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Research Article

A STUDY ON PREVALENCE OF CARDIAC AUTONOMIC NEUROPATHY IN DIABETES MELLITUS

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ABSTRACT

Introduction: Diabetes mellitus (DM) is a chronic condition characterized by hyperglycemia precipitating because of the complete or partial absence of the insulin hormone. DM has been often associated with a wide range of complications (viz., cardiovascular diseases, nephropathy, retinopathy, and neuropathy), all of which can result in morbidity, disability, and even mortality.[1,2] Cardiac autonomic neuropathy (CAN) is described as impairment of autonomic nerve fibers that innervate the heart and blood vessels resulting in abnormalities of heart rate and vascular dynamics. [3] The presence of CAN increases the risk for severe hypoglycemia, silent myocardial ischemia, stroke, preoperative morbidity, and mortality even in minor surgical procedures.[4,5]
Aim: To study the prevalence of cardiac autonomic neuropathy in patients of diabetes mellitus
Materials and Methods: This cross sectional study was conducted in Department of Medicine, Santosh Medical College and Hospital, Uttar Pradesh. 100 individuals who were diagnosed case of Type 2 Diabetes Mellitus and cardiac autonomic neuropathy after approved ethical standards and fulfilling inclusion and exclusion criteria were taken for the study. The Kruskal-Wallis test followed by Tukey's post-hoc tests was used to compare continuous variables.
Results: Mean age of the patients was 50.15±9.04 years. Out of which 44.4% males and 46.9% were females. Cardiac autonomic neuropathy were more in patients having raised HbA1c (>7%), raised total leucocyte count, blood sugars. There was a significantly higher incidence of HbA1c with cardiac autonomic neuropathy as compared to no cardiac autonomic neuropathy. HbA1c with CAN showed M.D+ S.D. = 1.07, 8.48±1.59, HbA1c without CAN showed M.D.+ S.D. = 8.06±0.64
Conclusions: This study concluded that prevalence of CAN was 46% in diabetes patients and definite CAN being 67.4%. Even though cardiac autonomic neuropathy can be detected by various invasive tests, noninvasive tests remain a key tool to detect it in the remote settings in a cost-effective and user-friendly manner without making people visit higher centers.

INTRODUCTION

India has been labeled as the "Diabetes capital" of the world, owing to the share of highest number of people with diabetes (Sukla *et al*, 2016).[6] Diabetes mellitus (DM) is a recognized cardiovascular risk factor leading to accelerated atherosclerosis, associated with endothelial dysfunction and insulin resistance as well as with non specific inflammatory markers.[7] Around the world, almost 350 million people suffer from diabetes, and these estimates are expected to be doubled by the year 2030 if no active intervention are taken. DM has been often associated with a wide range of complications (viz., cardiovascular diseases, nephropathy, retinopathy, and neuropathy), all of which can result in morbidity, disability, and even mortality (American Diabetes Association, 2004; Zucchi *et al*, 2005).[8,9] The autonomic nervous system plays a crucial role in the maintenance of normal body homeostasis (Jeyaraman, 2012).[10] Autonomic neuropathy is one of the least recognized, dreaded and troublesome complications of diabetes, related to poor metabolic control and longer period since initial diagnosis, which can cast a serious negative impact on the quality of life of diabetes patients (Rao, 2012; Freeman, 2014).[11,12] It can involve cardiovascular, gastrointestinal or urogenital systems. CAN is described as impairment of autonomic nerve fibers that innervate the heart and blood vessels resulting in abnormalities of heart rate control and vascular dynamics (Vinik *et al*, 2013)[13]. The presence of CAN increases the risk for severe hypoglycemia, silent myocardial ischemia, stroke, perioperative morbidity, and mortality even in minor surgical procedures (Yun *et al*, 2014; Kadoi, 2010).[14,15]

The aim of our work was to assess the metabolic disorders of diabetes leading to diffuse and widespread damage of

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peripheral and autonomic nerves, and small vessels. CAN is associated with a high risk of cardiac arrhythmias and with sudden death.

Aims and objectives

To find out the prevalence of Cardiac autonomic neuropathy (CAN) in patients with Diabetes Mellitus.

MATERIAL AND METHODS

This was a cross sectional study, conducted in tertiary care setting during the period from February 2018 to March 2019. 100 subjects were taken into consideration who was diagnosed type 2 Diabetes mellitus with cardiac autonomic neuropathy. The subjects were evaluated and selected after detailed medical history, physical examination, systemic examination and routine investigations to rule out any underlying diseases.

Inclusion criteria

The present study was composed of randomly selected 100 subjects having diabetes mellitus for more than 5 year

Exclusion criteria

1. Patients with diseases like Leprosy, Syphilis, Shingles, HIV, Gullianbarre syndrome.
2. Diseases like Liver failure, Sarcoidosis, Amyloidosis.
3. Malnourishment, vitamin B12 deficiency cases.
4. Oncological disease or Paramalignant syndrome.
5. Hereditary Neuropathy and Chronic Alcoholic person.
6. VI.Patient on treatment with anticholinergic, adrenergic antagonists and vasoconstrictive agents that can affect the results of autonomic function tests.
7. Exposure to toxins as Lead, chemotherapies.
8. Persons having ESRD.
9. Patient having CAD or Acute MI or congenital heart disease.
10. Gestational diabetes mellitus

The patients in the study were subjected to

1. A complete detailed history and general physical examination, fundus examination.
2. Basic Anthropometry (weight, Height, Waist circumference)
3. Fasting and Post Prandial Blood sugar and GTT estimation done using GOD-POD method.
4. Lipid profile.
5. Complete blood count.
6. Renal function tests.
7. Liver function tests.
8. Urine routine and microscopy.
9. Urine for microalbuminuria.
10. Echocardiography if required.
11. X-ray chest (PA view).
12. ECG to diagnose or to rule out CVD with Cardiovascular autonomic reflex tests (CART) as recommended by AHA.
13. Beat to Beat Heart rate variability.
14. Heart rate response to standing.
15. Heart rate response to Valsalva maneuver.
16. Systolic blood pressure response to standing or change in posture (Orthostatic Hypotension)
17. Diastolic blood pressure response to isometric exercise.

Resting ECG was taken for all the patients. Individuals in the study group were subjected to ECG recordings. Preferred lead is lead II.

On the basis of the results of Cardiovascular autonomic reflex tests (CART) patients were classified into 3 groups:

a. Early – two borderline test results or one abnormal result on Heart rate test
b. Definite- Two or more abnormal results on Heart rate test
c. Severe- development of Orthostatic Hypotension

This classification is important as those patients with initial stages of CAN should have a more intensive glycemic control while patients with severe CAN should have a less aggressive glycemic control due to the risk of asymptomatic hypoglycemia.

Data Analysis

The collected data was entered Microsoft Excel computer program. The results are presented in frequencies, percentages and mean ± SD. The continuous variables were compared by using Mann-Whitney U test between two strata. The Kruskal-Wallis test followed by Tukey's post-hoc tests was used to compare continuous variables among the strata. The Spearman correlation coefficient was calculated. The p-value<0.05 will be considered significant. All the analysis will be carried out on SPSS 16.0 version (Chicago, Inc., USA).

RESULTS

Table 1 Distribution of Prevalence of CAN

CAN	No. (n=100)	%
Present	46	46.0
Absent	54	54.0

Table-1 shows the distribution of Prevalence of CAN. The prevalence of CAN was found to be 46%.

Table 2 Distribution of severity of CAN

Severity of CAN	No. (n=46)	%
Early	13	28.3
Definite	31	67.4
Advance	2	4.3

Table-2 & Fig.1 shows the distribution of severity of CAN. Definite CAN was among majority of patients (67.4%) followed by early (28.3%) and advance (4.3%).

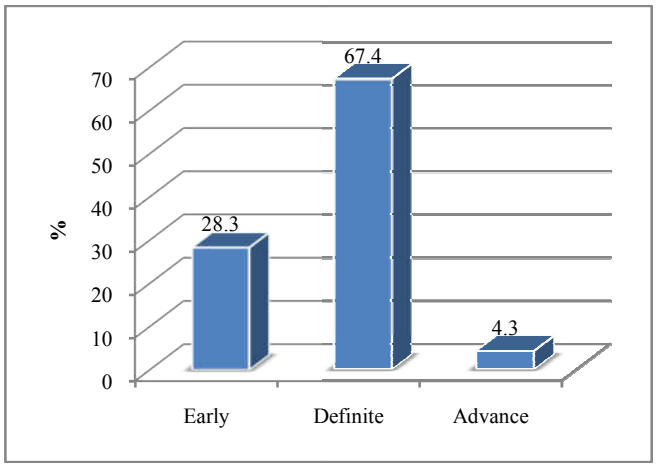

Fig 1 Distribution of severity of CAN

Table 3 Association of prevalence of CAN with age

Age in years	No. of patients		Prevalence of CAN				p-value[1]
			With CAN		Without CAN		
	No.	%	No.	%	No.	%	
<40	9	9.0	1	11.1	8	88.9	0.11
40-50	46	46.0	22	47.8	24	52.2	
51-60	34	34.0	16	47.1	18	52.9	
>60	11	11.0	7	63.6	4	36.4	
Mean±SD	50.15±9.04		50.80±9.04		44.30±6.99		

[1]Chi-square test

Table-3 shows the association of prevalence of CAN with age. More than one third of patients were between 40-50 years (46%) followed by 51-60 (34%), >60 (11%) and <40 (9%). The mean age of patients was 50.15±9.04 years. There was no significant (p>0.05) association of prevalence of CAN with age. The mean age of CAN and without CAN was 50.80±9.04 and 44.30±6.99 years.

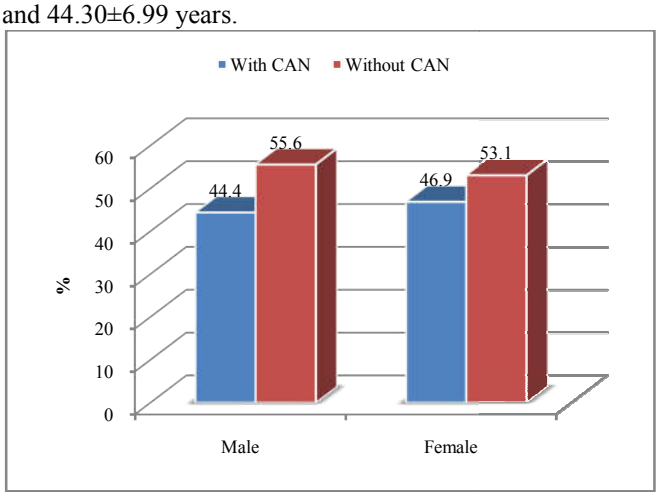

Fig 2 Association of prevalence of CAN with gender

Fig.2 shows the association of prevalence of CAN with gender. The prevalence of CAN was higher among females (46.9%) than males (44.4%). There was no significant (p>0.05) association of prevalence of CAN with gender.

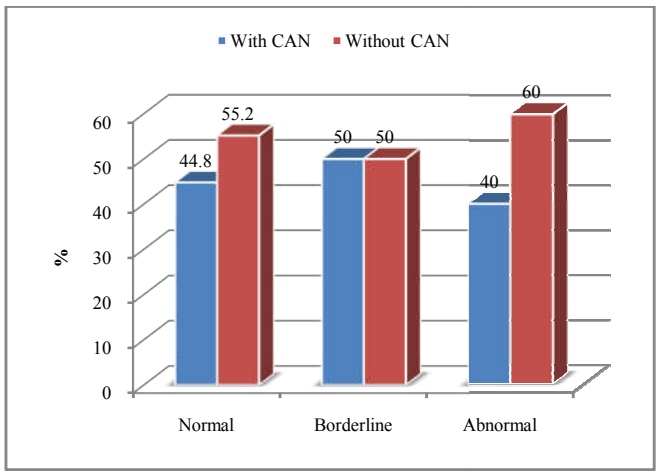

Fig 3 Association of prevalence of CAN with Cardiovascular Autonomic Function parameter-Orthostatic hypotension

Fig.3 shows the association of prevalence of CAN with Cardiovascular Autonomic Function parameter-orthostatic hypotension. Orthostatic hypotension was abnormal among 40% patients.

There was no significant (p>0.05) association of prevalence of CAN with orthostatic hypotension.

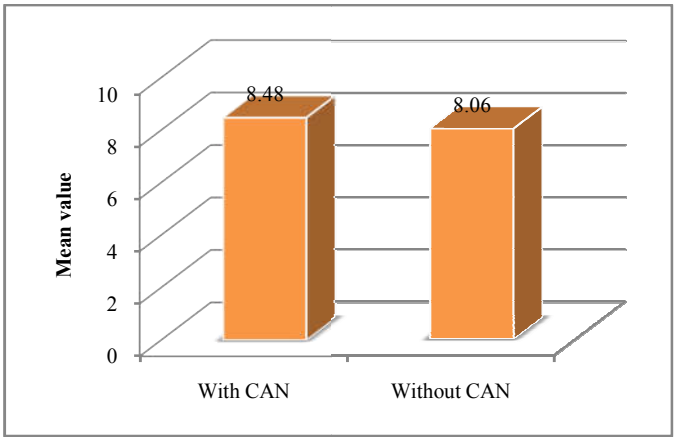

Fig 4 Comparison ofHba1C with CAN and without CAN

Fig.4 shows the comparison of HbA1C with CAN and without CAN. HbA1C was insignificantly (p>0.05) higher among patients with CAN (8.48±1.59) than without CAN (8.06±0.64).

DISCUSSION

Diabetes mellitus constitutes a growing concern to population all over the world because of its well-known chronic complications particularly the triad of neuropathy, retinopathy and nephropathy, which have close correlation with the metabolic abnormalities. Cardiac autonomic neuropathy (CAN) probably contributes to the poor prognosis of cardiovascular disease in type 1 and type 2 diabetes mellitus (Töyry *et al*, 1996; Orchard *et al*, 1996). The main risk factor for autonomic neuropathy was poor glycemic control, but hyperinsulinaemia also had predictive role in the development of parasympathetic autonomic neuropathy. Interestingly, both parasympathetic and sympathetic neuropathies predicted 10 year cardiovascular mortality independent of conventional risk factors. Based on the CAN Subcommittee of the Toronto Consensus Panel on Diabetic Neuropathy (Spallone *et al*, 2011), CAN is defined as the impairment of cardiovascular autonomic control in patients with established diabetes mellitus following the exclusion of other causes. A better understanding of predictive risk factors for CAN incidence and progression is crucial for the development of new strategies for follow-up as well as of novel therapeutic targets.

In the present study, the prevalence of CAN was found to be 46%. Gupta and Gupta (2017) found that CAN was present in 54 patients (54%) out of 100 patients. Barthwal *et al* (1997) reported prevalence of cardiac dysautonomia as 36.2% in Indian diabetic patients whereas Mathur and Gupta (2006) reported prevalence of definite CAN as 58%. Kumar *et al* (2000) and Veglio (1993) reported prevalence of cardiac dysautonomias 60% and 63.7% respectively. Most of the studies done among diabetic patients had a CAN prevalence of 50-60% which corresponds to the results of the present study. Behera and Vishnu (2018) observed that 57.5% of the case had evidence of Cardiac autonomic neuropathy.

Definite severity of CAN was among majority of patients (67.4%) followed by early (28.3%) and advance (4.3%) in this study. Gupta (2017) found that out of 54 (54%) patients having CAN, 16 (16%) had early CAN, 14 (14%) had definite CAN and24 (24%) had severe CAN. Mathur and Gupta (2006) reported 58% CAN among diabetics including 20% having early CAN, 30% having definite CAN and 8% having severe CAN. Another study by Ahire*et al* (2014) reported severe CAN as 20%. Early and definite cardiac dysautonomia was

present in33.3% and 23.3% respectively. Prevalence of severe CAN was comparatively higher in the present study which might be due to late reporting of diabetic subjects where the CAN had already set in. Angadi *et al* (2016) reported that definite CAN was in 8% patients.

Atypical CAN with other combination of abnormalities was seen in 32% patients.

Pillai and Madhavan (2015) evaluated 50, type 2 diabetes mellitus patients and found that 21 (42%) had severe autonomic neuropathy and 12 (24%) had early autonomic neuropathy by the autonomic function tests. In a study by Taha *et al* (2014)out of 150 cases, 106 cases had CAN. Early CAN in 35, definite CAN in 40, severe CAN in 31 patients. Agarwal *et al* (2011) reported the prevalence of CAN in their study as 70%. Among them, early neuropathy was seen in 37%, definite neuropathy in 40% and severe autonomic dysfunction in 22.9% patients.

CONCLUSION

1. The prevalence of CAN was found to be 46%.
2. Definite CAN was among majority of patients (67.4%) followed by early (28.3%) and advance (4.3%).
3. More than one third of patients were between 40-50 years (46%) followed by 51-60 (34%), >60 (11%) and <40 (9%).
4. The mean age of patients was 50.15±9.04 years.
5. The prevalence of CAN was higher among patients of age >60 years (63.6%) followed by 40-50 (47.8%), 51-60 (47.1%) and <40 (11.1%).
6. There was no significant ($p>0.05$) association of prevalence of CAN with age.
7. The mean age of CAN and without CAN was 50.80±9.04 and 44.30±6.99 years.
8. More than half of patients were females (64%).
9. The prevalence of CAN was higher among females (46.9%) than males (44.4%).
10. There was no significant ($p>0.05$) association of prevalence of CAN with gender.
11. There was no significant ($p>0.05$) association of prevalence of CAN with Cardiovascular Autonomic Function parameters.
12. HbA1C was insignificantly ($p>0.05$) higher among patients with CAN (8.48±1.59) than without CAN (8.06±0.64).

Overall, this study concluded that prevalence of CAN was 46% in diabetes patients and definite CAN being 67.4%.Even though cardiac autonomic neuropathy can be detected by various invasive tests, noninvasive tests remain a key tool to detect it in the remote settings in a cost effective and user friendly manner without making people visit higher centers.

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