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Electrocardiographic Revelations: Investigating Cardiac Autonomic Neuropathy among Geriatric Diabetes with Microvascular Complications

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ABSTRACT

Background: Cardiac Autonomic Neuropathy (CAN) is a severe yet underdiagnosed complication of diabetes mellitus, especially in geriatric patients with microvascular complications. It results from autonomic dysfunction affecting the cardiovascular system, increasing the risk of arrhythmias, silent myocardial infarction, and sudden cardiac death. Despite its clinical significance, routine CAN screening is limited. Early detection using non-invasive tools like electrocardiography (ECG) and Ewing tests is essential for risk mitigation. This study assesses the prevalence, risk factors, and clinical implications of CAN in geriatric diabetic patients with microvascular complications.

Methods: A cross-sectional study was conducted on 160 diabetic patients aged ≥50 years with at least one microvascular complication. Cardiac autonomic function was evaluated using ECG analysis and Ewing tests. Demographic, clinical, and treatment profiles were compared between CAN-positive and CAN-negative patients using statistical analyses, including chi-square tests, Fisher's exact tests, and logistic regression.

Results: CAN prevalence was highest in patients with combined microvascular complications (n=29), followed by neuropathy (n=24), nephropathy (n=19), and retinopathy (n=15). Key risk factors included prolonged diabetes duration (16–20 years: 25%), smoking (31%), alcohol consumption (41%), and ECG abnormalities such as prolonged QT intervals (20.7%) and T-wave changes (20.7%). Patients with CAN had worse cardiovascular profiles.

Conclusion: CAN is highly prevalent in geriatric diabetic patients with microvascular complications. Early screening using ECG and Ewing tests is crucial for timely intervention and cardiovascular risk reduction.

KEYWORDS: Cardiac Autonomic Neuropathy, Diabetes Mellitus, Microvascular Complications, ECG Abnormalities, Geriatric Population, Ewing Tests.

INTRODUCTION

Diabetes mellitus (DM) is a chronic metabolic disorder characterized by persistent hyperglycemia secondary to defects in insulin secretion and/or action [1]. DM is an important global health problem and a main cause of morbidity and mortality. The incidence of DM has been reported to be rising alarmingly driven by the increasing geriatric population, obesity, and sedentary lifestyles [2]. Chronic hyperglycemia with DM leads to a number of systemic complications that are commonly categorized as macrovascular complications, including cardiovascular disease, and microvascular complications, which include neuropathy, retinopathy, and nephropathy [3].

Microvascular complications are hallmark manifestations of DM, severely affecting quality of life. Diabetic

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neuropathy impacts both peripheral and autonomic nerves and produces functional impairment, including pain, sensory loss, and dysfunction related to the autonomic nervous system [4]. Hyperglycemia-induced damage in the retina through microvascular damage is the leading cause of blindness among working-age adults. Nephropathy, characterized by albuminuria and declining renal function, continues to be a major cause of end-stage renal disease globally [5]. Together, these complications pose great risks for the patients, especially in older adults with longstanding diabetes [6].

Among the microvascular complications, the most underappreciated yet impactful one is cardiac autonomic neuropathy, (CAN). CAN can be defined as the damage to the autonomic nerves in charge of the cardiovascular system [7]. The consequences are impaired heart rate variability, intolerance to exercise, and even silent myocardial ischemia which can raise the risk of sudden cardiac death [8]. However, the potential seriousness of this complication leaves it often underdiagnosed, mostly because its clinical features often present subclinically in geriatric patients [9]. The underdiagnosis is compounded by limited awareness, lack of routine screening, and the overlapping nature of symptoms with other cardiovascular conditions [10].

Against the backdrop of a significant disparity in the previously gained knowledge relating to the prevalence and severity of CAN in geriatric diabetic patients with microvascular complications, this study employs non-invasive diagnostic tools such as electrocardiography (ECG) and Ewing tests to inform on the association between diabetic microvascular complications, neuropathy, retinopathy, and nephropathy with cardiac autonomic dysfunction [11]. Identifying these associations will be helpful for clinicians developing targeted interventions that might reduce cardiovascular risks and thereby enhance patient outcomes among this vulnerable population.

Methodology

This study is a cross-sectional study in tertiary care hospital conducted among geriatric patients aged 50 years or older with a diagnosis of diabetes mellitus (DM) and its associated microvascular complications. It is proposed to be conducted over a span of six months to gather and analyze data. A total sample size of 160 participants was determined based on the calculations yielded by using RAOSOFT software; margin of error was given at 5%, and confidence interval was set at 95%. This increases the possibility of having power to detect significant associations between CAN and diabetic complications.

The inclusion criteria pertaining to the participants are specific to ensure that only an appropriate sample population is included. These patients should be above 50 years of age and also have either Type 1 or Type 2 DM. They should further have one of the following three microvascular complications: diabetic neuropathy, diabetic retinopathy, or diabetic nephropathy. All the participants will be required to have metformin for diabetes management and they must give consent before joining the study. On the contrary, individuals less than 50 years old, with severe comorbidities like cardiovascular diseases or liver failure, and patients on medications for diseases other than diabetes would not be included in the study. Moreover, this exemption covers those who are significantly impaired cognitively in a manner that could impact their capacity to participate.

Ewing's Test is the principal test which will be used to evaluate CAN [12]. The test contains several components designed to assess autonomic function by analyzing the heart rate changes elicited by deep breathing, standing and the Valsalva maneuver, along with blood pressure changes due to standing and sustained handgrip. Abnormal responses to any of these tests indicate potential presence of CAN [13]. Additional confirmatory tests for diagnosing CAN are electrocardiogram metrics. Some of the key parameters analyzed include the HRV, the lengthening of QT, and variability in the R-R interval during stress tests such as deep breathing or the Valsalva maneuver [14].

This study procedure starts by seeking ethical clearance from the Institutional Ethics Committee to ensure compliance with ethical standards in conducting research on human subjects. Afterwards, the participants will be informed of the purpose and procedure of the study; signed forms will be obtained for their consent. For

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data collection, structured interviews will be held, making use of a validated questionnaire comprising 20 questions related to symptoms of microvascular complications and CAN. Besides that, pertinent medical history that will be obtained from the participants' medical records will be also analyzed for better data extraction.

This will be supported by recording baseline ECGs for each participant with standardised procedure, assessing a variety of cardiac parameters including HRV and QT intervals. The scores from the Ewing test will also be collected during this stage [15]. After getting all the data, analyses will be completed through SPSS version 26. Summaries of findings from the Ewing test are done using descriptive statistics while examining associations of demographic variables and CAN prevalence used chi-square tests. Fisher's Exact test will evaluate relationships between ECG abnormalities and CAN presence, while logistic regression analysis will identify predictors of CAN based on clinical characteristics.

The research outcome is expected to provide an overview of the prevalence of CAN among geriatric diabetic patients with microvascular complications, identifying specific risk factors involved in its development. Such knowledge shall be used as a basis to ensure targeted screenings and interventions that shall enhance cardiovascular outcomes for such populations.

Results

The demographic, clinical, and treatment profiles of diabetic patients with and without Cardiac Autonomic Neuropathy (CAN) across neuropathy, retinopathy, nephropathy, and combined microvascular complications were analyzed. Among the four groups, combined microvascular complication patients exhibited the highest prevalence of CAN (n=29), followed by neuropathy (n=24), nephropathy (n=19), and retinopathy (n=15). Gender distribution revealed a consistent male predominance in retinopathy (CAN: 8; without CAN: 14) and nephropathy (CAN: 10; without CAN: 9) groups, while females were more prevalent in neuropathy (CAN: 15; without CAN: 9) and combined complications (CAN: 15; without CAN: 7).

Age distribution showed that the 61–65 age group was the most affected across all complications, particularly in neuropathy (CAN: 9; without CAN: 8), retinopathy (CAN: 7; without CAN: 5), and nephropathy (CAN: 9; without CAN: 6), whereas the combined complications group had a slightly broader age distribution with noticeable representation in the 71–75 and 76–80 ranges. Duration of diabetes varied significantly, with the majority of non-CAN patients across all groups having diabetes for 5–10 years. In contrast, patients with CAN often exhibited longer durations, particularly 16–20 years in neuropathy (n=9) and combined complications (n=8), and 11–15 years in nephropathy (n=9).

Lifestyle factors such as smoking and alcohol consumption were consistently higher in the CAN groups across all complications. Smoking was particularly prevalent in combined complications (CAN: 10) and neuropathy (CAN: 6), whereas alcohol use was highest among CAN patients with combined complications (n=12). Non-CAN patients, however, exhibited lower smoking and alcohol rates.

Regarding anti-diabetic medication regimens, Metformin in combination with other agents dominated across all groups, with variations reflecting differences in treatment strategies. For neuropathy patients with CAN, Glimepiride + Metformin was most common (n=12), while retinopathy and nephropathy CAN patients relied more on Metformin alone or in combinations like Vildagliptin + Metformin. Combined complications showcased a more diverse treatment landscape, with a notable use of newer agents such as Dapagliflozin (CAN: 2; without CAN: 4) [Table 1].

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Variables		Neuropathy		Retinopathy		Nephropathy		Combined Microvascular Complications	
		CAN +ve (n=24)	CAN -ve (n=16)	CAN +ve (n= 15)	CAN -ve (n=25)	CAN +ve (n=19)	CAN -ve (n=21)	CAN +ve (n = 29)	CAN -ve (n=16)
Gender	Male	9	7	8	14	10	9	14	9
	Female	15	9	7	11	9	12	15	7
Age	61-65	9	8	7	5	9	6	8	5
	66-70	8	3	2	5	3	6	5	4
	71-75	4	3	4	8	2	6	6	3
	76-80	1	1	2	2	2	2	6	2
	81-85	2	1	1	5	3	1	4	2
Duration	5-10	9	9	11	20	6	18	9	10
	11-15	3	4	3	3	9	2	7	4
	16-20	9	2	0	1	4	1	8	2
	21-25	2	1	1	1	0	0	3	0
	26-30	1	0	0	0	0	0	2	0
Smoking History	Smoking	6	1	5	9	6	5	10	7
	Non-Smoking	18	15	10	16	13	16	19	9
Alcoholic History	Alcoholic	4	2	6	6	4	3	12	5
	Non-Alcoholic	20	14	9	19	15	18	17	11
Anti diabetic drugs	Insulin + Metformin	0	5	0	3	0	0	0	0
	Gliclazide + Vildagliptin	1	1	0	1	1	2	0	0
	Glimepiride + Vildagliptin	1	1	2	2	1	1	2	3
	Vildagliptin + Metformin	2	1	3	3	2	2	3	1
	Metformin	4	1	4	7	4	6	7	1
	Glimepiride + Metformin	12	2	1	2	3	5	7	1
	Glimepiride	1	1	1	1	0	0	0	0
	Glipizide + Metformin	0	3	1	2	1	1	0	0
	Metformin + Voglibose	1	0	2	0	4	1	5	2
	Gliclazide + Metformin	0	0	0	1	2	1	0	0
	Glimepiride + Vildagliptin + Metformin	0	0	2	3	0	0	4	1

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	Glibenclamide	0	0	0	0	1	2	0	0
	Dapagliflozin	0	0	0	0	0	0	2	4

Table 1: Distribution of Clinical and Demographic Characteristics in Patients with Microvascular Complications (neuropathy, retinopathy, and nephropathy), Stratified by CAN Status

ECG abnormalities were prominent among CAN patients, with combined complications exhibiting the highest occurrence across all categories, including T-wave changes (n=8), ST changes (n=5), R-wave progression issues (n=5), and prolonged QT intervals (n=6). Neuropathy and nephropathy patients also showed significant T-wave and ST changes, whereas retinopathy patients had relatively lower abnormalities in these parameters [Table 2].

ECG Findings	Total ECG Abnormalities			
	Neuropathy patients with CAN (n=24)	Retinopathy patients with CAN (n=15)	Nephropathy patients with CAN (n=19)	Combined Microvascular Complications (n=29)
Low T-wave, Flattened T wave, Inverted T wave	7	3	6	8
ST-Elevation, ST Depression	7	5	4	5
R-R Interval, Poor R wave progression	4	4	2	5
Prolonged QT-Interval, Abnormal Q wave	4	3	4	6
Others(LVH secondary repolarization, septal ischemia, Left ventricular hypertrophy ,Left axis deviation)	2	-	3	5

Table 2 : Total ECG Abnormalities in patients with CAN

The results show that the patients with CAN showed distinct patterns of longer diabetes duration, higher smoking and alcohol consumption, and more severe ECG abnormalities compared to those without CAN. Combined microvascular complications displayed the most severe clinical manifestations, reflecting a cumulative burden of disease. This analysis underscores the need for vigilant monitoring and tailored management strategies for diabetic patients with CAN, particularly those with multiple complications.

Discussion

This study has given a detailed exploration into demographic, clinical, and therapeutic features of diabetic patients with and without Cardiac Autonomic Neuropathy (CAN), with a specific focus on prevalence, risk

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factors, and complications. Making comparisons between the current research with previous literature, the results of the study support and extend the current understanding related to the multifaceted role of CAN in the diabetic patient. The discussion that follows integrates study findings with reviews of critical literature, allowing for meaningful comparison that holds implications for the clinical practice.

In the present study, the highest prevalence of CAN was seen with combined microvascular complications of neuropathy, nephropathy, and retinopathy, and diabetes duration of 16–20 years was an ongoing risk factor. These results were consistent with Davis et al. (2024), who found that of the FDS2 participants, 15.3% had definite CAN; its presence was significantly associated with longer diabetes duration, higher BMI, and co-morbid conditions that included albuminuria and heart failure [16]. Both studies lend support to the prognostic significance of CAN since Davis et al. reported that CAN is associated with a 2.42-fold increased risk of all-cause mortality. Similarly, our research showed that patients with CAN had worse ECG abnormalities and cardiovascular risks, especially those who had combined complications; it supports the idea that CAN contributes dramatically to mortality and morbidity. Our results of common T-wave alterations, ST-segment shifts, and long QT intervals in patients with CAN are similar to the finding by Khandoker et al. (2023) when they noted that 60% of diabetic patients presented with CAN who had an ST segment depression sign of myocardial ischemia [17]. Prasanna Karthik et al. (2015) identified that severe

CAN has a strong association with abnormal ECG abnormalities whereby it presents with higher mean scores of CAN and prolonged QT intervals [18]. Besides ours, these studies emphasize the need for vigilant monitoring of ECG for early potential myocardial ischemia and other cardiovascular risks among diabetic patients with CAN.

Our study found a strong correlation with longer duration of diabetes and CAN, corresponding to the observation of John et al. (2022), where deterioration of parameters of heart rate variability with disease duration is indicative of progressive worsening of autonomic dysfunction [19]. Lifestyle factors, like smoking and alcohol consumption, were more common among the patients diagnosed with CAN in our study groups as well. Such behaviors have been associated with vascular and autonomic damage, as suggested by Serhiyenko et al. (2018), that proper lifestyle interventions are the most important interventions in CAN management [20].

Combination therapies like Glimepiride + Metformin were used commonly in the management of patients with CAN, pointing out the complexity of the advanced diabetic management. But there should be noted that Hansen et al. 2017 and David S.H. et al. 2022 indicated a possible role of metformin in deteriorating CAN due to vitamin B12 deficiency [21,22]. Both studies associated long-duration use of metformin with low levels of vitamin B12 and worsening autonomic dysfunction, and hence the monitoring of such patients is crucial, along with supplementation in long-term metformin-treated patients.

Emerging diagnostic tools for CAN might include continuous monitoring of HRV. These are promising markers to identify early autonomic dysfunction. HRV analysis in patients with endstage renal disease has proven utility, which should expand potential applicability towards large diabetic populations, as shown by Min et al. (2021) [23]. As a support for our study, it goes without saying that these advanced diagnostic techniques should be integrated with the conventional techniques such as ECG and cardiovascular reflex tests in order to improve early detection and stratification of risk.

Conclusion

This study reveals the heavy burden of Cardiac Autonomic Neuropathy (CAN) in the geriatric diabetic population afflicted with microvascular complications, especially in those who are afflicted with a combination of neuropathy, retinopathy, and nephropathy. The findings hence focus on the fact that a more prolonged duration of diabetes, greater prevalence of smoking and alcohol consumption, and particular anti-diabetic regimens hold a very strong association with the presence of CAN. Besides, specific ECG abnormalities like T wave changes, ST segment shifting, and QT prolongation were more significant in CAN

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patients, which means that patients with CAN are at greater risk of cardiovascular diseases. As per the literature, this article supports the association between CAN and adverse cardiovascular outcomes but has a point to be placed on the early detection via non-invasive studies, such as Ewing tests and ECG. The study advocates routine screening, targeted management strategies, and lifestyle interventions to mitigate the effects of CAN in diabetic populations. The outcomes and intervention strategies for long-term care and morbidity must be further studied in such vulnerable groups.

Declaration

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Conflict of Interest:
The authors declare no conflict of interest related to this research.

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Data Availability:
The data supporting the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions:

1. Archana Venkatesan: Conceptualization, data collection, manuscript writing, and analysis.
2. Mownika Rajasekar: Data acquisition, statistical analysis, and manuscript review.
3. Krishna Ravi: Supervision, study design, manuscript review, and approval of the final version.

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