

## Study of Cardiovascular Autonomic Dysfunction in Type 2 Diabetes Mellitus

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### Abstract

**Background:** Type 2 Diabetes mellitus is the most common metabolic and endocrine disorder that is characterized by hyperglycemia (high blood sugar) in the context of insulin resistance and shortage of insulin. Obesity and lack of physical activity is thought to be the primary cause of type 2 diabetes and known to cause chronic complications particularly neuropathy, retinopathy, and nephropathy. One of the most over looked of all serious complications of diabetes is Cardiovascular Autonomic Neuropathy (CAN) which encompasses damage to the autonomic nerve fibers. **Aim:** The present study aims at assessing cardiovascular autonomic efficiency in diabetic people of urban region. **Methods:** cardiovascular autonomic activity was assessed with help of Ewing's autonomic function test parameters. Age matched 50 non diabetic and 50 diabetic subjects were included in this study. **Results:** It was observed that heart rate response to deep breathing, immediate standing and Valsalva manouvre in diabetic groups showed significant difference when compared to control group. It also shows that blood pressure response to immediate standing and resting systolic blood pressure were significantly increased in diabetic groups. **Conclusion:** we found that diabetic people exhibit autonomic dysfunction

**Keywords:** Type 2 diabetes mellitus, autonomic function test, cardiovascular autonomic neuropathy

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### I. Introduction

Diabetes mellitus (DM) is a pandemic clinical condition. Estimates indicate that the total number of people with DM will double from 171million in 2000 to 366 million in 2030. By 2030, more than 75% of people with DM will live in developing countries. The greatest relative increase is expected to occur in countries in the Middle East, sub-Saharan Africa, and India (1) Type 2 Diabetes mellitus is the most common metabolic and endocrine disorder that is characterized by hyperglycemia (high blood sugar) in the context of insulin resistance and shortage of insulin. Type 2 diabetes makes up about 90% of cases of diabetes, with the other 10% due primarily to diabetes mellitus type 1 and gestational diabetes. Obesity and lack of physical activity is thought to be the primary cause of type 2 diabetes and known to cause chronic complications particularly neuropathy, retinopathy, and nephropathy. Diabetic Autonomic Neuropathy (DAN) is among the least recognized and less understood complication of diabetes mellitus despite its significant impact on survival and quality of life in people with diabetes (2,3) One of the most over looked of all serious complications of diabetes is Cardiovascular Autonomic Neuropathy (CAN) which encompasses damage to the autonomic nerve fibers that innervate the heart and blood vessels resulting in abnormalities in heart rate control as well as defect in central and peripheral vascular dynamics (4,5,6). Diabetic autonomic neuropathy in patients with diabetes is an irreversible complication, but early detection is important, because although the condition cannot be reversed, intensive diabetes care may delay it further development (2). There are many studies done on the evaluation of autonomic nervous system activity in type 2 diabetes mellitus in developed countries. There is scarcity of comparable study from developing countries like India. Hence this study is carried out.

### II. Materials And Methods

The present study was conducted in the department of physiology, Rajah muthiah medical college, Annamalai University, Annamalai nagar. This study was undertaken after approval by the Institutional ethical committee overseeing human studies. Experiments were done in accordance with Helsinki declaration of 1975. 50 patients of Type 2 diabetes mellitus in the age groups 25-75 years of both sexes were selected for this study. The control group comprises 50 healthy subjects of both sexes. All the subjects in the study and control groups were subjected to detailed clinical examination and other relevant investigations as required. Diabetic patients with systemic diseases and kidney failure, heart diseases were excluded from the study. The control group

subjects were free from diabetes mellitus, hypertension, heart diseases or any other illness expected to interfere with cardiovascular autonomic function. Written informed consent was obtained from each subject prior to inclusion in the study. In addition to routine general examination the height and the weight of the subjects were noted. Body mass index was calculated as weight (kg) /height (m<sup>2</sup>). The autonomic functions were assessed using five simple non-invasive cardiovascular reflex tests proposed by Ewing et al (7). Three tests for parasympathetic function and two tests for sympathetic function were used for the study.

**I. Parasympathetic function tests**

**Heart rate response to deep breathing**

Before beginning the test, subjects were taught to breathe six breaths a minute, five seconds for each inhale and five seconds for each exhalation in sitting posture. An electrocardiogram was recorded throughout the period of deep breathing. The onset of inspiration and expiration was marked. R-R interval was measured during expiration and inspiration. The difference between maximum and minimum heart rate was calculated. A difference of 18 beats or more per minute was taken as normal, less than this was taken as an abnormal response.

**Heart rate response to immediate standing**

On changing the posture from supine to standing heart rate increases immediately by 10 -20 beats per minute. This response is detected by recording ECG in supine and standing postures. Subject was made to lie down in supine posture. Subject was asked to relax completely for a minimum period of 10 minutes. Basal heart rate was recorded. Subject was asked to stand up immediately and change in heart rate is noted and the point at starting to stand is also marked. The shortest R-R interval around the 15<sup>th</sup> beat and the longest R-R interval around the 30<sup>th</sup> beat after starting to stand are measured. The characteristic response is expressed by the 30:15 ratios. In the present study 1.04 and above was taken as normal. 1.01 to 1.03 was taken as borderline response. Less than 1.00 was taken as abnormal response.

**Heart rate response to Valsalva maneuver:**

The test is performed by the patients blowing into a mouthpiece connected to a sphygmomanometer and holding it at a pressure of 40 mm Hg for 15 seconds (in sitting position) while a continuous electrocardiogram is recorded. The result is expressed as Valsalva ratio (8), which is the longest R-R interval after the manoeuvre, to the shortest R-R interval during the manoeuvre.

**II. Sympathetic function test**

**Blood pressure response to standing:**

The test was performed by measuring the patient's blood pressure with a sphygmomanometer while he is lying down quietly and again when he stands up. The postural fall in blood pressure is taken as the difference between the systolic blood pressure during lying and the systolic blood pressure during standing. In the present study a mean fall in systolic blood pressure of 30 mm Hg or more was taken to indicate postural hypotension (abnormal response). Postural fall of systolic blood pressure of 10 mm Hg or less was taken as normal. And the value 11 to 29 mm Hg was taken as borderline.

**B.P response to sustained handgrip**

The subject was then asked to maintain the handgrip (isometric contraction) at 30 percent of that maximum up to three minutes in sitting position. Blood pressure was recorded at the beginning and at the end of the procedure. The rise of diastolic blood pressure was calculated. In the present study a rise of diastolic blood pressure of 16 mm Hg or more was taken as normal, 11 to 15 mm Hg was taken as borderline and 10 mm Hg or less than that was taken as an abnormal response.

**Statistical analysis:**

The students 't' test was used to compare mean values of autonomic function test parameters between study and control group. A P value of < 0.05 was taken as significant.

**III. Results**

**Table 1.** Effects on parasympathetic functions between control and study groups

Parasympathetic function tests	Control group	Study group
Resting H.R	74.18 ±7.21	82.10±9.21
H.R Response to deep breathing	27.21±12.21	19.15±12.21*
H.R Response to immediate standing	1.19±19.11	1.05±12.10*
H.R response to Valsalva manoeuvre	1.29±29.31	1.16±0.12*

H.R = Heart rate \* P < 0.0001

In the present study 50 subjects of type 2 diabetes patients were selected after using proper exclusion criteria. The mean age in control and study group was 54 years. The mean height in control and study group was 150 and 154.73 cms respectively; mean weight of control and study group were 62.78kg and 64.91kg respectively, the BMI in control and study group were 25.04 and 25.32 respectively. The mean weight of the study group is higher than the control group. There is no significant difference with respect to age between study and control groups.

Table 1 shows the effects on parasympathetic efficiency between control and study group. In the present study Heart rate response to deep breathing between control and Study group ( $P < 0.0001$ ) was significant. It also shows that Heart rate response to immediate standing was decreased significantly in study (diabetic) group. Valsalva ratio was significantly reduced in study group ( $P < 0.0001$ ). All parasympathetic function tests showed significant P Values.

**Table 2.** Effects on sympathetic functions between control and study groups

Sympathetic function tests	Control group	Study group
Resting systolic B.P	122.07±18.27	134.27±11.21*
Resting diastolic B.P	74.07±9.22	86±7.04
B. P response to immediate standing	6.09±4.35	10.8±10.16*
B.P response to sustained handgrip	18.90±8.32	21.33±37.10

B.P = Blood Pressure \*  $P < 0.05$

Table 2 shows resting systolic blood pressure between control and study group was significant. No significant change was observed in resting diastolic blood pressure. Blood pressure response to immediate standing between control and study group was statistically significant. There is no significant difference between control and study group in sustained handgrip test.

#### IV. Discussion

Autonomic neuropathy is a common complication of diabetes which is easily overlooked. Cardiovascular autonomic neuropathy (CAN) is associated with high rates of mortality & morbidity. [1, 2] So approaches to manage cardiovascular autonomic neuropathy could reduce mortality and morbidity of diabetic patients. CAN encompasses damage to the autonomic nerve fibers that innervate the heart & blood vessels, which may result in abnormalities in heart rate control and vascular dynamics (9). Autonomic dysfunction can occur early after diagnosis or even before diagnosis of diabetes (10). In the present study baseline systolic blood pressure was significantly reduced in study group. In the present study heart rate response to deep breathing was significantly reduced in study group (type 2 diabetic subjects) it was in agreement with Gnanadesigan et al (11), Chiranjeevi et al (12), AK Basu et al (13). Deep breathing test is the simplest and most widely performed measure of autonomic control of the heart. This test produces a specific, accurate and reproducible indirect measure of vagal cardiac function. In the present study it indicates autonomic damage. It was in agreement with Fareedabanu AB et al (14), Gnanadesigan et al.

The most commonly recognized autonomic dysfunction in diabetes is orthostatic hypotension or fainting when standing up. In the case of diabetic autonomic dysfunction, it is due to the failure of the heart and arteries to appropriately adjust heart rate and vascular tone to keep blood continually and fully flowing to the brain. The present study shows significant difference in heart rate response to immediate standing. It is in line with Gnanadesigan et al,

This study also showed that Valsalva ratio is lower in type 2 diabetic patients than control subjects this indicates decreased parasympathetic function. It was in agreement with Gnanadesigan et al, Komal K. Makwana1 et al (15). The present study showed that resting systolic blood pressure was increased significantly in diabetic group. It indicates autonomic imbalance. This study also showed that significant change was observed in blood pressure measurements after immediate standing in diabetic group. In the present study there is a fall in systolic blood pressure in diabetic subjects as compared to the controls. This indicates failure of baroreceptor reflex mechanism due to chronic hyperglycemia which affects autonomic nerves. It was in agreement with Gnanadesigan et al., In the present study, sustained handgrip test values were increased in diabetic people but it was not statistically significant. The results in handgrip test shows that the diabetic subjects were in borderline category. In the present study most common abnormal result was the deep breathing test. This test reflects the parasympathetic activity; this is the most sensitive test than other parameters. This indicates defect is more severe in parasympathetic activity. Autonomic neuropathy can occur in both Type 1 and Type 2 diabetes, which can modify the cardiovascular responses. (16,17)

## V. Conclusion

The present study indicates that there is statistically decrease in parasympathetic activity and increase in sympathetic activity in type 2 diabetic patients in urban areas. There is significant relationship between autonomic neuropathy and chronic diabetes mellitus in our study. We conclude that Ewing's clinical autonomic function tests were more sensitive in detecting early features of autonomic dysfunction in diabetic patients.

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