

Cardiovascular Autonomic Neuropathy in Patients with Diabetes in Cotonou, Benin: A Cross-Sectional Study

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Received Date: 24 July 2021 | **Accepted Date:** 20 August 2021 | **Published Date:** 31 August 2021

Citation: G C Jules, F J Soglo, A A S Cossi, D François. (2021) Cardiovascular Autonomic Neuropathy in Patients with Diabetes in Cotonou, Benin: A Cross-Sectional Study. *J. Endocrinology and Disorders*. 5(5): DOI:10.31579/2640-1045/083

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Abstract

Background: Diabetes mellitus is well known as a major risk factor for cardiovascular diseases. Cardiovascular autonomic neuropathy is one of the diabetes complications that has a major impact on cardiovascular morbidity and mortality in patients with diabetes.

Aim: To determine the prevalence of cardiovascular autonomic neuropathy in patients with diabetes attending the diabetic center in Cotonou and to identify its risk factors.

Materials and Methods: It was a cross-sectional study. Cardiovascular autonomic neuropathy was identified using deep breathing test, standing test and the blood pressure response to standing test (orthostatic hypotension). Chi square test was used for statistical analysis and difference was considered significant when $p < 0.05$.

Results : A total of 405 subjects were included in the study. Their mean age was 53.67 ± 11.68 years and the mean diabetes duration was 6.66 years. The prevalence of cardiovascular autonomic neuropathy was 65.9%. Regarding the severity of the complication in neuropathic patients, 51.7% of them had an early neuropathy, 41.2% have presented a moderate neuropathy and 7.1% have presented a severe neuropathy.

Factors associated with cardiovascular autonomic neuropathy were age of patients ($p = 0.0002$), diabetes duration ($p = 0.0012$), hypertension ($p = 0.0015$), dyslipidemia ($p = 0.027$) and high pulsed blood pressure ($p = 0.032$)

Conclusion: Cardiovascular autonomic neuropathy is a very frequent complication of diabetes mellitus. Unfortunately this complication of diabetes is not often explored in the patient's follow-up examination. As this complication is recognised to be associated with high cardiovascular morbidity and mortality, systematic screening can be recommended in patients with long duration of diabetes or presenting another cardiovascular risk factor.

Key words: diabetes ; cardiovascular autonomic neuropathy ; orthostatic hypotension ; microangiopathy

Introduction

The epidemic trend of the evolution of diabetes mellitus (DM) worldwide [1] is a worrying situation particularly in regard to its numerous complications [2, 3]. Because of these complications diabetes mellitus is considered as a very serious disease with high morbidity and mortality [4]. Through available data cardiovascular complications appear as the main cause of mortality in patients with diabetes, mainly the ischemic heart disease [5, 6]. Cardiovascular autonomic neuropathy has been recognised to increase cardiovascular morbidity and mortality in patients with diabetes [7, 8].

This complication is not often explored during classic patient's follow-up examination. No epidemiological study had been conducted in our population of patients. The present study aimed to determine the prevalence of cardiovascular autonomic neuropathy in patients with diabetes attending the diabetic center in Cotonou and to identify associated factors.

Materials and methods

It was a cross-sectional study with prospective data collection. Study population was constituted by patients with diabetes of both genders attending the diabetic center of Cotonou. Patients were included with their

own consent without distinction of type of diabetes. Sampling technique used was a two steps selection in the patient's medical file attending the center. Data data were collected using a questionnaire established for the needs of the study for individual interview and clinical examination. Cardiovascular autonomic neuropathy was defined according to the Toronto Consensus Panel on Diabetic Neuropathy [9]. To assess cardiac autonomic neuropathy, three tests were used: the two cardio-vagal tests (deep breathing test and standing test) and the blood pressure response to standing (orthostatic hypotension).

Inclusion criteria

All diabetic patients who attend the outpatient center and who have given their consent have been included.

Exclusion criteria

Patients with a known history of neuropathy and hereditary heart disease, pregnant women, patients with hyperthermia, and patients with a previously known respiratory pathology have been excluded.

Sample size

Sample size has been calculated using the Openepi software by considering $p=60$ (mean frequency of cardiac autonomic neuropathy). Then we obtained 369 subjects which were increased by 10% being 405 to minimize the possible bias due to possible missing data.

Deep breathing test

With the patient in supine position, he adapts to a deep and ample breath at a rate of about six cycles per minute. With the help of a pulse oximeter placed on one of his fingers, the highest heart rate that is reached during deep inspirations (HR max) and the minimum heart rate reached during deep expirations were recorded. The difference between the two heart rates was calculated. A difference more than 15 was considered normal and a difference less than 10 was considered abnormal [10].

Standing test

The patient initially in supine position gets up with the pulse oximeter still in one of his fingers. The heart rates at 15 and 30 seconds after orthostatism respectively HR max and HR min were taken and noted; then the difference between the two rates was calculated. A difference more than 15 was considered normal and a difference less than 10 was considered abnormal [10].

Blood pressure response to standing

Orthostatic hypotension has been defined as an excessive fall in BP level (a drop of > 20 mmHg systolic or/and > 10 mmHg diastolic BP) within 3 min of standing and a fall of 30 mmHg systolic BP when a person assumes a standing position

Patient was considered having cardiovascular autonomic neuropathy when one of the three tests was abnormal. Cardiac autonomic neuropathy was considered early when one cardiovagal test was abnormal, confirmed when the two cardiovagal tests were abnormal and severe when the abnormality of the two tests was associated with orthostatic hypotension. [9]. Factors investigated in this study of cardiovascular autonomic neuropathy were age and sexe of patients, diabetes duration, type of treatment, control of the diabetes and the presence of cardiovascular risk factors. Pulsed pressure was defined as the difference between systolic and diastolic pressure.

Statistical analysis were performed using the Chi square test. Difference observed was considered significant when $p \leq 0.05$. Logistic regression test was used for multivariate analysis for factors associated with cardiovascular autonomic neuropathy in univariate analysis.

Results

A total of 405 patients living with diabetes were included in this study. Women represented 72.8% of the study population and this population was largely dominated by type 2 diabetes. Characteristics of the population are shown in table 1.

	Mean \pm SD or N (%)
Age (year)	53.67 \pm 11.68
Sexe (Female)	294 (72.6)
Diabetes duration (year)	6.66 \pm 6.47
Abdomonal obesity (%)	304 (75.1)
High blood pressure (%)	188 (46.4)
Type 2 diabetes (%)	398 (98.27)

Table 1: Baseline characteristics of patients screened for CAN.

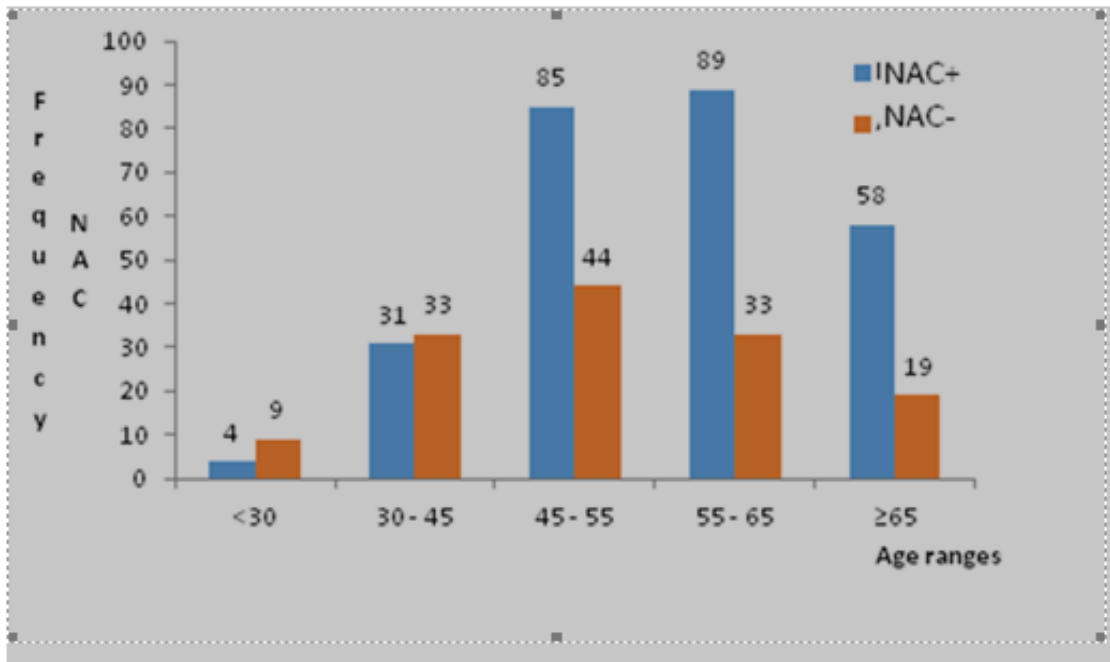


Figure 1: Age and cardiac autonomic neuropathy (CAN).

As shown in this figure, the prevalence of cardiac autonomic neuropathy increased with the age of patients and the statistical analysis has shown a

significant association between age and cardiac autonomic neuropathy with $p=0.002$.

Factors		Number investigated	Prevalence of cardiac autonomic neuropathy (%)	p
Sexe	M	111	67.6	0.668
	F	294	65.3	
Level of education	Non scolarised	156	66.7	0.374
	Primary level	107	71	
	Secondary level	110	62.	
	University level	32	56.3	
Diabetes duration (years)	< 5	216	58.8	0.0012
	≥ 5	189	74.1	
Diabetes treatment	Diete only	28	60.7	0.128
	Oral medication	300	66	
	Insuline	44	56.8	
	Oral medication + Insuline	33	81.8	
Diabetes control (HbA1c)	≤ 7%	33	65.6	0.594
	>7%	142	70.4	

Table 2: Associated factors with CAN

There was no association of sexe with cardiac autonomic neuropathy and wether the diabetes was treated with insulin or oral medication had no influence on the prevalence of cardiovascular autonomic neuropathy.

Factors		Population investigated	Prevalence of autonomic neuropathy (%)	p
Abdominal obesity	Yes	304	66.1	0.887
	No	132	63.6	
Alcohol consumption	Yes	19	63.2	0.794
	No	386	66.1	
Tobacco consumption	Yes	7	71.4	0.400
	No	398	65.8	
High blood pressure	Yes	188	73.9	0.0015
	No	217	59.0	

Pulsed blood pressure (mmHg)	<70	367	64.3	0.032
	≥70	31	81.6	
Dyslipidemia	Yes	81	80.2	0.027
	No	10	50.0	

Table 3: Cardiovascular risk factors and autonomic neuropathy

In cardiovascular risk factors investigated, only high blood pressure, pulsed blood pressure and dyslipidemia have shown significant association with cardiac autonomic neuropathy.

Discussion

Cardiovascular autonomic neuropathy is not investigated in routine follow-up of patients with diabetes. The current study found that the prevalence of cardiac autonomic neuropathy was 65.9%. High prevalences of 73%, 88% and 70% were also reported respectively by Low et al [11], Kenedy et al [12] and Wael et al [13]. However, low prevalences of 36% and 35% were reported respectively by Kempler et al [5] and Pop-Busui et al [14]. The difference observed in these studies can be related to the diagnostic criteria used by the different authors for the selection of patients with cardiovascular autonomic neuropathy. This disparity is thought to be due to the differences in the screening criteria used. Indeed, KEMPLER et al have used the active orthostatic test and blood pressure response to standing and POP-BUSUI et al used deep breathing test, Vasalva maneuver, blood pressure response to standing. In the current study, the criteria used were: the deep breathing test, the standing test and the blood pressure response to standing. Regarding the severity of the complication, a frequency of severe cardiovascular neuropathy was the lower (9.6%). The results of this study are in keeping with previous observational studies. Indeed, Ko et al [15] have found frequencies of 51.1%, 39.3% and 9.6% of respectively early, confirmed and severe cardiovascular autonomic neuropathy.

In our study, mean age of patients was 53.67±11.68 years, very closed to 53.03 years reported by Traoré et al [16] and closed to 55.2 years reported by Shera et al [3]. As reported by several authors [3, 17-19] prevalence of cardiovascular autonomic neuropathy increased significantly with age of patients. There was no association with the sexe of patients in the present study and these findings are in keeping with those reported by Kempler et al [5].

Prevalence of cardiovascular autonomic neuropathy was significantly associated with diabetes duration. Spallone et al [9], Vinik et al [19] and Valensi et al [20] have reported similar results. This is not surprising since diabetes duration has been reported as independent risk factor for cardiovascular autonomic neuropathy whatever the type of diabetes [21].

In the present study, prevalence of cardiovascular autonomic neuropathy was significantly higher in patients with high blood pressure. This result was conform to what has been reported by Boulton et al [22], Ko et al [15] and Ayad et al [23].

An other cardiovascular risk factor significantly associated with cardiovascular autonomic neuropathy was dyslipidemia. Same observation had been made by several other authors [12, 24, 25]. Dyslipidemia had also been reported as progressing factor of cardiovascular autonomic neuropathy [26].

Obesity is a factor currently described to be associated with cardiovascular autonomic neuropathy [20, 27, 28]. This association did not appear in our study certainly because in our analysis obesity was not isolated but pooled with overweight.

Conclusion

Cardiovascular autonomic neuropathy is a very frequent complication of diabetes mellitus but not often investigated in patients follow up. Our

study revealed a high prevalence of cardiovascular autonomic neuropathy in patients with diabetes and several factors were significantly associated to this complication. To contribute to reduce mortality in patients with diabetes, cardiovascular autonomic neuropathy must systematically be investigated in follow up examination of patients when risk factors are present.

Acknowledgments

Not applicable

Author's contributions

All authors contributed equally to the manuscript; all authors read and approved the final version of the manuscript.

Disclosure of potential conflicts of interest

The authors declared that they have no conflict of interest.

Funding

This study received no financial support.

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DOI: [10.31579/2640-1045/083](https://doi.org/10.31579/2640-1045/083)

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