Mellitus.
2. History of ischemic heart disease.
3. Cardiac arrhythmias.
4. Hypertension under beta-blocker therapy.
5. Chronic kidney disease.
6. Thyroid disorders.
7. Chronic alcohol consumption.
8. Smokers.
9. Patients on drugs affecting autonomic function.

Methodology: Detailed clinical history including age, sex, duration of diabetes, treatment history, and associated illnesses was recorded. General physical

examination and systemic examination were performed.

Venous blood samples were collected for estimation of glycated haemoglobin (HbA1c). Patients were advised to avoid caffeine, smoking, and vigorous physical activity prior to HRV recording.

Heart rate variability analysis was performed using a standard 5-minute resting electrocardiographic recording in supine position under controlled laboratory conditions.

Time domain parameters evaluated included:

1. SDNN (Standard Deviation of NN intervals)
2. RMSSD (Root Mean Square of Successive Differences)
3. NN50
4. pNN50

Patients were categorized according to HbA1c levels:

- HbA1c <7%
- HbA1c 7–9%
- HbA1c >9%

Patients were also categorized based on duration of diabetes:

- <5 years
- 5–10 years
- >10 years

Statistical Analysis: Data were entered into Microsoft Excel and analyzed using SPSS version 25. Quantitative variables were expressed as mean ± standard deviation. Categorical variables were expressed as percentages. Pearson's correlation coefficient was used to assess correlation between HRV parameters and HbA1c levels. Independent t-test and one-way ANOVA were used for comparison between groups. A p-value <0.05 was considered statistically significant.

Results

A total of 100 patients with Type 2 Diabetes Mellitus were included in the present study. All participants successfully underwent heart rate variability (HRV) analysis using 5-minute resting electrocardiographic recording. The demographic profile, glycaemic status, duration of diabetes, and HRV parameters were analyzed.

The baseline demographic and clinical characteristics of the study participants are presented in Table 1. The mean age of the participants was 54.18±9.62 years. Among the 100 participants, 58% were males and 42% were females. The mean duration of diabetes was 8.24±4.36 years, while the mean HbA1c level was 8.14±1.52%. The average body mass index (BMI) of the study population was 26.48±3.12 kg/m².

Table 1: Demographic and Clinical Characteristics of Study Participants

Variable	Value
Mean age (years)	54.18±9.62
Male	58 (58%)
Female	42 (42%)
Mean duration of diabetes (years)	8.24±4.36
Mean HbA1c (%)	8.14±1.52
Mean BMI (kg/m²)	26.48±3.12

The age-wise distribution of study participants is illustrated in Figure 1. The majority of patients belonged to the age group of 51–60 years (34%), followed by 41–50 years (26%).

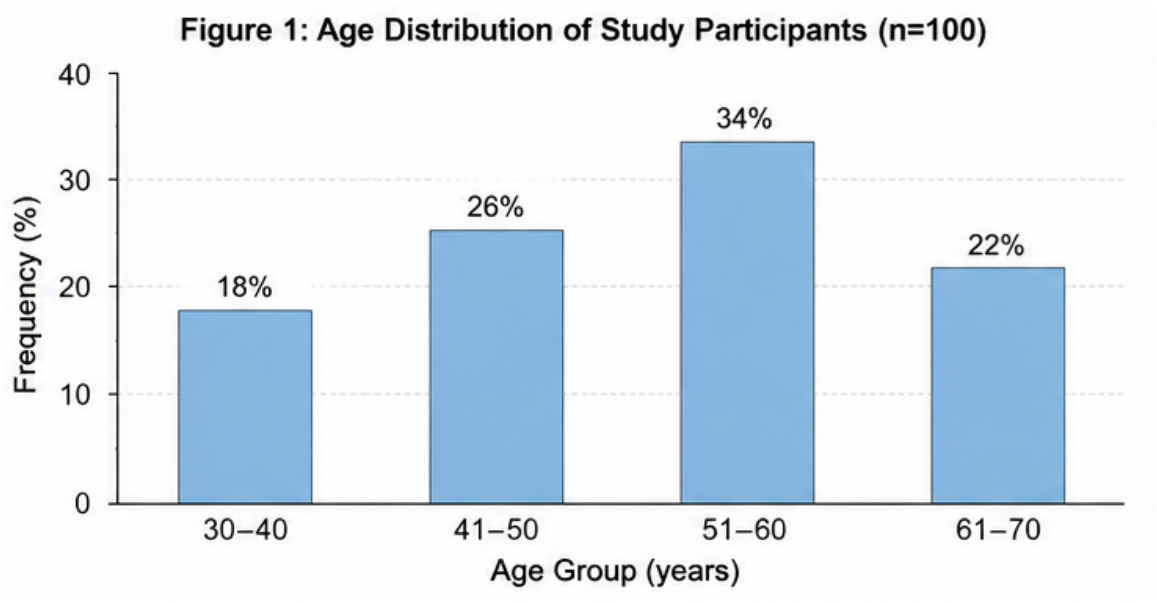

Figure 1: Age Distribution of Study Participants

The mean values of time domain HRV parameters including SDNN, RMSSD, NN50, and pNN50 are summarized in Table 2. The mean SDNN value among diabetic patients was 36.82±11.64 ms, while the mean RMSSD value was 28.16±10.42 ms.

Table 2: Mean Time Domain HRV Parameters Among Study Participants

HRV Parameter	Mean ± SD
SDNN (ms)	36.82±11.64
RMSSD (ms)	28.16±10.42
NN50	18.34±8.72
pNN50 (%)	7.24±3.84

The distribution of mean HRV parameters is depicted in Figure 2.

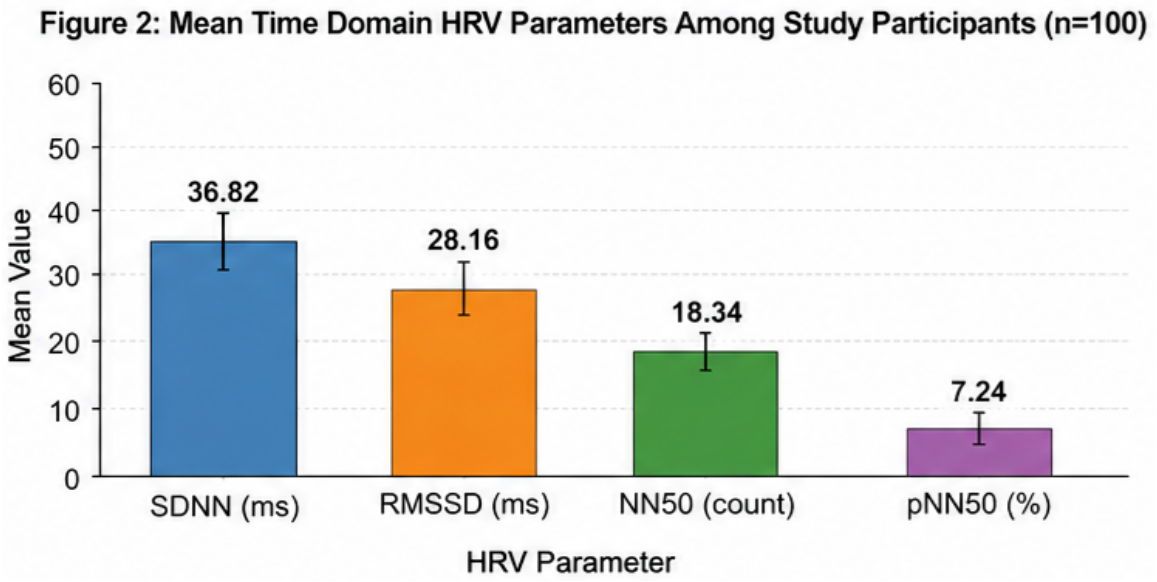

Figure 2: Mean Time Domain HRV Parameters

The association between glycated haemoglobin (HbA1c) levels and HRV parameters was evaluated using Pearson's correlation analysis. Significant negative correlations were observed between HbA1c levels and all major HRV parameters as shown in Table 3. SDNN demonstrated a moderate negative correlation with HbA1c ($r = -0.52$, $p<0.001$). RMSSD also showed significant inverse

correlation with HbA1c (r = -0.47, p<0.001). Similarly, NN50 and pNN50 demonstrated statistically significant negative correlations with HbA1c levels.

Table 3: Correlation Between HbA1c and HRV Parameters

HRV Parameter	Correlation Coefficient (r)	p-value
SDNN	-0.52	<0.001
RMSSD	-0.47	<0.001
NN50	-0.41	0.002
pNN50	-0.39	0.004

The inverse relationship between HbA1c levels and SDNN values is illustrated in Figure 3. Patients with HbA1c levels greater than 9% demonstrated markedly reduced SDNN values compared to patients with HbA1c less than 7%.

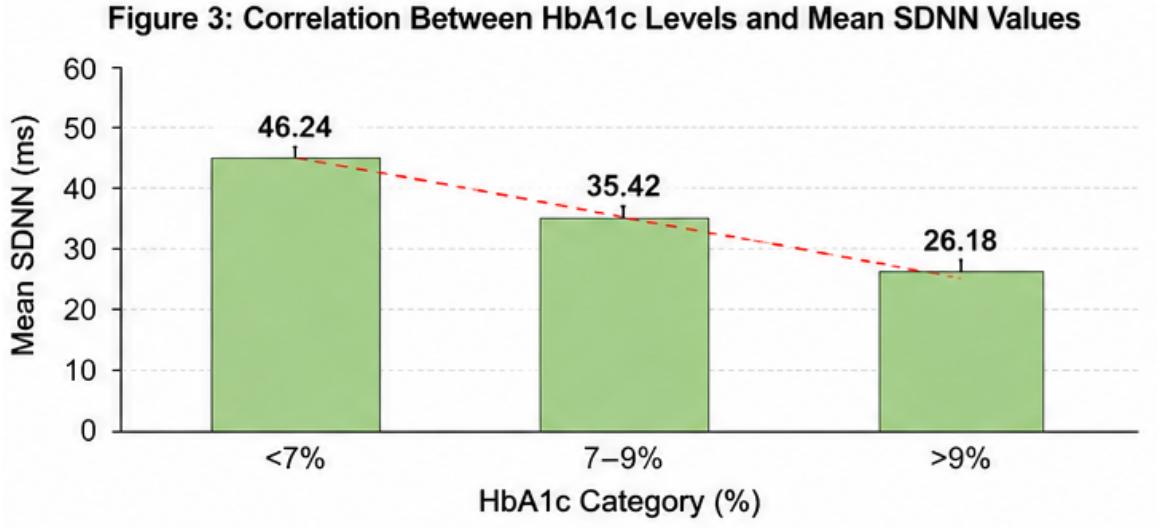

Figure 3: Correlation Between HbA1c Levels and Mean SDNN Values

Patients were further categorized according to duration of diabetes mellitus. Comparison of HRV parameters according to duration of diabetes is presented in Table 4. Patients with diabetes duration greater than 10 years demonstrated significantly lower SDNN and RMSSD values compared to patients with duration less than 5 years. The differences were statistically significant (p<0.001).

Table 4: Comparison of HRV Parameters According to Duration of Diabetes

Duration of Diabetes	SDNN (ms)	RMSSD (ms)	p-value
<5 years	44.82±10.12	34.26±8.42	<0.001
5–10 years	35.16±9.84	27.42±7.94	0.002
>10 years	24.84±8.64	18.36±6.52	<0.001

Figure 4 demonstrates the progressive decline in mean SDNN values with increasing duration of diabetes mellitus.

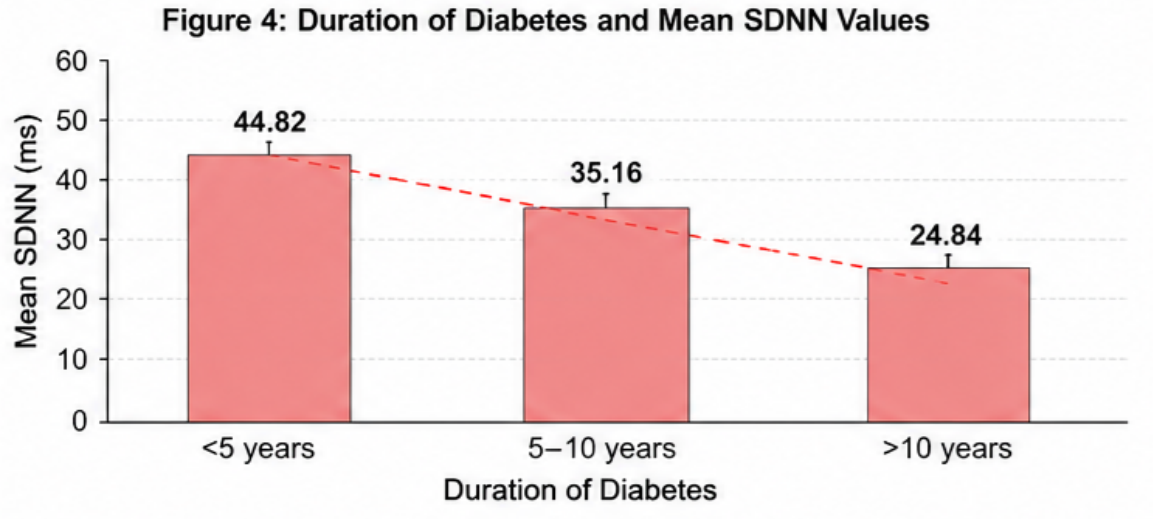

Figure 4: Duration of Diabetes and Mean SDNN Values

The study participants were also divided into controlled and uncontrolled diabetic groups based on HbA1c levels. Comparison of HRV parameters between the two groups is shown in Table 5. Patients with uncontrolled diabetes (HbA1c ≥7%) had significantly lower SDNN, RMSSD, and pNN50 values compared to patients with controlled diabetes (HbA1c <7%). The differences were statistically significant.

Table 5: Comparison Between Controlled and Uncontrolled Diabetes

Variable	HbA1c <7%	HbA1c ≥7%	p-value
SDNN (ms)	46.24±9.82	31.18±10.24	<0.001
RMSSD (ms)	35.12±8.44	24.28±8.16	<0.001
pNN50 (%)	9.18±3.22	5.82±2.94	0.003

Figure 5 illustrates the comparison of SDNN values between controlled and uncontrolled diabetic patients.

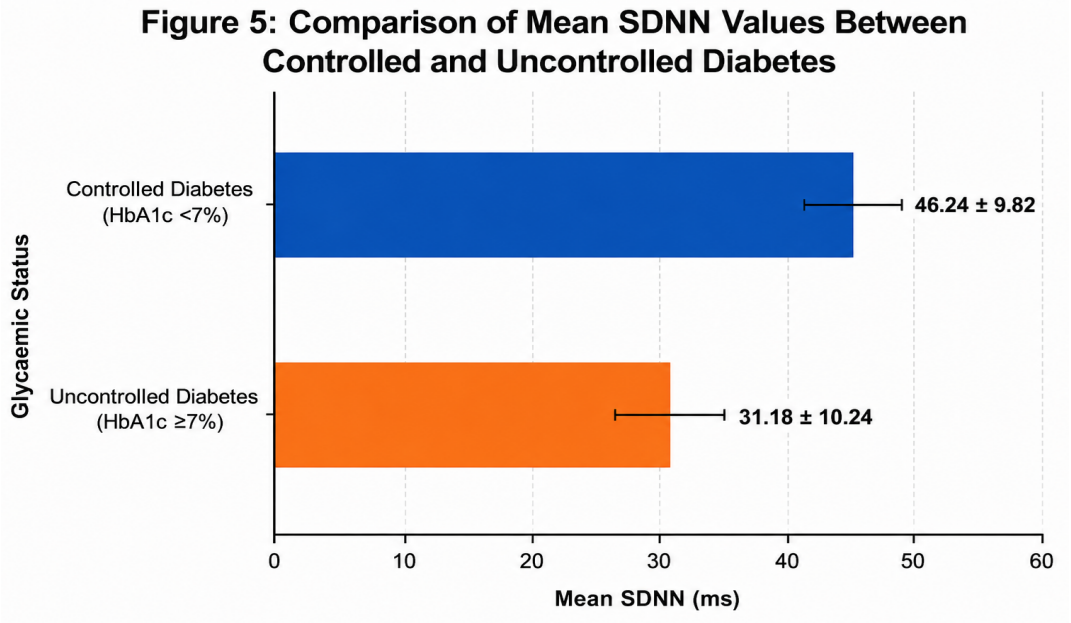

Figure 5: Comparison of Mean SDNN Values Between Controlled and Uncontrolled Diabetes

Overall, the present study demonstrated significant reduction in time domain heart rate variability parameters with worsening glycaemic control and increasing duration of Type 2 Diabetes Mellitus. Reduced HRV indices were strongly associated with elevated HbA1c levels and prolonged disease duration, indicating progressive cardiac autonomic dysfunction among diabetic patients.

Discussion

The present study evaluated the association between time domain parameters of heart rate variability with glycated haemoglobin levels and duration of Type 2 Diabetes Mellitus. The findings demonstrated significant reduction in HRV parameters among patients with poor glycaemic control and longer duration of diabetes, indicating progressive cardiac autonomic dysfunction.

In the present study, the mean age of participants was 54.18±9.62 years, which is comparable to previous studies evaluating autonomic dysfunction among diabetic patients.[9] The majority of participants belonged to the middle-aged and elderly population, reflecting the increasing prevalence of Type 2 Diabetes Mellitus with advancing age.

The mean HbA1c level observed in the present study was 8.14±1.52%, indicating suboptimal glycaemic control among a significant proportion of patients. Chronic hyperglycaemia has been implicated in the development of microvascular and neuropathic complications through mechanisms involving oxidative stress, advanced glycation end products, endothelial dysfunction, and neuronal ischemia.[10]

Heart rate variability analysis is widely regarded as a sensitive marker for assessing autonomic nervous system activity. In the current study, mean SDNN and RMSSD values were significantly reduced among patients with higher HbA1c levels. SDNN reflects overall autonomic modulation, whereas RMSSD primarily reflects parasympathetic activity.[11] Reduction in these parameters suggests impaired vagal tone and autonomic imbalance.

A significant negative correlation was observed between HbA1c levels and HRV parameters including SDNN, RMSSD, NN50, and pNN50. Similar findings have been reported by earlier investigators who demonstrated that poor glycaemic control contributes to deterioration of autonomic function.[12] Persistent hyperglycaemia may result in axonal degeneration, demyelination, and microvascular damage affecting autonomic nerve fibers.

The present study also demonstrated progressive reduction in HRV parameters with increasing duration of diabetes. Patients with duration of diabetes greater than 10 years showed markedly lower SDNN and RMSSD values compared to patients with shorter disease duration. Similar observations have been documented in previous studies evaluating diabetic autonomic neuropathy.[13]

Long-standing diabetes is associated with cumulative metabolic and vascular injury leading to progressive neuronal dysfunction. Chronic exposure to elevated glucose levels may impair neuronal blood flow, increase oxidative stress, and promote inflammatory changes, thereby worsening autonomic impairment over time.[14]

The findings of the present study support the hypothesis that cardiac autonomic dysfunction begins early in the course of diabetes and progresses with worsening metabolic control. Reduced parasympathetic activity is considered one of the earliest manifestations of cardiac autonomic neuropathy.[15]

Several investigators have emphasized the importance of HRV analysis as a screening tool for early autonomic dysfunction in diabetic patients. HRV analysis is non-invasive, reproducible, inexpensive, and easy to perform in clinical settings. Early identification of autonomic neuropathy may facilitate timely intervention and help reduce cardiovascular complications.[16]

Poor HRV has been associated with increased risk of arrhythmias, silent myocardial ischemia, exercise intolerance, and sudden cardiac death in diabetic patients. Therefore, regular autonomic function assessment may be beneficial in patients with poorly controlled diabetes and longer disease duration.[17]

The present study had certain limitations. The study was conducted at a single tertiary care center with relatively small sample size. Frequency domain HRV parameters were not evaluated. Longitudinal follow-up was not performed to assess progression of autonomic dysfunction over time. Further multicentric studies with larger sample sizes are recommended.

Despite these limitations, the present study highlights the significant relationship between glycaemic status, duration of diabetes, and autonomic dysfunction assessed through HRV analysis.

Conclusion

Poor glycaemic control and longer duration of Type 2 Diabetes Mellitus are significantly associated with reduction in time domain heart rate variability parameters, indicating progressive cardiac autonomic dysfunction. HRV analysis serves as a useful non-invasive tool for early detection of cardiac autonomic neuropathy in diabetic patients. Early screening and strict glycaemic control may help reduce cardiovascular morbidity and improve long-term outcomes in patients with Type 2 Diabetes Mellitus.

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