

# Clinical Profile of Cardiac Autonomic Neuropathy in Diagnosed Patients of Type 2 Diabetes Mellitus

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## Abstract

**Background:** Diabetes mellitus (DM) is a clinical syndrome characterized by hyperglycemia caused by relative or absolute deficiency of insulin<sup>1</sup>. Cardiac autonomic neuropathy is a complication of diabetes. Our study intends to study Cardiac Autonomic Neuropathy in diabetics attending our hospital. **Aims and Objectives:** To study the clinical profile of Cardiac Autonomic Neuropathy in type 2 DM. **Materials and Method:** The study was carried out in a tertiary care hospital. The data was collected from August 2013 to December 2015 in 54 patients. The history, examination and bedside tests were done and conclusions drawn. Tests performed included heart rate response to deep breathing, standing, valsalva maneuver; BP response to sustained handgrip and standing. **Results:** Of 54 patients studied, 25 (46.29%) had CAN. Of the 25 patients affected with CAN 3 were between age 41-50, 10 between 51-60, 10 in 61-70 and 2 in 71-80. Out of 25 patients having CAN in the study 14 (56%) are male and 11 (44%) are female. Mean age of patients having CAN was 10.36 as compared to 6.55 in those not having CAN. Our study gave the following. **Conclusions:** Cardiac Autonomic Neuropathy is one of the most common but under diagnosed complications of diabetes mellitus. Cardiac Autonomic Neuropathy is associated with both type 1 and type 2 Diabetes Mellitus. It correlates with the duration and age. Resting tachycardia is a signs of autonomic dysfunction. Heart rate response to deep breathing and B.P. response to sustained hand grip are the most sensitive and specific tests for diagnosis of autonomic dysfunction. Cardiac Autonomic Neuropathy is significantly associated with other microvascular complications of DM like Diabetic retinopathy and nephropathy.

**Keywords:** Cardiac Autonomic Neuropathy, Diabetes Mellitus, Diabetic Neuropathy, Diabetic Nephropathy, Diabetic Retinopathy

## 1. Introduction

One of the most overlooked but easily detectable of all serious complications of diabetes is Cardiac Autonomic Neuropathy. It results from damage to the autonomic nerve fibers that innervate the heart and blood vessels which results in abnormalities in heart rate control and vascular dynamics. Reduced heart rate variation is the earliest marker of CAN.

In a review of several epidemiological studies among individuals diagnosed with diabetes, it was shown that the 5 years mortality rate from this serious complication is five times higher for individuals with CAN than for individuals without cardiovascular autonomic involvement.

CAN manifests itself in various ways like Exercise intolerance Intraoperative cardiovascular lability Orthostatic hypotension Silent myocardial ischemia.<sup>2</sup>

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In the early 1970s, Ewing *et al.*,<sup>3</sup> proposed five simple non-invasive cardiovascular reflex tests (i.e., Valsalva maneuver, heart rate response to deep breathing, heart rate response to standing up, blood pressure response to standing up and blood pressure response to sustained and grip) which have been successfully applied in many studies.

Heart rate response to deep breathing is for the most part a function of parasympathetic activity, although the sympathetic nervous system may affect this measure. The parasympathetic activity plays the greatest role in the heart rate regulation for short-term standing. Response of heart rate to Valsalva maneuver is influenced by both parasympathetic and sympathetic activity. Sympathetic activity is assessed by measurements of blood pressure response to standing and blood pressure response to sustained handgrip<sup>4</sup>.

Autonomic function tests based on changes in heart rate variation and blood pressure regulation detect cardiovascular complications at early stages of involvement even in asymptomatic patients. Detection of CAN in late stage has poor prognosis in diabetic patients. Thus early prognostic capabilities offer a significant contribution to diagnosis and subsequent therapy<sup>5</sup>.

## 2. Methodology

The study was carried out in a tertiary care hospital. The protocol of the study was approved by the hospital ethics committee. The data was collected over 2 yrs from August 2013 to December 2015. A total of 54 patients were studied.

### 2.1 Inclusion Criteria

- 1. Known cases of type 2 Diabetes Mellitus admitted in hospital, both male and female above the age of 40 years.

### 2.2 Exclusion Criteria

- Patients with known cardiac pathologies like ischemic heart disease, myocardial infarction, arrhythmias, cardiac tumours.
- Patients with evidence of other diseases or conditions known to contribute to autonomic dysfunction such as HIV, Parkinsons disease, physical trauma, spinal injuries, drugs
- Patients who were not willing to give consent for the study.
- Patients who were not able to perform the bedside tests.

## 3. Results

Out of 54 patients studied 25 (46.29%) had CAN. Out of 25 patients affected with CAN 3 (12%) belonged to the age group 41-50, 10 (40%) belonged to the age group 51-60 and 10 (40%) belonged to 61-70. 2 (8%) patients in the age group 71-80 were found to have CAN. Out of 25 patients having CAN in the study 14 (56%) are male and 11 (44%) are female. In our study only 1 (14.28%) patient out of 7 having diabetes for <5 year duration had CAN. 16 (41.03%) patients out of 39 with diabetes for 6-10 years had CAN.

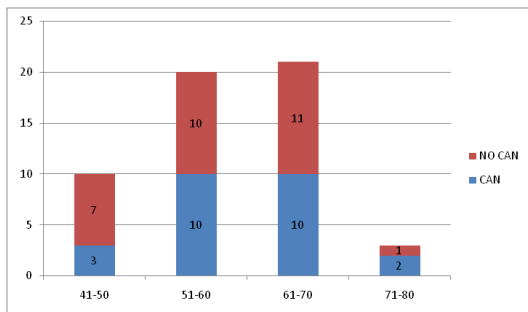
And all the 8 patients with diabetes more than 10 years had CAN. Mean age of patients having CAN was 10.36 as compared to 6.55 in those not having CAN. Out of 25 patients having CAN only 4 (16%) patients have no evidence of nephropathy while 21 (84%) patients had evidence of albuminuria pointing towards nephropathy. Whereas 19 (65.52%) out of 29 patients not having CAN had no evidence of nephropathy. 12 (48%) patients out of 25 having CAN have 2+ albuminuria. Among 54 diabetic patients under study, 25 patients developed Autonomic nervous dysfunction, of which 5 (20%) patients did not have significant changes in their retina, 12 (48%) patients had Non-Proliferative Diabetic Retinopathy (NPDR) and 8 (32%) patients had Proliferative Diabetic Retinopathy (PDR). Thus 20 out of 25 (80%) patients having CAN had evidence of retinopathy in the form of either NPDR or PDR. Maximum no of patients who presented with cardiac autonomic neuropathy had associated NPDR and retinopathy was detected in 80% patients having CAN in the form of either NPDR or PDR. Retinopathy was detected in only 5 (17.24%) patients without CAN. None of the diabetic patients not having CAN had PDR. Our study gave the following conclusions: Cardiac Autonomic Neuropathy is one of the most common but under diagnosed complications of diabetes mellitus. Cardiac Autonomic Neuropathy is commonly associated with type 1 Diabetes

Mellitus but incidence of autonomic dysfunction has been observed to be high even in Type 2 diabetes mellitus. Occurrence of Cardiac autonomic neuropathy very well correlates with duration of diabetes. Longer the duration of diabetes, more are the chances of developing autonomic dysfunction in type 2 DM. Physical parameters like age are associated risk factors for development of autonomic dysfunction. Resting tachycardia is one of the important clinical signs of autonomic dysfunction.

Heart rate response to deep breathing and B.P. response to sustained hand grip are the most sensitive and specific tests for diagnosis of autonomic dysfunction. Cardiac Autonomic Neuropathy is significantly associated with other microvascular complications of DM like Diabetic retinopathy and nephropathy. Early diagnosis of CAN with intensive control of diabetes will help in delaying the onset of symptoms in patients and help to avoid future complications of the disease.

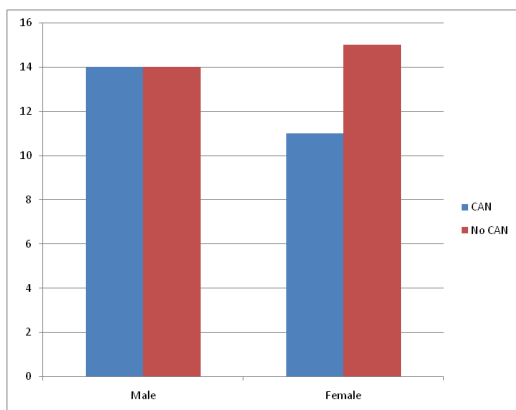
**Table 1.** Age distribution in patients having Cardiac Autonomic Neuropathy

Age(yrs)	CAN	No CAN	Total
41-50	3(12%)	7(24.14%)	10
51-60	10(40%)	10(34.48%)	20
61-70	10(40%)	11(37.93%)	21
71-80	2(8%)	1(3.45%)	3
<b>Total</b>	<b>25</b>	<b>29</b>	<b>54</b>



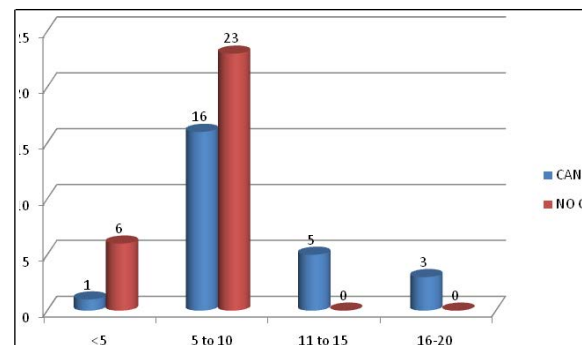
**Table 2.** Sex distribution in patients having Cardiac Autonomic Neuropathy

Sex	CAN	No CAN	Total
Male	14(56%)	14 (48.28%)	28
Female	11(44%)	15(51.72%)	26
<b>Total</b>	<b>25</b>	<b>29</b>	<b>54</b>



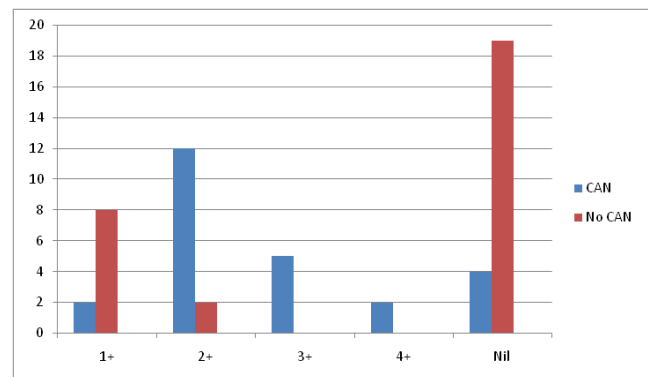
**Table 3.** Association between duration of diabetes (years) and Cardiac Autonomic Neuropathy (CAN)

Duration of Diabetes (years)	Cardiac Autonomic Neuropathy (CAN)		Total Patients
	Yes	No	
< 5	1(14.28%)	6(85.72%)	7
6-10	16(41.03%)	23(58.97)	39
11-15	5(100%)	0	5
16-20	3(100%)	0	3
<b>Total</b>	<b>25</b>	<b>29</b>	<b>54</b>
<b>Mean ± SD</b>	<b>10.36±4.04</b>	<b>6.55±2.09</b>	



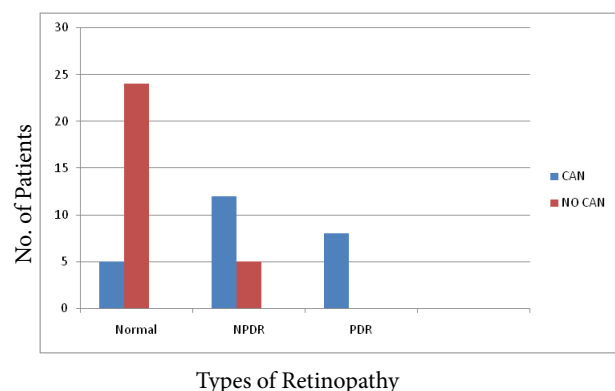
**Table 4.** Association between nephropathy and Cardiac Autonomic Neuropathy (CAN)

Albuminuria	Cardiac Autonomic Neuropathy (CAN)	
	Yes	No
1+	2(8%)	8((27.58%)
2+	12(48%)	2(6.90%)
3+	5(20%)	0
4+	2(8%)	0
Nil	4(16%)	19(65.52%)
<b>Total</b>	<b>25</b>	<b>29</b>



**Table 5.** Association between Retinopathy and Cardiac Autonomic Neuropathy.

Retinopathy	Cardiac Autonomic Neuropathy	
	Yes	No
Normal (0)	5	24
NPDR (1)	12	5
PDR (2)	8	0
<b>Total</b>	<b>25</b>	<b>29</b>

**Table 6.** Association between Retinopathy and Cardiac Autonomic Neuropathy

## 4. Discussion

In a present study the prevalence of Cardiac Autonomic Neuropathy was 46.29% (n=54) which very well correlates with the studies conducted by Basu AK *et al.*,<sup>6</sup> who had a prevalence of 54% and Sinha PK *et al.*,<sup>7</sup> (2012) had prevalence of 42.85%, whereas in a study conducted by Alexandra *et al.*,<sup>8</sup> (2010), the prevalence of CAN was as high as 62.26%. In the study by Ahmed AM *et al.*,<sup>9</sup> (2000) (n=120) CAN was diagnosed in 40% patients.

In our study maximum number of patients having CAN 23 (47.91%) were 51-60 yrs of age (40%) and 61-70 (40%) (n=54) which correlates with the study of Alexandra *et al.*,<sup>8</sup> (n=212) who had a similar result.

In the present study, there was significant association found between CAN and the duration of diabetes.

In a study conducted by Sinha PK *et al.*,<sup>7</sup> (2012) Kempler *et al.*,<sup>10</sup> (2002) (n=3007) Ahmed AM *et al.*,<sup>9</sup> (2000) (n=120), Spallone *et al.*,<sup>11</sup> (1997) (n=161) significant association was seen on multivariate analysis between CAN and duration of diabetes.

In the present study, nephropathy was detected in 84% patients having CAN which was comparable with

the study by Chandy A *et al.*,<sup>2008</sup> (n=174) where Diabetic Neuropathy was found to be associated with Nephropathy and 83.33% patients were affected.

In a study by Basu AK *et al.*,<sup>6</sup> (2011) (n=50) nephropathy was detected in 36% patients having DAN, which is significant (p<0.05). In a study by Kempler *et al.*,<sup>10</sup> (2002) (n=3007) and Spallone V *et al.*,<sup>11</sup> (1997) (n=161) significant correlations were observed between autonomic neuropathy and nephropathy.

In the present study there was a significantly higher incidence of retinopathy in patients with CAN (80%) as against those without CAN (17.24%) which was also seen in most of the studies conducted for the prevalence and associated complications of CAN.

According to the studies by Basu AK *et al.*,<sup>6</sup> (p<0.05), Magri CJ *et al.*,<sup>12</sup> Valensi P *et al.*,<sup>13</sup> Spallone V *et al.*,<sup>11</sup> Kempler *et al.*,<sup>10</sup> significant correlations were observed between autonomic neuropathy and the presence of retinopathy (P < 0.0001).

In a study by Kubo K. *et al.*,<sup>14</sup> findings suggest that progression of diabetic neuropathy is closely associated with progression of diabetic retinopathy.

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