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Cardiovascular Autonomic Neuropathy among Diabetic Patients in a Tertiary Care Hospital in Odisha: A Cross-sectional Study

Kishore Chandra Behera[1], Sanjeev Supakar[2], Jagnyaseni Panda[3], Arvind Ranjan Mickey[4]*

[1]Professor & HOD, Department of Community Medicine, SLN Medical College & Hospital, Koraput, Odisha, India
[2]Associate Professor, Department of Community Medicine, Bhima Bhoi Medical College & Hospital, Balangir, Odisha, India
[3]Associate Professor, Department of Physiology, MKCG Medical College & Hospital, Berhampur, Odisha, India
[4]Assistant Professor, Department of Anaesthesiology, SCB Medical College and Hospital, Cuttack, Odisha, India

***Address for Correspondence:** Dr Arvind Ranjan Mickey, Assistant Professor, Department of Anaesthesiology, SCB Medical College and Hospital, Cuttack, Odisha, India
E-mail: arvind.mickey@gmail.com

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ABSTRACT

Background: Diabetes mellitus is a chronic disease associated with both modifiable and non-modifiable risk factors and is notorious for causing several systemic complications, often without early symptoms. Among these, cardiovascular autonomic neuropathy (CAN) remains underdiagnosed despite its serious implications. The condition affects multiple organ systems and can present with subtle clinical signs, leading to delayed recognition and treatment.

Methods: A hospital-based cross-sectional study was conducted over two years at SLN Medical College and Hospital, Koraput, Odisha, involving 130 patients with a confirmed diagnosis of diabetes mellitus. Autonomic function was evaluated using cardiovascular reflex tests, including measurement of postural blood pressure changes, beat-to-beat heart rate variability, Valsalva ratio, and immediate heart rate response to standing. Data were analyzed using descriptive statistics.

Results: The study included 84 males and 46 females, mostly aged over 55 years. Moderate postural hypotension (10–20 mmHg drop in systolic BP) was observed in over half of the participants, while approximately a quarter exhibited a significant drop exceeding 30 mmHg. Around one-third demonstrated beat-to-beat heart rate variability of less than 10 beats per minute, indicating autonomic dysfunction. About 29% showed abnormal Valsalva ratios (<1.10), and 35% exhibited impaired heart rate response to standing (30:15 ratio<1.00), indicating prevalent cardiovascular autonomic neuropathy.

Conclusion: Cardiovascular autonomic neuropathy is a frequently overlooked yet serious complication among diabetic patients. Early detection using simple bedside autonomic tests can aid in timely diagnosis and management. Regular screening for CAN should be integrated into routine diabetic care, particularly in patients with longer disease duration and other comorbidities.

Key-words: Diabetes Mellitus, Cardiovascular Autonomic Neuropathy (CAN), Autonomic function tests, Postural hypotension, Valsalva ratio, Heart rate variability, Type 2 diabetes

INTRODUCTION

Diabetes mellitus is a complex chronic condition characterized not only by its risk determinants but also by its capacity to act as a predisposing factor for various systemic complications.

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Risk factors for diabetes are generally divided into two categories: non-modifiable factors such as age, gender, and family history, and modifiable ones including obesity, excessive caloric intake, physical inactivity, and alcohol use [1].

What makes diabetes particularly concerning is its often-asymptomatic nature in the early stages, leading to delayed diagnosis. This asymptomatic period, sometimes lasting 5–10 years, allows ongoing damage to organ systems without overt clinical signs, earning diabetes the designation of an "iceberg disease." By the time symptoms become evident, significant physiological

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damage may have already occurred. Therefore, early identification is vital to prevent associated complications [1].

Commonly recognized complications of diabetes mellitus include neuropathy, nephropathy, retinopathy, diabetic foot ulcers, cardiac complications, hypoglycemia related to treatment, and susceptibility to infections. However, less well-known but potentially more dangerous complications such as CAN often go unnoticed [2].

When diabetes persists over a long period, it is frequently associated with a broader range of complications, one of which is diabetic autonomic neuropathy. This form of neuropathy affects various systems, including the gastrointestinal, genitourinary, and cardiovascular systems. Its insidious presentation—with subtle or mild symptoms—means it often escapes detection and clinical attention [2].

CAN is a serious but underappreciated complication of diabetes. Both clinicians and patients may overlook it, partly due to a lack of comprehensive understanding of its natural history and epidemiological characteristics [3].

Several studies have shown that CAN is associated with multiple risk factors. Increasing age, longer duration of diabetes, and poor glycemic control have been consistently linked to a higher prevalence of CAN [4]. Additionally, this condition is often found in conjunction with microvascular complications such as diabetic microangiopathy and distal symmetric polyneuropathy. Factors contributing to reduced heart rate variability in individuals with type 2 diabetes mellitus include advancing age, prolonged duration of illness, smoking, and excess body weight [5].

In individuals with type 1 diabetes mellitus, the risk of developing CAN is significantly higher in the presence of hypertension, diabetic retinopathy, poor glycemic control, elevated HbA1c levels, and distal symmetrical polyneuropathy [6].

Given the importance of early detection and the underdiagnosis of this condition, the present study was undertaken to evaluate cardiovascular reflex abnormalities associated with diabetic autonomic neuropathy in patients attending SLN Medical College and Hospital, Koraput, Odisha—a tertiary care teaching hospital.

MATERIALS AND METHODS

Study Design and Setting- This hospital-based cross-sectional study was carried out over two years at SLN Medical College and Hospital in Koraput, Odisha. A total of 130 individuals with previously diagnosed diabetes mellitus were included in the study.

Data Collection- Participants underwent a detailed clinical history and physical examination with a particular focus on symptoms suggestive of autonomic dysfunction. Data were collected using a pre-tested and semi-structured questionnaire.

Inclusion criteria- Individuals with a confirmed diagnosis of diabetes mellitus and willingness to participate and provide written informed consent.

Exclusion criteria- Patients with chronic obstructive pulmonary disease, those on antihypertensive medications for hypertension, and individuals with a history of myocardial infarction.

Methodology- Each participant underwent the following autonomic function tests: measurement of postural blood pressure changes, assessment of beat-to-beat heart rate variation (R-R interval), Valsalva maneuver, and immediate heart rate response to standing. These assessments were conducted using a standard sphygmomanometer and continuous ECG monitoring.

Postural Hypotension Testing- For postural hypotension testing, blood pressure, and pulse were recorded after the patient had rested supine for three minutes. Upon standing, immediate measurements were repeated, and any drop in systolic blood pressure was recorded. Care was taken to avoid measurements immediately after insulin administration to prevent confounding vasodilatory effects.

Beat-to-Beat Heart Rate Variability- Beat-to-beat heart rate variability was assessed while the subject breathed deeply at a rate of six breaths per minute, optimizing heart rate variation. Continuous ECG recordings were used to calculate the difference between the maximum and minimum heart rates during inspiration and expiration. The variation was expressed as the difference between these extremes rather than the E/I ratio.

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Valsalva Maneuver- The Valsalva maneuver involved having the subject exhale forcefully with a closed nose and mouth while applying pressure on the abdomen. ECG was recorded continuously to determine the Valsalva ratio—the ratio of the longest R-R interval after the maneuver to the shortest R-R interval during the strain phase.

Immediate Heart Rate Response to Standing (30:15 Ratio)- For assessing the immediate heart rate response to standing, an ECG was recorded as the patient moved from a supine to an upright position. R-R intervals were measured at the 15th and 30th beats after standing, and the 30:15 ratio was used to interpret the vagal response. A value of 1.03 or higher was considered normal, while a ratio below 1.00 indicated probable vagal impairment.

Statistical Analysis- All data were entered into Microsoft Excel and analyzed using descriptive statistics such as percentages and proportions.

Ethical Approval and Consent- Before commencing the study, approval was obtained from the Institutional Ethics Committee. Informed consent was taken from each participant to ensure voluntary participation and adherence to ethical standards.

RESULTS

This hospital-based cross-sectional study was conducted at SLN Medical College and Hospital, a tertiary care institution, over two years from April 2017 to March 2022. The study included 130 individuals with a known diagnosis of diabetes mellitus.

Table 1 presents the distribution of study participants by age and sex. Among the 130 subjects, 84 were male and 46 were female. Most participants fell within the age group of over 56 years, accounting for 33.85% of the total, with 42.86% of males and 17.39% of females in this category. The next most common age group was 46–55 years, representing 28.46% of the sample, with 16.67% of males and 50% of females. The age groups 36–45 years, 26–35 years, and 18–25 years accounted for 16.73%, 12.88%, and 7.69% of the total participants, respectively.

Table 1: Age and sex wise distribution of study subjects

Age (years)	Male		Female		Total	
	No.	%	No.	%	No.	%
18-25	7	8.33	3	6.52	10	7.69
26-35	11	13.10	6	12.50	17	12.88
36-45	16	19.05	6	12.50	22	16.73
46-55	14	16.67	23	50.00	37	28.46
> 56	36	42.86	8	17.39	44	33.85
Total	84	100	46	100	130	130

Table 2 illustrates the changes in systolic blood pressure from lying down to standing position. Most participants (56.15%) experienced a moderate fall in systolic pressure (10–20 mmHg), while 24.62% had a marked drop exceeding 30 mmHg. Meanwhile, 19.23% of participants showed an increase of 10 mmHg upon standing.

Table 2: Blood pressure recordings during lying down and standing positions

Systolic blood pressure from lying down to standing position (mmHg)	No.	%
Fall of > 30 mmHg	32	24.62
Fall of 10-20 mmHg	73	56.15
Rise of 10 mmHg	25	19.23
Total	130	100

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Table 3 shows the beat-to-beat heart rate variability. Among the study population, 30.77% exhibited a variation of less than 10 beats, indicating potential autonomic dysfunction. Normal beat-to-beat variation was observed in 45.38% of participants, whereas 23.85% demonstrated borderline variation.

Table 3: Beat to beat variations among the study subjects

Beat to beat variation	No.	%
< 10 beats variation (autonomic damage)	40	30.77
Normal variation	59	45.38
Border line variation	31	23.85
Total	130	100

Table 4 presents the heart rate responses during the Valsalva maneuver. A normal response (Valsalva ratio> 1.21) was observed in 55.38% of participants. Borderline responses (ratio between 1.11 and 1.20) were seen in 15.38% of individuals, while 29.23% demonstrated an abnormal Valsalva ratio (less than 1.10), suggestive of autonomic impairment.

Table 4: Heart rate changes during Valsalva and Valsalva ratio

Valsalva ratio	No.	%
> 1.21 (normal response)	72	55.38
1.20 to 1.11 (border line response)	20	15.38
< 1.10 (abnormal response/autonomic damage)	38	29.23
Total	130	100

Table 5 summarizes the heart rate changes immediately after standing. A normal heart rate response (ratio≥1.03) was recorded in 40.77% of the subjects. Borderline responses (ratio 1.00–1.02) were seen in 23.85%, and an abnormal response (ratio<1.00), indicative of autonomic dysfunction, was observed in 35.38% of participants.

Table 5: Heart rate changes immediately after standing among study subjects

Heart rate changes immediately after standing	No.	%
Ratio 1.03 or above (normal response)	53	40.77
Ratio 1.00 to 1.02 (borderline response)	31	23.85
Ratio<1.00 (abnormal response/autonomic damage)	46	35.38
Total	130	

These findings collectively suggest a notable prevalence of cardiovascular autonomic dysfunction among diabetic patients in the study population.

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DISCUSSION

This hospital-based cross-sectional study was conducted at SLN Medical College and Hospital, Koraput, a tertiary care center, over two years. A total of 130 patients with known diabetes mellitus were included in the study. In the current analysis, most participants (60%) were male. Among male participants, the highest representation was from those aged above 55 years. In contrast, the predominant age groups among female participants were 45–54 years and above 55 years.

Postural hypotension was predominantly observed among individuals with a longer duration of diabetes, with an average disease duration of 13.5 years among those affected. The most significant drop in systolic blood pressure recorded upon standing was 50 mmHg. A quarter (25%) of participants exhibited a fall in systolic blood pressure of 30 mmHg or more, while 55% had a fall in the range of 10–20 mmHg. Interestingly, 20% showed a mild increase in blood pressure upon standing, not exceeding 10 mmHg.

In healthy individuals, normal respiratory-induced beat-to-beat variation in heart rate is typically 15 or more beats per minute. A reduction of this difference to fewer than 10 beats per minute suggests possible autonomic dysfunction. In the present study, 30% of patients had results indicative of autonomic dysfunction, 45% showed normal variation, and 25% exhibited borderline findings [4,5].

The Valsalva ratio is a recognized tool to evaluate autonomic function. A ratio of 1.21 or higher is considered normal, 1.11–1.20 is borderline, and 1.10 or lower is considered abnormal. In this study, 30% of patients had an abnormal Valsalva ratio, 15% had borderline responses, and the remaining 55% demonstrated normal responses [4].

The heart rate response to standing, particularly the 30:15 ratio, is another marker of autonomic function. A ratio of 1.03 or higher is normal, while 1.00 or less may suggest vagal impairment. In the current study, 40% showed normal responses, 35% had abnormal findings, and 25% were in the borderline category [4].

A study by Birajdar *et al.* reported an abnormal expiration-to-inspiration (E:I) ratio in 24 patients, an abnormal Valsalva ratio in 34 patients, and an abnormal 30:15 ratio in 38 individuals [7]. Only 8% of their cohort had postural hypotension, and 10 patients demonstrated abnormal results on the sustained handgrip test. Overall, 58% were diagnosed with CAN. They also found a significant association between CAN and overall autonomic neuropathy, though no significant relationship was seen with nephropathy or retinopathy. The authors noted that parasympathetic involvement was more prominent than sympathetic involvement.

Arif *et al.* observed that 36.7% of their type 2 diabetes participants with poor glycemic control exhibited features of CAN [3]. Their findings support the association between inadequate glycemic management and the occurrence of cardiovascular autonomic complications.

Khoharo *et al.* found the mean duration of diabetes in their study group to be approximately 13 years [8]. All participants exhibited prolonged QTc intervals, and the occurrence of CAN was significantly more common in those with diabetes for over five years. Furthermore, postural hypotension and heart rate variability were both significantly associated with the duration of diabetes. QTc interval prolongation correlated strongly with longer disease duration, heart rate abnormalities, and postural hypotension.

A prevalence of 60% for CAN was reported by Pappachan *et al.* [9]. Their analysis revealed that older patients had a 15.75-fold higher risk of developing CAN than younger individuals. They also found that patients with prolonged QTc intervals were 5.55 times more likely to have CAN. A disease duration of more than 10 years doubles the risk of CAN, and the presence of peripheral neuropathy increases the risk by 5.55 times.

Another study by Khoharo *et al.* observed a male predominance like our findings [10]. Their participants had a longer average duration of diabetes and higher HbA1c levels. They reported a 24% incidence of CAN. Kumhar *et al.* highlighted the diagnostic value of QTc dispersion, noting it as a simple, non-invasive, and cost-effective tool for identifying cardiac dysautonomia [11].

In contrast to our study, another investigation by Khoharo *et al.* reported equal representation of males and females [12]. Their study found a 40% incidence of CAN, with heart rate variability significantly associated with the duration of diabetes.

Finally, Khandoker *et al.* reported that individuals with CAN showed reduced Poincaré plot patterns [13]. They proposed that sample entropy (SampEn), a complexity-based heart rate variability measure, might be useful in detecting asymptomatic CAN.

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Cardiovascular autonomic neuropathy is often underdiagnosed despite being associated with increased morbidity and mortality in diabetes. Early detection using bedside autonomic function tests like the Valsalva maneuver and heart rate variability is cost-effective and clinically valuable [14,15].

CONCLUSIONS

This hospital-based cross-sectional study highlights a high prevalence of cardiovascular autonomic neuropathy (CAN) among patients with type 2 diabetes mellitus, with significant associations observed between CAN and factors such as prolonged duration of diabetes, postural hypotension, reduced heart rate variability, and abnormal Valsalva and 30:15 ratios. The findings underscore the importance of early screening for autonomic dysfunction in diabetic patients, particularly those with long-standing disease or poor glycemic control. Simple bedside tests like postural blood pressure measurement, heart rate variability assessments, and QTc interval analysis can serve as effective, low-cost tools for early detection of CAN. Early identification and timely intervention can help mitigate the risk of cardiovascular complications and improve overall prognosis in diabetic populations.

CONTRIBUTION OF AUTHORS

Research concept- Sanjeev Supakar, Jagnyaseni Panda
Research design- Jagnyaseni Panda, Arvind Ranjan Mickey
Supervision- Kishore Chandra Behera
Materials- Sanjeev Supakar, Jagnyaseni Panda
Data collection- Jagnyaseni Panda, Arvind Ranjan Mickey
Data analysis and interpretation- Kishore Chandra Behera
Literature search- Sanjeev Supakar, Jagnyaseni Panda
Writing article- Jagnyaseni Panda, Arvind Ranjan Mickey
Critical review- Kishore Chandra Behera
Article editing- Jagnyaseni Panda, Arvind Ranjan Mickey
Final approval- Kishore Chandra Behera

REFERENCES

[1] Behera BK, Vishnu K. Cardiac autonomic neuropathy in diabetes mellitus. Int J Res Med Sci., 2018; 6: 88–93. doi: 10.18203/2320-6012.ijrms20175501.
[2] Khandelwal E, Jaryal AK, Deepak KK. Pattern and prevalence of cardiovascular autonomic neuropathy in diabetics visiting a tertiary care referral center in India. Indian J Physiol Pharmacol., 2011; 55(2): 119–27.
[3] Arif ZA, Shaikh IA, Masood N. Cardiovascular autonomic neuropathy (CAN) in patients of type 2 diabetes mellitus: a tertiary care hospital-based study. Indian Heart J., 2014; 66(6): 751–54.
[4] Vinik AI, Ziegler D. Diabetic cardiovascular autonomic neuropathy. Circ., 2007; 115(3): 387–97.
[5] Maser RE, Mitchell BD, Vinik AI, Freeman R. The association between cardiovascular autonomic neuropathy and mortality in individuals with diabetes: a meta-analysis. Diabetes Care, 2003; 26(6): 1895–901.
[6] Maser R, Lenhard M, DeCherney G. Cardiovascular autonomic neuropathy: the clinical significance of its determination. Endocrinol., 2000; 10(1): 27–33.
[7] Birajdar SV, Chavan SS, Munde SA, Bende YP. A study of autonomic nervous system dysfunction among patients with diabetes mellitus: a cross-sectional study. Int J Adv Med., 2017; 4(2): 406–11.
[8] Khoharo HK, Halepoto AW. QTc-interval, heart rate variability and postural hypotension as indicators of cardiac autonomic neuropathy in type 2 diabetic patients. J Pak Med Assoc., 2012; 62(4): 328–31.
[9] Papachan JM, Sebastian J, Bino BC, Jayaprakash K, Vijaykumar K, et al. Cardiac autonomic neuropathy in diabetes mellitus: prevalence, risk factors and utility of corrected QT interval in the ECG for its diagnosis. Postgrad Med J., 2008; 84(990): 205–10.
[10] Khoharo HK, Ansari S, Shaikh IA, Qureshi F. Cardiac autonomic neuropathy in type 1 diabetes mellitus patients and its association with the duration of disease and glycemic control. J Coll Physicians Surg Pak., 2009; 19(4): 232–35.
[11] Kumhar MR, Agarwal TD, Singh VB, Kochar DK, Chadda VS. Cardiac autonomic neuropathy and its correlation with QTc dispersion in type 2 diabetes. Indian Heart J., 2000; 52(4): 421–26.
[12] Khoharo HK, Qureshi F. Frequency of cardiac autonomic neuropathy in patients with type 2 diabetes mellitus reporting at a teaching hospital of Sindh. J Coll Physc Surg Pak., 2008; 18(12): 751–54.
[13] Khandoker AH, Jelinek HF, Palaniswami M. Identifying diabetic patients with cardiac autonomic neuropathy by heart rate complexity analysis. Biomed Eng Online, 2009; 8: 3.

doi: 10.21276/SSR-IIJLS.2025.11.3.36

[14]sEleftheriadou A, Spallone V, Tahrani AA, et al. Cardiovascular autonomic neuropathy in diabetes: an update with a focus on management. Diabetologia, 2024; 67: 2611–25. doi: 10.1007/s00125-024-06242-0.

[15]Spallone V, Ziegler D, Freeman R, Bernardi L, Frontoni S, Pop-Busui R, et al. Cardiovascular autonomic neuropathy in diabetes: clinical impact, assessment, diagnosis, and management. Diabetes Metab Res Rev. 2011; 27(7): 639–53.