



## Study of Autonomic Function Tests in Type II Diabetes Mellitus

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### Abstract

**Introduction:** Diabetes mellitus is a chronic condition that has been around since far before the birth of Christ. The frequency of diabetes mellitus has dramatically increased in recent years both in India and globally. Because diabetes mellitus usually affects the nerve system, retinopathy, nephropathy, and neuropathy are the three pathological diseases that make up this disease. Although autonomic neuropathy is frequently asymptomatic, it is linked to a higher risk of mortality and other diabetes-related consequences. Dysfunction to the autonomic nervous system is thought to reflect cardiovascular reflex damage elsewhere. Present study was undertaken with an objective to assess autonomic nervous system abnormality in type II diabetes mellitus patients by using simple bedside autonomic function tests

**Materials and Methods:** Present study is a cross sectional prospective study conducted from duration 2017 to 2020. 100 Type II diabetic patient between age 25 – 45 years without any Co- morbidity or disease were enrolled. Total patients were divided into two groups based on duration of diabetes as group A & group B. tests of the autonomic nervous system were performed in all patients

**Observations and Results:** Statistically significant result found for Systolic (Lying down), Diastolic (Lying down), Systolic (Standing), Diastolic (Standing), Systolic CP & Diastolic CP between group A & group B (**P<0.05**). Mean  $\pm$  SD of VR found in group A was  $1.66 \pm 0.59$  & in group B was  $1.51 \pm 0.64$ . Mean  $\pm$  SD of HRR found in group A was  $1.41 \pm 0.52$  & in group B was  $1.28 \pm 0.44$ . Statistically significant result found for HRR (**P=0.01**).

**Conclusion:** In conclusion, the results of the present investigation showed that there exist active sympathetic and parasympathetic nervous systems abnormality in diabetics. Since both autonomic nervous system components are involved and there are symptoms, it is likely that these diabetics have had autonomic dysfunction from quite some time. For these, conventional autonomic function tests (AFT) can be utilized as a reliable method for evaluation.

**Keywords:** AFT, DM

### Introduction

Diabetes mellitus is a chronic condition that has been around since far before the birth of Christ. Many of the existing knowledge about the illness was known to ancient Indians Charaka and Sushruta, who gave it the name "Madhumeha" (rain of honey) because they recognised the sweetness of urine<sup>1</sup>. The frequency of diabetes mellitus has dramatically increased in recent

years both in India and globally. There are currently close to 40.9 million diabetics in India, and by the year 2025, there are projected to be close to 69.9 million<sup>2</sup>. There are probably issues involved with this heavy burden. In the context of insulin resistance and relative insulin shortage, type 2 diabetes mellitus— also known as non-insulin-dependent diabetes

mellitus or adult-onset diabetes—is a metabolic condition marked by elevated blood glucose levels. The incidence is quickly rising and is projected to double by 2030<sup>3</sup>. Because diabetes mellitus usually affects the nerve system, retinopathy, nephropathy, and neuropathy are the three pathological diseases that make up this disease<sup>4</sup>. Diabetes mellitus frequently results in neuropathy, which can impact both the autonomic nervous system and peripheral nerves. The primary cause of autonomic neuropathy is diabetes. Depending on the diagnostic technique, the features of the patient group, and the kind of diabetes being researched, its prevalence might range from 1% to 90%<sup>5</sup>. Although autonomic neuropathy is frequently asymptomatic, it is linked to a higher risk of mortality and other diabetes-related consequences. Although practically every region of the body is affected when autonomic nerves are damaged, the cardiovascular system is where the effects are most noticeable. Dysfunction to the autonomic nervous system is thought to reflect cardiovascular reflex damage elsewhere. Present study was undertaken with an objective to assess autonomic nervous system abnormality in type II diabetes mellitus patients by using simple bedside autonomic function tests (AFT)

### Material and Methods

Present study is a cross sectional prospective study conducted from duration 2017 to 2020 in the Department of Physiology, MGM's Medical College & Hospital. Institutional ethics committee permission was taken prior to commencement of present study. 100 type II diabetes mellitus patients fulfilling inclusion and exclusion criteria were enrolled. Study was explained to all participants and written informed consent was obtained from all.

### Inclusion Criteria

Type II diabetic patient between age 25 – 45 years without any Co- morbidity or disease.

### Exclusion Criteria

1. Associated diseases in which autonomic nervous system is affected like, Tabes dorsalis and leprosy etc.
2. Patients receiving drugs that are known to interfere with cardiac or respiratory function such as beta-blockers, sympathomimetic drugs, antihypertensives like alpha methyl dopa, diuretics etc.

3. Patients with comorbid conditions like ischemic heart disease, rheumatic heart disease, arrhythmia and cardiac failure.
4. Patients who cannot cooperate for various tests and physically handicapped patients and those unable to stand up quickly and maintain an erect posture

### Procedure

Patients were instructed not to have coffee, tea or any cold drink 12 hours before the tests. They were asked to come to the physiology laboratory at 9 am after having a light breakfast. Detailed history was taken on a standard proforma as duration of the disease, whether he/she on oral hypoglycemic drugs/insulin therapy. Reports of investigation (fasting blood sugar, post prandial blood glucose value and HbA1c value) were noted. Total patients were divided into two groups based on duration of diabetes as

- A. **Group A:** Type II diabetes patients with diabetes duration  $\leq 10$  years
- B. **Group B:** Type II diabetes patients with diabetes duration  $> 10$  years

Subjects were asked to relax in supine position for 30 minutes. At the time of examination, the participants weight and height was measured. BMI was computed as weight / height<sup>2</sup> ( kg/m<sup>2</sup> ). tests of the autonomic nervous system were performed in all patients

### Methods of assessment of autonomic function test

#### Tests for parasympathetic damage

1. **Immediate heart rate response to standing (30:75 ratio):** The test is simple to use and requires only a standard electrocardiograph and ability of patients to stand-up a continuous ECG recording and measurement of the R-R interval at beat 15 and 30 after standing to give 30:15 ratio.
2. **Valsalva ratio:** The patients lay comfortably and resting ECG was recorded for 15 seconds. Later the patient was asked to blow into a mouth piece connected to a manometer so as to keep the pressure up to 40 mmHg and to maintain it for 15 seconds while a continuous ECG recording was done. After 30 seconds ECG was monitored again for 15 sec. The Valsalva ratio was calculated as longest R-R interval after release to shortest R-R interval during manoeuvre.

Tests for sympathetic damage

- 1. Blood pressure response to standing:** When patients stand, 2 min after standing decline in systolic blood pressure by more than 20 mmHg and by more than 10mmHg for diastolic blood pressure is considered abnormal.
- 2. Cold pressure test:** Simulation of sympathetic system may be caused due to physical or mental stress. Dipping a hand in cold water acts as a pain stimulus and causes rise in blood pressure.

**Operational definition**

Diagnosis of diabetes mellitus was made by criteria given American diabetics association 2014<sup>6,7</sup>.

**Observation and Result**

**Table 1: Distribution of cases according to baseline characteristics**

Sr No	Group A Mean ± SD	Group B Mean ± SD	t value	P value
<b>Age (Years)</b>	48.25 + 11.45	54.00 + 09.05	2.786	0.006 (S)
<b>Height (cm)</b>	143.7 + 07.06	154.5 + 08.84	6.75	<0.0001 (S)
<b>Weight (Kg)</b>	53.84 + 04.60	54.66 + 07.45	0.66	0.50 (NS)
<b>BMI (kg/m2)</b>	22.53 + 02.89	22.96 + 03.51	0.66	0.50 (NS)

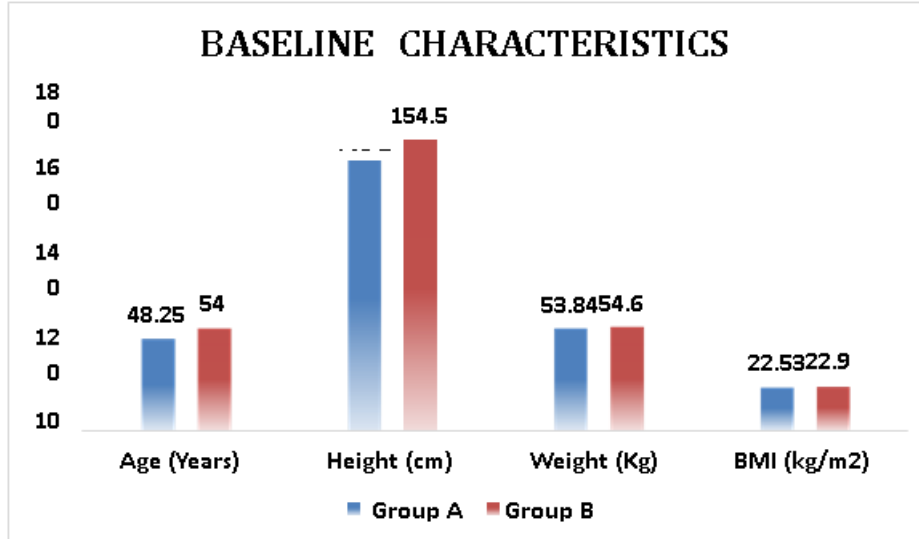
Table 1 shows distribution of cases according to baseline characteristics. Mean ± SD of age (years) found in group A was 48.25 + 11.45 & in group B was 54.00 + 09.05. Mean ± SD of Height (cm) found in group A was 143.7 + 07.06 & in group B was 154.5 + 08.84. Mean ± SD of Weight (Kg) found in group A was 53.84 + 04.60 & in group B was 54.66 + 07.45. Mean ± SD of BMI (kg/m2) found in group A was 22.53 + 02.89 & in group B was 22.96 + 03.51 (Graph 1).

Subjects were diagnosed as having fasting serum glucose values > 126 mg/dl, post- prandial blood glucose value >200 mg/dl and glycated hemoglobin (HbA1c values) > 7 %.

**Statistical analysis**

Statistical analysis was performed us-ing SPSS software, version 20. Data are expressed as mean ± SD and frequency with percentages N (%).  $\chi^2$ -test was used to evaluate qualitative data and to study association between two variables. Statistical significance was assumed if P value less than 0.05.

**Graph 1: Distribution of cases according to baseline characteristics**

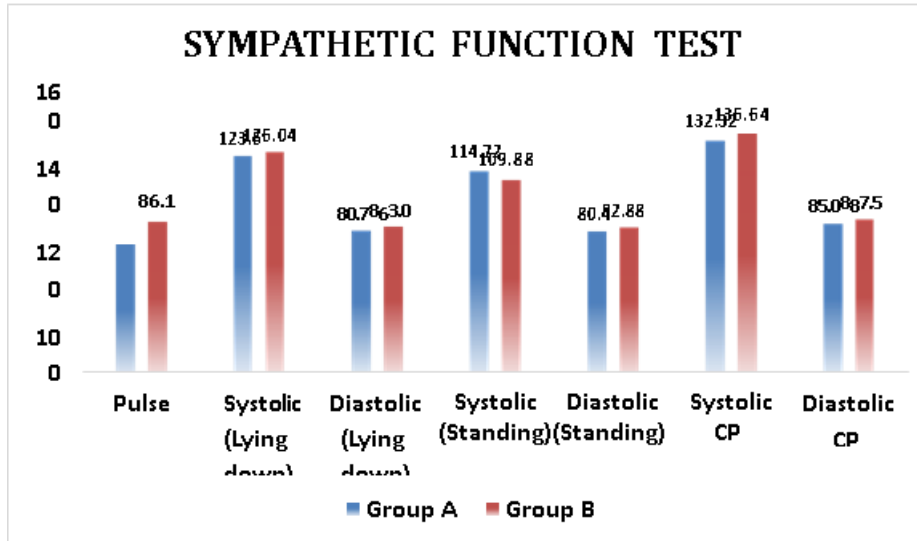


**Table 2: Distribution of cases according to sympathetic function test**

Sr No	Group A Mean ± SD	Group B Mean ± SD	t value	P value
<b>Pulse</b>	73.64 ± 17.73	86.1 ± 5.65	4.735	<0.0001
<b>Systolic (Lying down)</b>	123.6 ± 5.59	126.04 ± 7.44	1.854	0.066
<b>Diastolic (Lying down)</b>	80.76 ± 3.44	83.04 ± 5.49	2.488	0.014
<b>Systolic (Standing)</b>	114.72 ± 7.50	109.88 ± 10.79	-2.604	0.01
<b>Diastolic (Standing)</b>	80.4 ± 3.72	82.88 ± 5.58	2.61	0.01
<b>Systolic CP</b>	132.32 ± 5.38	136.64 ± 4.77	4.248	<0.0001
<b>Diastolic CP</b>	85.08 ± 4.08	87.56 ± 5.70	2.502	0.01

Table 2 shows distribution of cases according to sympathetic function test. Statistically significant result found for Systolic (Lying down), Diastolic (Lying down), Systolic (Standing), Diastolic (Standing), Systolic CP & Diastolic CP between group A & group B (P<0.05) (Graph 2)

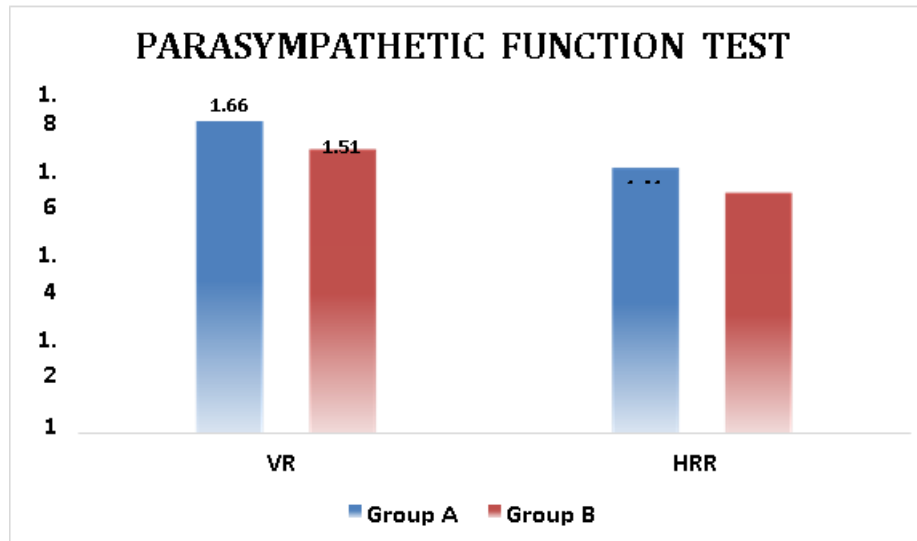
**Graph 2: Distribution of cases according to sympathetic function test**



**Table 3: Distribution of cases according to parasympathetic function test**

Sr No	Group A Mean ± SD	Group B Mean ± SD	t value	P value
<b>VR</b>	1.66 ± 0.59	1.51 ± 0.64	1.854	0.066
<b>HRR</b>	1.41 ± 0.52	1.28 ± 0.44	2.488	0.014

Table 3 shows distribution of cases according to parasympathetic function test. Mean ± SD of VR found in group A was 1.66 ± 0.59 & in group B was 1.51 ± 0.64. Mean ± SD of HRR found in group A was 1.41 ± 0.52 & in group B was 1.28 ± 0.44. Statistically significant result found for HRR (P=0.01) (Graph 3)

**Graph 3: Distribution of cases according to parasympathetic function test**

## Discussion

Autonomic nervous system (ANS) innervates almost all organ systems and is primarily involved with homeostatic regulatory mechanisms. Nerve dysfunction or neuropathy associated with diabetes mellitus (DM) is called diabetic neuropathy. Autonomic neuropathy due to DM involves various systems, such as gastrointestinal, cardiovascular, sudomotor, genitourinary, and metabolic systems. Cardiac autonomic neuropathy results from injury to the autonomic nerve fibers that innervate the heart and blood vessels, which in turn results in altered heart rate (HR) control and vascular dynamics. With the help of classical AFTs, subjects who are at risk of cardiac complications are found out and early intervention can be done to prevent morbidity and mortality due to DM. Present study was undertaken with an objective to assess autonomic nervous system abnormality in type II diabetes mellitus patients by using simple bedside autonomic function tests (AFT).

In present study mean  $\pm$  SD of age (years) found in group A was  $48.25 \pm 11.45$  & in group B was  $54.00 \pm 09.05$ . Mean  $\pm$  SD of Height (cm) found in group A was  $143.7 \pm 07.06$  & in group B was  $154.5 \pm 08.84$ . Mean  $\pm$  SD of Weight (Kg) found in group A was  $53.84 \pm 04.60$  & in group B was  $54.66 \pm 07.45$ . Mean  $\pm$  SD of BMI (kg/m<sup>2</sup>) found in group A was  $22.53 \pm 02.89$  & in group B was  $22.96 \pm 03.51$  (**Table 1**) (**Graph 1**). In similar study by **Sucharita S et al (2011)**<sup>8</sup> total of 23 (15 male and 8 female) patients with type 2 diabetes of 10-15 years duration and their age and

gender matched controls (n=23) were recruited. **Jayabal M et al (2015)**<sup>9</sup> in their study included cases with average age of  $48.53 \pm 5.12$  years (mean  $\pm$  SD) and that of the volunteers was  $47.10 \pm$

$3.59$  years. **Pathak A t al (2017)**<sup>11</sup> included 50 cases and 50 controls with mean age of cases  $54.92$  years and of controls,  $53.82$  years. Out of 50 cases, 29 (58%) were male and 21 (42%) were females, and in controls, 31 (62%) were male and 19 (38%) were females. The mean weight of cases was  $62.24$  kg and in controls was  $60.74$  kg. The mean BMI of cases was  $24.82$  kg/m<sup>2</sup> and of controls were  $23.48$  kg/m<sup>2</sup> (SD  $\pm 2.83$ )

In present study Statistically significant result found for Systolic (Lying down), Diastolic (Lying down), Systolic (Standing), Diastolic (Standing), Systolic CP & Diastolic CP between group A & group B (**P<0.05**) (**Table 2**) (**Graph 2**). In present study mean  $\pm$  SD of VR found in group A was  $1.66 \pm 0.59$  & in group B was  $1.51 \pm 0.64$ . Mean  $\pm$  SD of HRR found in group A was

$1.41 \pm 0.52$  & in group B was  $1.28 \pm 0.44$ . Statistically significant result found for HRR (**P=0.01**) (**Table 3**) (**Graph 3**)

In similar study by **Sucharita S et al (2011)**<sup>8</sup> they found Peripheral nervous examination (n=16) revealing that 38% (n=6) had mild peripheral neuropathy and 25% (n=4) had moderate peripheral neuropathy. Out of 10 diabetics who tested positive for peripheral neuropathy 9 presented with at least



one autonomic symptom and cardiac sympathetic involvement and 6 diabetics had cardiac parasympathetic involvement based on conventional clinical autonomic tests. Peripheral nervous examination revealed negative results for six diabetics, out of which four had cardiac parasympathetic involvement and five had sympathetic involvement. **Jayabal M et al (2015)9** in their study results showed that significant impairment was present in patients with type 2 diabetes than in healthy volunteers, and it was more pronounced for parasympathetic system than for sympathetic system. **Juhi Agrawal et al (2019)10** Showed in their results that there is decrease in cardiovascular autonomic functions more in diabetic patients with NPDR as compared to diabetic patients without retinopathy. **Pathak A t al (2017)11** found Regarding the various autonomic functions, HR response to deep breathing was the most sensitive test to determine autonomic neuropathy. In 34 (68%) individuals, it is abnormal, while in 16 (32%) patients, it is normal. An aberrant HR response to standing (30.15 ratio) followed, with 26 (52%) patients having an abnormal reaction and 24 (48%), a normal response. 7 (14%) patients had abnormal HGT, while 43 (86%) patients had normal HGT. Twenty patients (40%) had aberrant vasospasms, while thirty patients (60%) had normal vasospasms. Postural hypotension was the autonomic neuropathy test with the lowest sensitivity. In 6 (12%) cases, this was abnormal, while in 44 (88%) cases, it was normal.

## Conclusion

In conclusion, the results of the present investigation showed that there exist active sympathetic and parasympathetic nervous systems abnormality in diabetics. Since both autonomic nervous system components are involved and there are symptoms, it is likely that these diabetics have had autonomic dysfunction from quite some time. For these, conventional autonomic function tests (AFT) can be utilised as a reliable method for evaluation. To get a firm conclusion, a more in- depth investigation including a larger sample size of DM patients is necessary.

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