Original Article

Prevalence of Cardiac autonomic neuropathy in patients with Type 2 diabetes mellitus and Peripheral neuropathy in a Tertiary care teaching hospital in central Kerala

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ABSTRACT

Background: Diabetes mellitus is a group of metabolic disorders characterized by hyperglycemia. Complex combinations between environmental and genetic factors cause various types of diabetes mellitus. Complications from diabetes mellitus, such as cardiac autonomic neuropathy, are common. Unbalanced autonomic function, which manifests as cardiac autonomic neuropathy, is a significant predictor of cardiovascular events in the diabetic patients.

Objectives: To study the prevalence of cardiac autonomic neuropathy in patients with type 2 diabetes mellitus with peripheral neuropathy in a tertiary care teaching hospital.

Methodology: Observational Cross-sectional hospital-based study done in 131 type 2 diabetes mellitus patients who presented to the General Medicine outpatient and inpatient departments of a tertiary care teaching hospital of central Kerala from December 2020 to April 2022. The data was entered in MS excel sheet and was analyzed using SPSS software.

Results: In the present study the mean age was 62.24 years. Among participants, 96.2% had HbA1c levels above 6.5%. Mean duration of living with diabetes is13.40 years. We observed that 65.6% of the patients in our study population had Cardiac autonomic neuropathy. Despite having peripheral neuropathy, 34.4% of participants exhibited normal cardiac sympathetic and parasympathetic function.

Key Words: *Cardiac autonomic neuropathy, peripheral neuropathy, Type 2 diabetes mellitus*

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INTRODUCTION

A series of widespread metabolic conditions known as diabetes mellitus characterized by hyperglycemia. Over the past ten years, type 2 diabetes has become frighteningly more common. Diabetes-related metabolic dysregulation results in secondary pathophysiologic alterations in a number of organ systems that place a heavy burden on both the diabetic patient and the healthcare system. The hormone insulin, which is released by the pancreas, regulates the body's blood sugar levels. Multiple diverse kinds of diabetes mellitus are brought on by intricate interactions between environmental and genetic variables. Depending on the cause of diabetes, lower insulin secretion, decreased glucose absorption, and increased glucose synthesis are all variables that can lead to hyperglycemia [1]. A prevalent condition with a prevalence that increases noticeably with age and increasing levels of obesity is type 2 diabetes [2].

Diabetes mellitus frequently results in complications like cardiac autonomic neuropathy. An major predictor of cardiovascular events in the diabetic population is autonomic imbalance, which appears as cardiac autonomic neuropathy [3] The most researched and clinically significant form of diabetic neuropathy is symmetric polyneuropathy. The parasympathetic and sympathetic nervous systems are the two main parts of the autonomic nervous system. To regulate heart rhythm, cardiac electrophysiology, and the constriction and dilation of blood vessels, these may function separately or in concert [4]. Cardiovascular liability during surgery, orthostasis, resting tachycardia, exercise intolerance, and silent myocardial infarction are only a few of the many clinical features of cardiac autonomic neuropathy. It is a very crippling condition that frequently reduces chances of survival in patients with diabetes. When autonomic imbalance is detected, suitable control measures should be adopted in the form of dietary changes, physical exercise, and the appropriate use of medication. In patients with long-term diabetes, cardiac autonomic dysfunction is an under diagnosed cause of mortality and morbidity [5].

The rationale behind this study is to identify those cases in order to prevent further complications.

MATERIALS AND METHODS

A Cross-sectional hospital-based study done in 131 type 2 diabetes mellitus patients who presented to the General Medicine outpatient and inpatient departments of a tertiary care teaching hospital of central Kerala from December 2020

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to April 2022. Ethical clearance wastaken.

SAMPLE SIZE
Considering the prevalence of cardiac autonomic neuropathy among patients with type 2 diabetes and peripheral neuropathy as 82.5% from the study "Cardiac autonomic neuropathy in type 1 and type 2 diabetes patients" by Anca et al [6], with a confidence interval of 95% CI and power of 80 % with an acceptable error of 7% with an attrition of 10%, total sample size calculated is 125. Software used is win Pepi, version 11.38

INCLUSION CRITERIA
Patients with type 2 diabetes mellitus (As diagnosed by American Diabetes Associationcriteria) with more than 5 years duration and associated with peripheral neuropathy. Those who give consent to participate in this study.

EXCLUSION CRITERIA
Age more than 80 years

Chronic alcohol consumption with CAGE score >1

History of neurotoxic poisoning in the last 5 years (e.g., Neurotoxic insecticides) 4.Vitamin B 12 deficiency determined by Vitamin B12 assay. Previous history of chronic renal failure

Documented intake of drugs causing peripheral neuropathy such as Amiodarone, Lithium,Dapsone, Ethambutol, Phenytoin, Chloroquine in the last 2 years.

Patients taking drugs causing orthostatic hypotension and tachycardia such Vasodilators, Anti parkinsonian agents, Alpha receptor blockers, Calcium channel blockers, Sildenafil. Major diagnosed psychiatric illnesses.9. Thyroid disorders

METHODOLOGY
Patients who satisfy the inclusion and exclusion criteria was subjected to evaluation after getting informed consent. The Cardiac Autonomic Neuropathy System Analyzer (CANS 504, Diabetic Foot Care) was used to assess cardiac autonomic neuropathy. Standard operation protocol was followed. The Digital Biothesiometer (VIBRODOP, Diabetic foot care India) was used to measure peripheral neuropathy by positioning the probe at certain spots on the soles of the feet and evoking a vibration sense. The results were tabulated for and scores are calculated.

DATA COLLECTION AND ANALYSIS
Manual collection of the data as printouts from the machines after completion of the procedure. Collected Data were compiled in MS Excel and analyzed using SPSS 22 software. Prevalence was evaluated. Data were analyzed using frequencies and percentages.

RESULTS
In our study, the average age was 62.24 years with standard deviation 7.653. The minimum and maximum age was 42 and 76 years respectively. Study population mainly consists of female population (51.1%). Male participants were 48.9 %. (Table.1)

Table 1: Distribution of sex

Sex	Frequency	Percent
Male	64	48.9%
Female	67	51.1%

HbA1C
Among 131 study population of type 2 diabetic mellitus patients, 126 participants (96.2%) hadHbA1c level more than 6.5%. Here the average HbA1c was 8.532% with standard deviation1.679. The minimum and maximum HbA1c was 6.3% and 13.0% respectively (Table.2)

Table 2: Distribution of HbA1C

HbA1c (%)	Frequency	Percent
< 6.5	5	3.8%
> 6.5	126	96.2%

DURATION OF DIABETES
Here the mean (median) duration of diabetes was 13.40 (11.00) years with standard deviation 7.418. The minimum and maximum duration of diabetes was 5 and 43 years respectively. Cumulatively 69 (52.7%) of patients have

diabetes for more than 10 years

<p align="center">Table 3: Distribution of duration of diabetes</p>

Duration (Years)	Frequency	Percent
Up to 10	62	47.3%
11 - 20	52	39.7%
Above 20	17	13.0%

PERIPHERAL NEUROPATHY

In the study population 73 (55.7%) participants had severe peripheral neuropathy. 31(23.7%) participants were experiencing moderate peripheral neuropathy and 27 (20.6%) participants found to have mild peripheral neuropathy. (Fig.1)
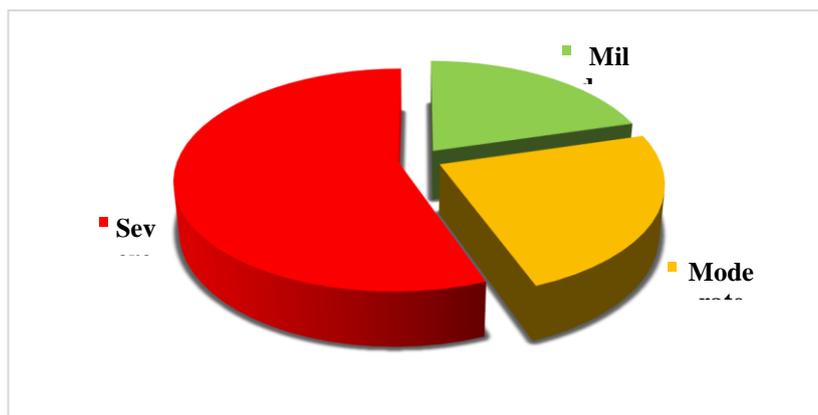

<p align="center">Fig 1: Distribution of severity of peripheral neuropathy</p>

CARDIAC AUTONOMIC NEUROPATHY

Among the patients with type 2 diabetes mellitus and peripheral neuropathy, we found that 86 (65.6%) of them are having cardiac autonomic neuropathy (Table.4)

<p align="center">Table 4: Prevalence of cardiac autonomic neuropathy</p>

Cardiac Autonomic Neuropathy	Frequency	Percent
Normal	45	34.4%
Abnormal	86	65.6%

CARDIAC AUTONOMIC NEUROPATHY AND GENDER

Among 64 male patients 40 (62.5%) participants were suffering from CAN. Similarly, among67 female participants, 46 (68.7%) was suffering from CAN. (Fig.2)
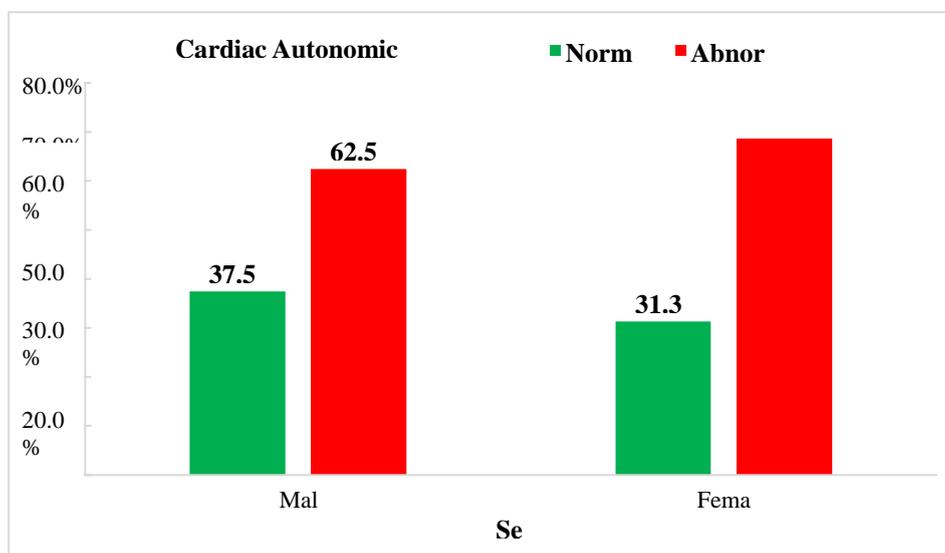

<p align="center">Fig. 2: Prevalence of cardiac autonomic neuropathy among different sex</p>

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SEVERITY OF CARDIAC AUTONOMIC NEUROPATHY

Among the 86 participants who were suffering from CAN, 38 (29%) of them are at early stage of CAN, a small proportion of 7 (5.3%) patients were suffering from moderate level of CAN. Whereas 41 (31.3%) participants was definite cardiac autonomic neuropathy (Table.5)

Table 5: Distribution of severity of cardiac autonomic neuropathy

Severity	Frequency	Percent
Normal	45	34.4%
Early	38	29.0%
Moderate	7	5.3%
Definite	41	31.3%

DISCUSSION

This study was done in a group of 131 patients. Study period is from December 2020 to April 2022 as per thesis protocol, taking all the consecutive cases of in-patient and outpatient departments of a tertiary care teaching hospital of central Kerala.

The mean age in the present study was 62.24 years with standard deviation of 7. 65. The minimum and maximum age was 46 and 76 years respectively. In a similar cross-sectional study conducted by Tahniyah Haq et al, in which they studied the patients with type 2 diabetes mellitus who also have peripheral neuropathy frequently have cardiac autonomic neuropathy; the mean age of the study group was 55.58 years, with a standard deviation of 10.73 years [7].

In a related study, Bhuyan AK et al [8]. looked at type 2 diabetes mellitus (DM) patients with a mean age of 53.3 and a standard deviation of 10.37 years to determine the prevalence and risk factors for cardiac autonomic neuropathy (CAN). The minimum and maximum ages were 36 and 72 respectively [8].

In the present study, out of 131 participants, 67 were females which constitutes 51.1% and 64 were males which constitutes 48.9%. In the study done by Tahniyah Haq et al [7], 50% were males and 50% were females. In the study conducted by Bhuyan AK et al [8], 60 were males and 40 were females (Total = 100) 96.2% of the patient in the present study has HbA1C of more than 6.5% and 3.8% has less than 6.5%. Average HbA1c was 8.532% with standard deviation of 1.679. The minimum and maximum value was 6.3% and 13% respectively. Another study done by Meghanad Meher et al aimed to find the impact of glycemic control over cardiac autonomic neuropathy, the average HbA1c was 9.54% with standard deviation of 2.18 [9].

The mean duration of diabetes was 13.40 years with standard deviation of 7.418. Among this, 47.3% were up to 10 years duration, 39.7% were between 11 and 20 years and 13% were with duration of diabetes more than 20 years. Study by Tahniyah Haq et al mean duration of diabetes was 14.15 years with standard deviation of 7.99 [7] In a similar study by P. Valensi et al done to evaluate the Factors Involved in Cardiac Autonomic Neuropathy in Diabetic Patients duration of diabetes in years was 9.3 with a standard deviation of 0.9 5 [10].

The primary objective of our study was to estimate the prevalence of cardiac autonomic neuropathy in patients with type 2 diabetes mellitus having peripheral neuropathy. At the end of our study, we found that the prevalence of CAN is 65.6% in our study population. CAN was found in 86 patients out of 131 study population with different grades of severity. Among the patients diagnosed with cardiac autonomic neuropathy, 46 were females and 40 were males. In the similar study conducted by Tahniyah Haq et al, all patients with peripheral neuropathy had some grade of CAN with prevalence of 100% [7]. In the study done by Bhuyan AK et al, the prevalence of CAN was found to be 70% [8]. Both the studies show a higher prevalence then the present study. Another study done by Spallone et al based on clinical impact, assessment, diagnosis, and management on Cardiovascular autonomic neuropathy in diabetes, found that the prevalence of confirmed CAN is around 20% which shows a lower prevalence than the present study [11] Peripheral neuropathy is the most important complication of diabetes, especially in patients with uncontrolled diabetes. Vibration perception threshold is a simple handheld screening device for the diagnosis of peripheral neuropathy. It is classified as mild, moderate and severe. In this study 20.6% patients have mild, 23.7% have moderate and 55.7% have severe peripheral neuropathy. Patients with severe neuropathy are significantly high in number in our study population. This association has got significant role in the management of diabetes as long-standing neuropathy leads to serious complications. This result emphasizes on strict control of diabetes in order to prevent these complications. In a previous study by Tahniyah Haq et al, they found that, 13% of the participants in the study were without peripheral neuropathy, 34.4% of those were with subclinical neuropathy and 49.3% of those were with symptomatic peripheral neuropathy [7].

It is very important to diagnose autonomic dysfunction as it may leads frequent and lethal complications of diabetes mellitus. Dysautonomia can results in arrhythmias and sudden cardiac death. It can also increase the risk of myocardial ischemia, cerebrovascular accident and associated morbidities. In the current study 31.3% patient had definite

involvement of cardiac autonomic neuropathy.5.3% had moderate and 29% had early involvement of dysautonomia.45 patients (34.4%) had normal cardiac sympathetic and parasympathetic function even though they have peripheral neuropathy as a complication. Another study conducted by Bhuyan AK et al diagnosed early CAN in 25%, definite CAN in 24%, and 21% with severe CAN [8].

A cross-sectional study by Tahniyah Haq et al carried out on 62 adult type 2 diabetic patients, all patients with peripheral neuropathy had some grades of CAN and more than half of them (>50%) had severe CAN [7].

CONCLUSION

The mean age in this study was 62.24 years with standard deviation of 7. 653. Out of 131 patients 51.1% were females and 48.9% were males. The mean duration of diabetes was 13.40 years with standard deviation of 7. 418. Among this 47.3% were up to 10 years duration, 39.7% were between 11 and 20 years and 13% were with duration of diabetes more than 20 years. The prevalence of CAN is 65.6% in our study population. CAN was found in 86 patients out of 131 study population with different grades of severity.20.6% patients have mild,23.7% have moderate and 55.7% have severe peripheral neuropathy. Patients with peripheral neuropathy are prone for developing cardiac autonomic neuropathy. As severity of peripheral neuropathy increases, severity cardiac neuropathy also increases. Cardiac autonomic neuropathy is a frequent and life-threatening complication of diabetes mellitus. This study emphasizes the importance of prevention and control diabetes in order to prevent these life complications.

RECOMMENDATIONS

Early detection of undiagnosed cardiac autonomic neuropathy to prevent further complications. Changes in medical counselling and patient education in chronic diabetic patients regarding autonomic neuropathy Further study to evaluate association of Peripheral Neuropathy and Cardiac Autonomic Neuropathy.

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