



A Study of Autonomic Neuropathy in Chronic Diabetes Mellitus in a Teaching Hospital

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Abstract

Diabetic autonomic neuropathy is one of the important complications with increased risk of cardiovascular morbidity and mortality. The present study aimed to investigate diabetic autonomic neuropathy in chronic diabetic patients with tests. It is prospective, observational study was conducted in the Department of General Medicine, Prathima Institute of Medical Sciences, Nagunur, Karimnagar. The following tests were performed to find the autonomic neuropathy in patients. (1) Heart Rate variations during Deep Breathing, (2) Heart Rate variations during Postural Changes, (3) Heart Rate variations during Valsalva maneuver, (4) Diastolic BP variation in response to Sustained Hand Grip Exercise. The laboratory investigations included FBS, Urine Analysis, Kidney & Liver Function Tests, HbA_{1c}, ECG, 2D ECHO were done. The mean age of the patients in the type I DM patients was 37.5 years and mean type II DM patients was 49.5 years. The total number of patients n=55 and out of which n=20 type I DM and Type II DM were n=35. Heart rate variations to postural changes were found to be abnormal in 54.54%, Valsalva ratio was found to be abnormal in 72.72%, Abnormal DBP was found in 21.81% of the patients. Within the limitations of the present study, we conclude that Diabetic Autonomic Neuropathy (DAN) affects a significant of diabetic patients both type I DM and type II DM. The incidence tends to increase as the duration of diabetes mellitus increases. Hence autonomic nervous system tests to determine DAN should be included in the routine examination of chronic diabetics at least once a year to determine its presence and delay its progression.

Keywords: Diabetic Autonomic Neuropathy [DAN], Chronic Diabetes Mellitus, Teaching Hospital.

Introduction

Diabetic autonomic neuropathy (DAN) is among the least understood complications of diabetes despite its significant negative impact on survival and quality of life in people with diabetes^[1]. A clinical symptom of autonomic neuropathy generally occurs in cases of long-standing

diabetes. Symptoms suggestive of autonomic dysfunction may be common and frequently be due to other causes rather than to true autonomic neuropathy. Subclinical autonomic dysfunction can, however, occur within a year of diagnosis in type 2 diabetes patients and within two years in type 1 diabetes patients^[2]. The reported

prevalence of DAN varies, depending on whether studies were carried out in the community, clinic, or tertiary referral center^[1,3]. The variance among prevalence studies also reflects the type and number of tests performed and the presence or absence of signs and symptoms of autonomic neuropathy. Other factors that account for the marked variability in reported prevalence rates include the lack of a standard accepted definition of DAN, different diagnostic methods, variable study selection criteria, and referral bias. Additional complicating factors include the wide variety of clinical syndromes and confounding variables such as age, sex, duration of diabetes, glycemic control, diabetes type, and another factor. Studies have indicated the variability of DAN from a low of 7.7% to a high of 90% depending on criteria used.^[1] A subtype of the peripheral polyneuropathies that accompany diabetes, DAN can involve the entire autonomic nervous system (ANS). ANS vasomotor, viscera motor and sensory fibers innervate every organ. In many DAN may be subclinical and it is manifested by dysfunction of one or more organ systems (e.g., Cardiovascular, Gastrointestinal Genitourinary, Sudomotor, or Ocular) Many organs are dually innervated, receiving fibers from the parasympathetic and sympathetic divisions of the ANS. DAN typically occurs as a system-wide disorder affecting all parts of the ANS.^[4] Indeed, because the vagus nerve (the longest of the ANS nerves) accounts for 75% of all parasympathetic activity, and DAN manifests first in longer nerves, even early effects of DAN are widespread. Because of its association with a variety of adverse outcomes including cardiovascular deaths, cardiovascular autonomic neuropathy (CAN) is the most clinically important and well-studied form of DAN. The introduction over 20 years ago of simple, noninvasive tests of cardiovascular autonomic function has supported the extensive clinical and epidemiologic investigation of DAN.

Material and Methods

It is prospective, observational study was conducted in the Department of General Medicine, Prathima Institute of Medical Sciences, Nagunur, Karimnagar. Institutional Ethical committee permission was obtained for the study. Written consent was obtained from all the participants of the study. A total of n=40 patients diagnosed with type I and type II diabetes were included in the study. The patients showing the signs and symptoms of diabetic autonomic neuropathy were included in the study. Exclusion criteria were coronary artery disease, hypertension, heart failure, respiratory disease, patients on antidepressants, neuroleptics, etc. The clinical assessment of autonomic neuropathy was performed in patients along with a complete history and examinations of Cardiovascular system (postural tachycardia, exercise intolerance, giddiness), GIT (Diarrhea, Constipation, Dysphagia, Xerostomia) Urinary symptoms (retention, incontinence). The following tests were performed to find the autonomic neuropathy in patients

1. Heart Rate variations during Deep Breathing
2. Heart Rate variations during Postural Changes
3. Heart Rate variations during Valsalva maneuver
4. Diastolic BP variation in response to Sustained Hand Grip

The laboratory investigations included FBS, Urine Analysis, Kidney & Liver Function Tests, HbA_{1c}, ECG, 2D ECHO were done.

Results

The mean age of the patients in the type I DM patients was 37.5 years and mean type II DM patients was 49.5 years. The total number of patients n=55 and out of which n=20 type I DM and Type II DM were n=35 shown in table 1.

Table 1: Age and sex-wise distribution of the cases in the study

Age Group	Type I DM		Total	Type II DM		Total
	Male	Female		Male	Female	
20 – 30	3	2	05	0	0	00
31 – 40	5	3	08	2	1	03
41 – 50	4	3	07	14	10	24
51 – 60	0	0	00	2	1	03
61 – 70	0	0	00	3	2	05
Total	12	8	20	21	14	35

The HbA1c values were measured during the study in both groups of patients. Most of the patients in Type I DM had the values in the range of 7.0 to 7.5 % the mean value was 7.2% in this group and in the type II DM patients most of the patients had HbA1c values in the range of 7.6 –

7.9 and the mean value was 7.8% the other relevant information is given in table 2. The BMI was also calculated in both groups. In the type, I group the mean BMI was 23.5 and the mean BMI in type II was 28.9.

Table 2: Showing the HbA1c levels in patients with DM

HbA1c %	Type I DM		Total	Type II DM		Total
	Male	Female		Male	Female	
6.0 – 6.5	0	0	00	1	0	01
6.6 – 6.9	1	0	01	3	0	04
7.0 – 7.5	5	3	08	3	3	06
7.6 – 7.9	4	2	06	9	5	14
8.0 – 8.5	1	2	03	2	3	05
8.6 – 8.9	1	1	02	2	2	04
>9.0	0	0	00	1	1	02

The duration of diabetes mellitus was recorded in both the group of patients with diabetic autonomic neuropathy. In the type, I DM a patient the mean duration was found to 9.5 years and in type II the

mean duration was 7.5 years. Most of the patients in the study were having durations ranging from 6 – 10 years shown in table 3.

Table 3: Duration of the diabetes mellitus in patients with DAN

Duration in years	Type I DM		Total	Type II DM		Total
	Male	Female		Male	Female	
0 – 5	0	1	01	4	3	07
6 – 10	5	6	11	8	5	13
11 – 15	5	0	05	6	3	09
16 – 20	2	1	03	3	3	06
> 20	0	0	00	0	0	00
Total	12	8	20	21	14	35

An assessment of diabetic nephropathy was done by collecting 24 hours of urine samples for albuminuria. Normoalbuminuria was found in n=11 patients of type I DM microalbuminuria in n=6 patients and macroalbuminuria was found in

n=3. In the type II DM patients normoalbuminuria was found in n=31 patients, microalbuminuria in n=3 and macroalbuminuria in n=1 patient shown in table 4.

Table 4: Showing the presence of albuminuria in patients of the study

Albuminuria	Type I DM		Total	Type II DM		Total
	Male	Female		Male	Female	
Microalbuminuria	5	1	06	1	2	03
Macroalbuminuria	2	1	03	1	0	01
Normoalbuminuria	5	6	11	19	12	31
Total	12	8	20	21	14	35

Deep breathing can evaluate changes in the heart rate provoked by deep breathing at the rate of 6 breaths per minute. The subject is asked to lie in the supine position and instruct to inhale through nostrils for 5 seconds and exhale for 5 seconds the complete cycle is repeated for 6 times per minute. Care must be taken to prevent hyperventilation.

Calculation of respiratory sinus arrhythmia (RSA) was done. RSA amplitude is defined as the difference between the end of expiration and end of inspiration in heart rate. The normal values of RSA depend on the age of the patient hence the values were accordingly classified as normal, borderline and abnormal shown in table 5.

Table 5: Respiratory Sinus Arrhythmia on deep breathing exercise

Respiratory Sinus arrhythmia	Type I DM		Total	Type II DM		Total
	Male	Female		Male	Female	
Normal	2	1	03	3	2	05
Borderline	2	1	03	8	2	10
Abnormal	8	6	14	10	10	20
Total	12	8	20	21	14	35

Heart rate variations are physiological compensatory mechanisms due to the gravitational redistribution of blood due to active change in posture from supine to standing. Due to decreased stroke volume and venous return heart rate increases by 10 - 15 beats per minute. These changes were monitored by ECG leads attached to the subject and recording of ECG during posture changes. Evaluation of changes in heart rate 30/15

ratio is performed during the initial phase of adaptation to orthostasis (45 sec), it is calculated as a quotient of the maximal approximately 30th heartbeat to minimal near 15 heartbeats the RR intervals in this period and the 30/15 ratio should be at least 1.04 but it tends to decrease with age^[5] Here the normal values were calculated and shown in table 6.

Table 6: Heart rate variations [HRV] to postural changes

HR variation to posture	Type I DM		Type II DM		Total
	Male	Female	Male	Female	
Normal	4	2	11	8	25
Abnormal	8	6	10	6	30
Total	12	8	21	14	55

Valsalva maneuver consists of forced expiration against the resistance with the expiratory pressure during strain at 40 mm Hg for 15 seconds. The subject is laid in the supine position and instructed to blow into an aneroid manometer and keep the pressure of 40mmHg for 15 seconds he should be allowed to see the gauge to adjust strain. The

subject is given feed regarding pressure and time left. It may be repeated twice after 3 minutes rest. The VR ratio is calculated as the longest RR interval after VM/ Shortest RR interval during VM. The normal values were determined for age and sex and recorded in table 7.

Table 7: showing the results of the Valsalva ratio in patients of the study

Valsalva Ratio	Type I DM		Total	Type II DM		Total
	Male	Female		Male	Female	
Normal	2	1	03	3	2	05
Borderline	2	1	03	2	1	03
Abnormal	8	6	14	16	11	27
Total	12	8	20	21	14	35

The Diastolic response to handgrip is measured and the subject is asked to hold the handgrip dynamometer in dominant hand and allowed to compress with maximum effort for 4-5 seconds and isometric contraction was recorded. Total of 3 attempts with a pause for 15 seconds was given the mean of the three reading was calculated as T

max the maximum tension. After 5 minutes the subject is asked to perform at 30% of the Tmax and during the test, DBP was recorded from the non-exercised arm, and each participant was instructed to perform normal respiration the recorded values are shown in table 8.

Table 8: Diastolic Blood Pressure [DBP] response to handgrip exercise

DBP response to handgrip	Type I DM		Total	Type II DM		Total
	Male	Female		Male	Female	
Normal	7	5	12	11	9	19
Borderline	2	1	03	6	2	08
Abnormal	3	2	05	4	3	07
Total	12	8	20	21	14	35

Discussion

Diabetic Autonomic Neuropathy (DAN) is a common complication seen in chronic diabetic patients. It affects the autonomic nervous system including all visceromotor, vasomotor, sensory fibers. The manifestations can vary depending on whether it is clinical or subclinical and the organs involved. The most commonly affects systems are the gastrointestinal tract and the cardiovascular system. The present conducted was conducted on n=55 patients of both types I DM and type II DM. They were showing signs and symptoms suggestive of autonomic neuropathy. The association of autonomic neuropathy with HbA1c, BMI, Albuminuria was studied. Autonomic neuropathy was assessed using 5 standard tests. It has been advocated that abnormality of more than one test is necessary for the diagnosis of autonomic neuropathy. Symptoms of DAN do not occur until long after the onset of diabetes. Symptoms suggestive of DAN may be common and also be due to other causes rather than true autonomic neuropathy. Subclinical autonomic dysfunctions can occur within a one year of

diagnosis in type II diabetes and can occur within two years in type I DM^[6]. The association of cardiovascular autonomic neuropathy is clinically important and hence studied extensively. In the present study the mean age of the patients in the type I DM patients was 37.5 years and mean type II DM patients was 49.5 years. S Agarwal et al;^[7] have found the patients were (80%) from the age group 50 -60 years. In the present study, we found that the duration of diabetes has a significant impact on the occurrence of DAN, here we found most of the patients with DAN were having diabetes from 5 to 16 years. A study by M. J. Sampson et al;^[8] for the progression of diabetic autonomic neuropathy over a decade in insulin-dependent diabetics found that may take more than a decade for the symptoms of DAN to appear and sometimes it may not progress further. In the present study, microalbuminuria was found in 16.36% of the patients and macroalbuminuria was found in 7.27% of the patients. Other studies have reported the incidence of nephropathy in patients with Diabetic Autonomic Nephropathy^[9]. In the present study patients were checked symptoms

suggestive of autonomic neuropathy it was found that constipation was in 63.63%, Gastroparesis in 20% of patients, palpitations were reported by 45.45%, incomplete voiding of urine 18.18%, incontinence 9.09% and sudomotor dysfunctions like anhidrosis, hyperhidrosis, hypothermia in 20% of the patients, postural hypotension in 36.36% of the patients it shows that the most common symptoms were related to cardiovascular and gastrointestinal symptoms. The results are similar to other studies in this filed ^[4, 10-12].

Conclusion

Within the limitations of the present study, we conclude that Diabetic Autonomic Neuropathy (DAN) affects a significant of diabetic patients both type I DM and type II DM. The incidence tends to increase as the duration of diabetes mellitus increases. Hence autonomic nervous system tests to determine DAN should be included in the routine examination of chronic diabetics at least once a year to determine its presence and delay its progression.

Conflict of Interest: None

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