

#### 4 original article

## EVALUATION OF SYMPATHETIC CARDIO VASCULAR REFLEXES IN DIABETIC PATIENTS & ITS CORRELATION WITH DURATION OF DISEASE

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### ABSTRACT

**INTRODUCTION:** Diabetes mellitus has severe complication like retinopathy, neuropathy nephropathy. Sympathetic neuropathy is chronic diabetic complication which silently leads to morbidity & mortality. As there are numerous range of autonomic function tests we need to be focused & specific for what we are looking for. Sympathetic neuropathy which creates great load of morbidity needs to be evaluated & treated specifically.

**OBJECTIVE:** To evaluate sympathetic nervous system in diabetic patients and look for effect of duration of disease on sympathetic neuropathy.

**METHOD:** The present study was carried out on the 500 study subjects divided into three case groups (according to duration of disease i.0-5 year ii.5-10 year iii. >10 year) & one non diabetic healthy control group. They were assessed for sympathetic neuropathy by Ewing's battery test.

**RESULTS:** The diabetic group shows more deranged sympathetic function tests than control group. The sympathetic function tests diversified to abnormality as the duration of disease increases. The sympathetic neuropathy is most prevalent in study group having disease for than 10 years.

**CONCLUSION:** Sympathetic neuropathy is prevalent & progressive with duration of diabetes.

**KEY WORDS:** Autonomic neuropathy, Sympathetic Function Test, Diabetes Mellitus

### INTRODUCTION:

India faces a great health challenge named Diabetes. Diabetes is an iceberg disease. It is causing sever burden to Indian economy due to the high prevalence rate & its complication.

The recent statements of World Health Organization (WHO) says that India already have the largest number of diabetic subjects (nearly 40 million) and it is predicted that this number would reach almost 80 million by the year 2030. The International Diabetes Federation says that number of people with diabetes in India currently around 41 million is expected to rise to 70 million by 2025. India & china makes major contribution of total diabetic patient load of world which is 75%. Complication of diabetes cardiovascular disease, retinopathy, nephropathy, and neuropathy makes the condition worsened. Autonomic neuropathy remains undiagnosed for years if not looked specifically by constellation of tests. The complication arising because of sympathetic dysfunction like dizziness, fainting, postural hypotension, erectile dysfunction hampers the life style of patient.<sup>I, II, III</sup> In this study we assessed the sympathetic nervous system in diabetic patients and non diabetic using Ewing's battery test. We have also correlated the effect of duration of disease on sympathetic functions test in diabetic patients.

## **MATERIALS AND METHODS**

After the permission of IRB committee, 500 study subjects were chosen from medicine outpatient department of Sir Takhtasinhji Hospital, Medical College Bhavnagar were divided into four groups, 3 groups of diabetic patient according to duration of disease & one group of control- non diabetic patients.

The diabetic group was subdivided in three groups according to duration of disease in Group I (0- 5 year), Group II (5- 10 year), Group III(10-15) year. Subjects in each group were examined and sympathetic nervous system's evaluation was done by instrument CANS analyzer -304 by Diabetic Foot Care India Pvt. Ltd. Subjects between 30 to 70 years of age were included. Subjects who did not give consent, hypertensive, suffering from disease that can cause sympathetic neuropathy (leprosy, alcoholic neuropathy, thyroid disorders) suffering from any other disease (HIV, TB, leprosy), taking any drug that can cause neuropathy all were excluded after taking proper history. Subjects with addiction like nicotine, alcohol were also excluded. We had taken all the precautions all the factors affecting sympathetic nervous system like sleep, food , drug, temperature can be avoided or matched in case & control. Sympathetic nervous system evaluation was done in every subject in morning between 9am to 11am only.<sup>IV,V,VI</sup> Battery of following tests was performed by each subject.

1) Resting systolic & diastolic Blood Pressure (BP) (greater than or equal to 130 mmHg systolic BP and 85 mmHg of diastolic BP is considered abnormal or pre hypertensive). 2) Systolic and diastolic BP fall in response to standing (fall in SBP >20 mmHg and fall in DBP > 10 mmHg it is said orthostatic hypotension). 3) Rise in diastolic blood pressure in response to isometric exercise handgrip test (A value of more than 15mmHg rise in diastolic BP is taken as normal. Less than 10 mmHg rise in diastolic BP is taken as sympathetic insufficiency. 10 -15 mmHg is considered borderline.<sup>VII,IX,X</sup>

## **OBSERVATION AND RESULTS**

Statistical tools: We compared the outcome between the controls and each group of patients of diabetes mellitus using Graph Pad.com. Data were analyzed with same tool. We used Student's t-test for comparison. The level of significance was set at  $P < 0.05$ , and 95% confidence intervals.

**TABLE 1** Sympathetic Function Test in controls and cases (groups according to duration of disease, group I-0 to 5 year, group II-6 to 10 year, group III- more than 10 year) (values are in mean and standard deviation)

Tests	controls	Group I(0-5 years)	Group II(5-10 years)	Group III(>10 years)
Resting SBP(mmHg)	117.48±10.94	121.35±10.58	129.12±14.25	132.85±15.35
P value		<0.05	<0.05	<0.05
T value		2.56	5.31	6.55
RDBP(mmHg)	73.84±7.48	76.71±8.01	83.10±10.00	87.44±10.72
P value		<0.05	<0.05	<0.05
T value		2.26	6.03	8.38
Fall in SBP on standing (mmHg)	5.15±4.78	5.30±4.67	9.06±6.60	10.32±7.75
P value		<0.05	<0.05	<0.05
T value		0.21	3.89	4.47
Fall in DBP on standing)	2.84±3.43	3.24±2.77	5.63±3.09	6.45±3.76
P value		0.38	<0.05	<0.05
T value		0.86	5.43	6.09
Rise in DBP on hand grip test (mmHg)	15.20±5.55	13.3±6.42	8.94±6.34	6.33±5.76
P value		<0.05	<0.05	<0.05
T value		2.05	4.22	7.31

## DISCUSSION

Diabetes mellitus is a strong risk factor for cardiovascular disease. DAN is a risk factor that independently increases cardiovascular risk in people with diabetes mellitus. The present study indicates abnormal sympathetic function in diabetic group.

The reasons of neuropathy are metabolic insult to nerve fibers, neurovascular insufficiency, and autoimmune damage. Hyperglycemic activation of the polyol pathway may lead to accumulation of sorbitol and alteration in NAD: NADH ratio resulting in direct neuronal damage vasoconstrictor like protein kinas C gets activated and reduces neuronal blood flow.

Vascular endothelium damage due to altered immunity & free radical production leads to vasoconstriction.<sup>XIII</sup>

The autonomic nervous system regulates blood pressure (BP), heart rate, thermoregulation, respiration, gastrointestinal, bladder, and sexual function. Autonomic dysfunction can be due to many diseases that affect autonomic nervous system. The clinician's role is not just to seek out symptoms of autonomic imbalance, but it is then necessary to determine if these symptoms are really due to involvement of autonomic systems. In the past, methods to evaluate sympathetic nervous system were irreproducible, non specific & invasive. The interiors of rural India where specific set up is not available we need tests that can be performed with simple, small portable instruments & which give sensitive, specific, reliable & reproducible results.<sup>X</sup> That's why in these study we have focused on tests like Resting Blood pressure, Fall in BP while standing, Rise in BP on hand grip test because this test require simple set up only can be assessed by even health assistants.<sup>VIII</sup>

The control group Resting Systolic BP is  $117.48 \pm 10.94$  mmHg. The mean value of resting systolic blood pressure is also increasing with duration of diabetes (group 1- mean value -  $121.35 \pm 10.58$  mmHg, group 2- mean value -  $129.12 \pm 14.25$  mmHg, group 3- mean value -  $132.85 \pm 15.35$ ). The Resting Diastolic BP in control group were  $73.84 \pm 7.48$  mmHg & in diabetics (Group 1- mean value  $76.71 \pm 8.01$  mmHg , group 2- mean value  $83.10 \pm 10.00$  mmHg, Group 3-  $87.44 \pm 10.72$  mmHg ). As we can see comparison all diabetic case group with healthy controls show difference in BP is significant. One important cause is that dysfunction of the vascular endothelium causes cardiovascular diseases.<sup>XIII</sup>

The test called fall in Systolic BP & Diastolic BP on standing which is performed to assess postural hypotension was also performed. The mean of fall in Systolic Blood Pressure in control group was  $5.15 \pm 4.78$  mmHg. The mean value of fall in systolic blood pressure also increases as duration of diseases increases (table 1 shows that group 1- mean value -  $5.30 \pm 4.67$  mmHg , group 2- mean value  $9.06 \pm 6.60$  mmHg, group 3- mean value  $10.32 \pm 7.75$  mm hg ).  $2.84 \pm 3.43$  mmHg is fall in Diastolic BP on standing in controls. The mean value of fall in diastolic blood pressure also increases as duration of diseases increases (table 1 shows that group 1- mean value -  $3.24 \pm 2.77$  mmHg , group 2- mean value  $5.63 \pm 3.09$  mmHg, group 3-  $6.45 \pm 3.76$  mm hg ). As we can see comparison all diabetic case group with healthy controls show difference in BP is significant. These results also shows that fall in BP is increasing as duration of disease is increasing. The reason for postural hypotension is slowing of sympathetic vascular reflexes due to nerve damage.<sup>XIII, XIV</sup>

Table 1 shows that rise in BP after hand grip isometric test in controls is  $15.20 \pm 5.55$  mmHg group 1- mean value -  $13.3 \pm 6.42$  mmHg , group 2- mean value  $8.94 \pm 6.34$  mmHg, group 3- mean value  $6.33 \pm 5.76$  mm hg ). P value suggests that difference is significant.

In a study it was found that in patients with type II diabetes showed a decline in exercise induced pressure response in subjects with cardiac autonomic neuropathy. We analyze data of both group mean value of resting BP & fall in systolic blood pressure and diastolic blood pressure on standing both are higher in diabetic group. Mean value of rise in DBP on hand grip test is higher in controls. This result suggests altered sympathetic tone. These results indicate sympathetic dysfunctions because process of decrease in venous return is exaggerated vessels are dilated due to decreased sympathetic tone. This may be due to damage to sympathetic nerves by diabetes. This result indicates impaired sympathetic functions in diabetics, as diastolic blood pressure is purely sympathetic function.<sup>XV, XVI</sup> As we have discussed the resistance vessel which are responsible for maintaining diastolic blood pressure have only sympathetic nerve supply.<sup>XI</sup> Table 1 shows sympathetic function tests are altered in diabetic patient than controls. Group 3 patients who have diabetes more than 10 years are at the most risk with worst scenario of morbidity. By comparing the results of three diabetic groups and correlating the results the final inference says that sympathetic neuropathy worsens as duration of disease increases.<sup>IV</sup>

The recent study of Meyer M.F. shows that impaired vasomotion which is cumulative result of sympathetic dysfunction & vascular damage is early sign of diabetic neuropathy, precedes sensory neuropathy. So, diagnosing sympathetic neuropathy on early stage may help us to focus our treatment narratives on high risk patients who have more chances of prognosis.<sup>XI, XII</sup>

## **CONCLUSION AND SUMMARY**

Present study shows that there is significant difference in sympathetic function test in diabetic & normal persons. The results are indicating that there is sympathetic neuropathy in diabetics which is progressively increasing as duration of disease increases.

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