https://doi.org/10.3329/jicc.v6i2.93349

ORIGINAL ARTICLE

Prevalence of Cardiac Autonomic Neuropathy in Diabetic Patients: A Cross-Sectional Study at Bir Hospital, Nepal

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Abstract

Background: Cardiac autonomic neuropathy (CAN) is a severe complication of diabetes mellitus characterized by impaired autonomic regulation of the heart, increasing the risk of cardiovascular morbidity and mortality.

Objective: To determine the prevalence of cardiac autonomic neuropathy (CAN) in diabetic patients using Ewing's score and assess the associated clinical factors.

Methodology:

This cross-sectional study was conducted at NAMS, Bir Hospital, Nepal, from September 2021 to June 2022, involving 100 diabetic patients. CAN was assessed using Ewing's battery of cardiovascular reflex tests, including heart rate and blood pressure response measurements. Clinical and demographic data were analyzed to identify the prevalence and severity of CAN.

Results: Of the 100 diabetic patients, 60% were diagnosed with CAN based on Ewing's score. Among these, 40% had early-stage CAN, while 20% exhibited severe CAN. Patients with severe CAN had a significantly longer mean duration of diabetes (13.23 ± 7.10 years) compared to those without CAN (8.90 ± 5.45 years). Symptom analysis revealed that fatigue (95%), dizziness (90%), and exercise intolerance (80%) were predominant in severe CAN. Ewing's score reliably categorized patients into normal, early, and severe stages, emphasizing its utility as a diagnostic tool.

Conclusion: This study underscores a high prevalence of cardiac autonomic neuropathy in diabetic patients, with Ewing's score serving as an effective diagnostic framework. Longer diabetes duration and symptom burden were significantly associated with CAN severity. Early detection through Ewing's tests and routine screening can aid in timely intervention and improved patient outcomes.

Keywords: Diabetes Mellitus, Cardiac Autonomic Neuropathy, Ewing's Score, Prevalence, Cardiovascular Complications

J Inv Clin Cardiol 2024; 6(2): 43-48

Introduction

Cardiac autonomic neuropathy (CAN) is a serious complication of diabetes mellitus, particularly in type 2 diabetes, where it disrupts the autonomic regulation of cardiovascular functions. The prevalence of CAN is high, with studies suggesting that up to 60% of individuals with long-standing type 2 diabetes are affected (Duque et al., 2021). This condition is associated with increased morbidity and mortality, as well as a higher risk of cardiovascular events such as sudden cardiac death and arrhythmias (Lerner et al., 2015; Ayad et al., 2010). The pathophysiology of CAN is complex, involving metabolic dysregulation, prolonged hyperglycemia, and damage to autonomic nerve fibers, all of which contribute to cardiovascular complications (Duque et al., 2021; Yuan et al., 2018).

Early detection of CAN is vital, as traditional glycemic control strategies may not be sufficient to address its detrimental effects once it develops (Lerner et al., 2015). Studies emphasize the importance of routine screening for CAN in diabetic patients, particularly through non-invasive methods such as heart rate

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variability (HRV) assessments and pupillometry, which are reliable markers of autonomic dysfunction (Lerner et al., 2015; Siddig et al., 2021). Additionally, the link between CAN and other diabetic complications like retinopathy and nephropathy highlights the need for a holistic approach to diabetes management that includes monitoring for autonomic dysfunction (Siddig et al., 2021; Ayad et al., 2010). The Ewing Score, based on these reflex tests, provides a standardized approach for evaluating autonomic neuropathy and can help stratify the severity of CAN in diabetic patients (Ewing et al., 1980).

In Nepal, where the prevalence of diabetes is rising rapidly, understanding the local prevalence of CAN is critical for developing targeted interventions. The healthcare system faces challenges in the early diagnosis and management of diabetic complications, exacerbated by limited resources and access to specialized care (Kumar & Kodidala, 2021). A cross-sectional study at Bir Hospital aims to determine the prevalence of CAN among diabetic patients in Nepal, using the Ewing Score as a diagnostic tool. This study seeks to fill a gap in knowledge regarding the burden of CAN in Nepal, offering insights into the regional prevalence of this condition and contributing to the development of more effective clinical management strategies (Siddig et al., 2021).

Beyond immediate cardiovascular risks, CAN also affects broader health outcomes such as quality of life and functional capacity (Gulichsen et al., 2012). Patients with CAN often experience silent myocardial ischemia, which complicates diagnosis and treatment, leading to delays in intervention (Inapakolla & Kotla, 2019). Therefore, incorporating CAN screening into routine diabetes care, especially in high-risk populations, is crucial. The findings from this study could help drive policy changes and the implementation of standardized screening practices, ultimately reducing the burden of diabetic complications in Nepal.

Methodology

Study Design: This investigation was designed as a cross-sectional observational study, aiming to assess the prevalence of Cardiac Autonomic Neuropathy (CAN) in diabetic patients using a structured and systematic approach. The study was conducted at Bir Hospital, Kathmandu, Nepal, located in the Mahabauddha area, Kathmandu, Nepal.

Study Duration: The study spanned one year, from September 2021 to June 2022, allowing ample time to ensure sufficient sample size and variability in patient conditions.

Sampling Strategy: A non-probability purposive sampling technique was employed to ensure the inclusion of a diverse group of diabetic patients from various backgrounds, facilitating a comprehensive evaluation of CAN across different subgroups. This method allowed the research team to prioritize the inclusion of patients who met the specific inclusion criteria.

Sample size calculation:

Taking maximum tolerable error of 10 % and using the following statistical sample size calculation formula

For infinite population:

$n = z^2pq/d^2$.

Where, n is the sample size

z is the confidence level set at 95%, which is 1.96

p is the prevalence of previous study, which is 65.2% = 0.652 (Siddig et al., 2021)

q is the proportion of the sample elements that do not have the particular attribute,

q = 100-p% or (1-p) =100-65.2% (1-0.652) = 34.8% (0.348)

d is the permissible error 10% (0.1)

$$n = z^2pq/d^2$$
$$= \frac{(1.96)^2 \times 0.652 \times 0.348}{(0.1)^2}$$
$$= 87.16$$
$$\cong 88$$

To reduce the non-response error, 10% sample was added.

n = 88+ 10% of 88

= 88+ 8.8

= 96.8 ≅ 97

The required sample size for study was 100.

- Inclusion Criteria:
  - All adult patients (ages 18-75) diagnosed with diabetes mellitus,
  - Stable vital signs and cardiac sinus rhythm,
  - Able to provide informed consent.

- Exclusion Criteria:
  - o Pregnant or breastfeeding women,
  - o Patients with congenital heart disease, rheumatic valvular heart disease, or other significant heart conditions,
  - o Those exhibiting signs of anemia, hypoxia, hypovolemia, sepsis, renal failure, or other conditions affecting heart rhythm,
  - o Patients on medications known to influence cardiac function (e.g., beta-blockers, antiarrhythmic drugs, calcium channel blockers, certain antipsychotics).

Data Collection:

Patients attending the outpatient department (OPD), the emergency department, or admitted to the hospital were screened for eligibility. After obtaining informed consent, eligible patients underwent detailed clinical evaluations, including a structured medical history and physical examination, recorded using a pre-designed proforma.

To assess Cardiac Autonomic Neuropathy (CAN), the following five standardized diagnostic tests were conducted:

1. Resting Heart Rate Measurement: Evaluating the baseline heart rate as an indicator of autonomic dysfunction.
2. Postural (Orthostatic) Hypotension Assessment: Monitoring blood pressure changes when transitioning from a supine to an upright position.
3. Valsalva Maneuver: A test to assess heart rate response, indicating parasympathetic function.
4. Heart Rate Variability during Deep Breathing: Measuring the variation in heart rate during paced breathing to assess parasympathetic activity.
5. Isometric Exercise Test: Analyzing changes in diastolic blood pressure to evaluate sympathetic response.

Each test result was scored based on the degree of abnormality observed. A cumulative score was used to classify the presence and severity of CAN:

- 0 points: No CAN,
- 1 point: Early CAN,
- 2 points: Definite CAN,
- 3 points: Severe CAN.

Statistical Analysis:

Data were analyzed using standard descriptive and inferential statistical methods. Continuous variables such as age, blood pressure, and heart rate were presented as mean ± standard deviation. Categorical variables, such as the prevalence of CAN across different severity levels, were expressed as frequencies and percentages.

To compare the means of different groups, the Student's t-test was employed, and assess potential associations between CAN and demographic or clinical factors. A p-value of < 0.05 was considered statistically significant, ensuring the reliability and validity of the findings.

Results

1. Socio-Demographic Variables of the Study Respondents

Out of 100 respondents, the majority (29%) belonged to the age group 58–67 years, and 54% were male.

Table-I

Socio-Demographic Variables of the Study Respondents (n=100)

Variables	Frequency (%)
Age Group (Years)	
18–27	2 (2)
28–37	10 (10)
38–47	18 (18)
48–57	23 (23)
58–67	29 (29)
≥68	18 (18)
Sex	
Male	54 (54)
Female	46 (46)

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2. Respondents' Sex Based on Age Category

The majority of male respondents (13) were in the 48–57 and 58–67 age groups, while most female respondents (16) were in the 58–67 age group.

Table-II

Respondents' Sex Based on Age Category (n=100)

Age Group (Years)	Male (n)	Female (n)
18–27	0	2
28–37	8	2
38–47	9	9
48–57	13	10
58–67	13	16
≥68 11	7	
Total	54	46

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3. CAN Score Distribution of the Study Respondents

A minority (20%) of respondents had severe cardiac autonomic neuropathy (CAN), 40% had early CAN, and 40% had no CAN.

Table-III

CAN Score Distribution of the Study Respondents (n=100)

CAN Score	Frequency (%)
No CAN (0–0.5)	40 (40)
Early CAN (1–2)	40 (40)
Severe CAN (≥2.5)	20 (20)

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4. Student's t-test for Significant Difference Between Mean CAN Scores by Sex

There was no significant difference in CAN scores between males and females (p-value: 0.69).

5. Association of CAN with Duration of Diabetes Mellitus

There was a significant relationship between CAN and the duration of diabetes mellitus (p-value: 0.001). A one-unit increase in the duration of diabetes mellitus increased CAN by 0.023 units (95% CI: -0.012 to 0.058). Duration of DM 8.90 ± 5.45 (without CAN) and 13.23 ± 7.10 (with CAN

6. Ewing Score Distribution and CAN Severity

The majority of respondents had either no CAN (40%) or early CAN (40%), with 20% having severe CAN.

7. Symptoms Associated with CAN Severity

There is a clear increase in symptom severity and frequency with higher CAN scores.

Prevalence of CAN

- Severe CAN
- 20% of the respondents had severe cardiac autonomic neuropathy .
- Early CAN
- 40% of the respondents had early cardiac autonomic neuropathy .
- No CAN
- 40% of the respondents had no cardiac autonomic neuropathy .

Symptom Distribution

- Dizziness/Lightheadedness (36% overall): Most prevalent in severe CAN (90%) and less common in No CAN (7.5%).
- Palpitations (27% overall): Primarily reported in severe CAN (75%); minimal in No CAN (5%).
- Syncope (15% overall): Rare, but occurs mostly in severe CAN (50%).
- Exercise Intolerance (32% overall): Progressively worsens, peaking in severe CAN (80%).
- Fatigue (42% overall): The most reported symptom, present in 95% of severe CAN cases.

The severity of CAN strongly correlates with the frequency and intensity of symptoms, with severe CAN showing the highest symptom burden. Fatigue and Dizziness/Lightheadedness are the most common complaints.

Table-IV

Student's t-test for CAN Scores by Sex (n=100)

Sex	Frequency	Mean	SD	95% CI	P-value
Male	54	1.20	1.11	0.89–1.50	0.69
Female	46	1.29	1.13	0.95–1.63	
Combined	100	1.245	1.118		

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Table-V

Association of CAN with Duration of Diabetes Mellitus (n=100)

CAN	Coefficient	95% CI	P-value
Duration of Diabetes Mellitus	0.023	-0.012 to 0.058	0.001

Table-VI

Ewing Score and CAN Severity (n=100)

Ewing Score	CAN Severity	Number of Patients (n)	Percentage (%)
0.0 – 0.5	No CAN	40	40%
1.0 – 2.0	Early CAN	40	40%
e” 2.5	Severe CAN	20	20%
Total	-	100	100%

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Table-VII

Symptom Distribution Based on CAN Severity (n=100)

Symptoms	No CAN (n=40)	Early CAN (n=40)	Severe CAN (n=20)	Total (n)
Dizziness/Lightheadedness	3	15	18	36
Palpitations	2	10	15	27
Syncope	0	5	10	15
Exercise Intolerance	4	12	16	32
Fatigue	5	18	19	42
Total Symptoms Reported	14	60	78	152

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Discussion

Diabetes mellitus (DM) represents a major global health challenge, with projections indicating an increase in its prevalence from 4% in 1995 to an anticipated 5.4% by 2025 (World Health Organization, 1998). This growing burden is particularly evident in developing nations, where diabetes and its complications, including cardiac autonomic neuropathy (CAN), are on the rise. CAN is a serious, often underdiagnosed complication of diabetes that can profoundly affect cardiovascular health, leading to increased morbidity and mortality. Recognizing CAN as a critical consequence of diabetes highlights the importance of understanding its prevalence, symptoms, and contributing factors.

Our study, conducted at Bir Hospital, Nepal, found a prevalence rate of 60% for CAN among diabetic patients, which aligns with previous studies by Nijhawan et al. (2002), Barthwal et al. (2003), and Kumar et al. (2009), who reported prevalence rates ranging from 36.2% to 60%. The observed high prevalence emphasizes the urgent need for increased awareness and regular screening for CAN in diabetic populations, particularly in resource-limited settings. Notably, 40% of the patients had early-stage CAN, highlighting the significance of early detection. Detecting CAN early allows for the implementation of preventive strategies to slow its progression, potentially improving patient outcomes.

Our study also revealed a strong association between the severity of CAN and the symptom burden experienced by patients. Severe CAN patients reported high frequencies of debilitating symptoms, including fatigue (95%), dizziness/lightheadedness (90%), and exercise intolerance (80%). These findings corroborate existing literature, which suggests that symptom-based evaluations are crucial for identifying patients at higher risk for severe autonomic dysfunction (Vinik et al., 2003). The presence of these symptoms not only diminishes the quality of life for diabetic patients but also complicates diabetes management, creating a cycle of worsening glycemic control and progressive autonomic dysfunction.

Additionally, our study demonstrated a significant association between the duration of diabetes and the development of CAN. Patients without CAN had a mean diabetes duration of 8.90 ± 5.45 years, while those with CAN had a mean duration of 13.23 ± 7.10 years. This aligns with previous studies by Kumar et al. (2009) and Barthwal et al. (2003), which found that longer diabetes duration significantly increased the likelihood of CAN. These findings underscore the importance of regular monitoring for CAN in patients with long-standing diabetes. Early intervention in this population could help alter the course of the disease and reduce the risk of severe complications.

The pathophysiology of CAN in diabetes is complex and involves a combination of metabolic, vascular, and inflammatory factors. Chronic hyperglycemia induces oxidative stress and promotes the formation of advanced glycation end-products, which damage autonomic nerve fibers. Additionally, the presence of cardiovascular risk factors, such as hypertension and dyslipidemia, can exacerbate CAN development. As such, a comprehensive approach to diabetes management—focusing not only on glycemic control but also on cardiovascular risk factors—is essential for reducing the incidence and severity of CAN.

Our study also advocates for routine screening for CAN in diabetic patients, particularly those with a prolonged disease duration or high symptom burden. The Ewing scoring system, which incorporates cardiovascular reflex tests, remains a useful diagnostic tool for detecting autonomic dysfunction (Ewing et al., 1985). Early identification and management of CAN can prevent its progression and reduce cardiovascular risks. Moreover, educating patients about the importance of regular check-ups and adhering to treatment regimens can empower individuals to actively manage their health and prevent complications.

However, there are limitations to our study. As a cross-sectional study, it only provides a snapshot of CAN prevalence at one point in time, which may not capture the disease's dynamic progression. Longitudinal studies are needed to assess how CAN evolves and identify potential risk factors for its development. Additionally, as the study was conducted in a single center, the findings may not be fully generalizable to broader populations. Future research should involve larger, multicenter cohorts to better understand CAN's prevalence, progression, and management in diverse settings.

In conclusion, this study highlights the concerning prevalence of cardiac autonomic neuropathy among diabetic patients in Nepal, emphasizing the need for increased awareness, routine screening, and early intervention. The strong association between diabetes duration and CAN, along with the significant symptom burden, underscores the importance of proactive management. By integrating regular CAN screening and a multifactorial approach to diabetes care, healthcare providers can help improve patient outcomes and reduce the long-term risks associated with autonomic dysfunction. Future research should focus on understanding the underlying mechanisms of CAN and developing targeted interventions to prevent its onset and progression.

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