Research Article

Sympathetic cardiovascular function integrity in children with parental history of diabetes mellitus

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Abstract

Introduction: Type 2 DM has a strong genetic component. Individuals having parents with type 2 DM have an increased risk of diabetes; if both parents have type 2 DM, the risk approaches 40%. The autonomic nervous system regulates the electrical and contractile activity of myocardium via interplay of sympathetic and parasympathetic activity. Sympathetic nerves of heart are derived from the upper thoracic 5 segments of the spinal cord. In general, sympathetic stimulation increases the overall activity of the heart. This is accomplished by increasing both the rate and force of heart contraction. **Amis and Objectives:** To study Sympathetic cardiovascular Function Integrity in children with parental history of diabetes mellitus. **Materials and Method:** The study procedure was carried out on healthy volunteer medical students of age group 18 to 25 years. They were first categorized into two groups, control (without parental history of diabetes mellitus) and subject (with parental history of diabetes mellitus). The sample size was 70 in the control group and 70 in the subject group. All participants were examined after explaining the study procedure. The cardiovascular tests to measure cardiovascular autonomic response were performed. These tests were explained and demonstrated to the participants before performing on them. Tests Done For Assessing Sympathetic Activity were Blood pressure response to standing (Orthostasis) test, Hand grip test and QTc interval test. The mean and standard deviation (S D) was calculated for all the parameters. The data was entered using Microsoft Excel (2007). Statistical analysis was done using SPSS version 10.The statistical test used were (as per the requirement of the data). **Results:** The age distribution and sex distribution was nearly same in the study and control group. Mean resting pulse, mean SBP and DBP was slightly more in study group as compared to control group and the difference was not significant statistically. While assessing sympathetic activity Orthostasis and Mean QTc interval test showed no statistically significant difference in study and control group whereas sustained handgrip test showed statistically significant difference in study and control group. **Conclusion:** Early subclinical sympathetic autonomic neuropathy may develop in children of type 2 diabetic parents without the presence of long term hyperglycemia. It could be due to inherited susceptibility genes for sympathetic autonomic neuropathy which could be expressed before or even without development of diabetes mellitus.

Keywords: Sympathetic cardiovascular Function, diabetes mellitus

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INTRODUCTION

India leads the world with largest number of diabetic subjects earning the dubious distinction of being termed the "diabetes capital of the world".[1] Diabetes mellitus comprises a heterogeneous group of hyperglycemic disorders. The hyperglycemia is the consequence of a relative or absolute deficiency of insulin and a relative or absolute excess of glucagon. Diabetes is associated with late complication involving the eyes, kidneys, nerves and blood vessels. It is the leading cause of acute blindness and a major cause of renal failure, gangrene, myocardial infarction, and stroke.[2] Type 2 DM has a strong genetic component. Individuals having parents with type 2 DM have an increased risk of diabetes; if both parents have

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type 2 DM, the risk approaches 40%. Insulin resistance, as demonstrated by reduced glucose utilization in skeletal muscle, is present in many nondiabetic, first-degree relatives of individuals with type 2 DM. The disease is polygenic and multifactorial since in addition to genetic susceptibility, environmental factors such as obesity, nutrition, and physical activity modulate the phenotype. Diabetes leads to development of cardiovascular and cerebrovascular diseases[3]. Increased risk of mortality is strongly associated with the presence of cardiovascular autonomic neuropathy in individual with diabetes[4]. The autonomic nervous system regulates the electrical and contractile activity of myocardium via interplay of sympathetic and parasympathetic activity[5]. Sympathetic nerves of heart are derived from the upper thoracic 5 segments of the spinal cord. In general, sympathetic stimulation increases the overall activity of the heart. This is accomplished by increasing both the rate and force of heart contraction. Parasympathetic stimulation causes mainly opposite effects i.e. decreased heart rate and strength of contraction. To express these effects in another way, sympathetic stimulation increases the effectiveness of the heart as a pump, as required during heavy exercise, whereas parasympathetic stimulation decreases heart pumping. Thus the present study was conducted in the young healthy individuals with parental history of diabetes mellitus to study the cardiovascular sympathetic autonomic response.

AMIS AND OBJECTIVES

To study Sympathetic cardiovascular Function Integrity in children with parental history of diabetes mellitus.

MATERIAL S AND METHOD

A study was carried out on volunteer medical students in the department of physiology in tertiary health care institute. After receiving the approval from the Committee for Academic Research and Ethics (CARE), Medical students of age group 18 – 25 years fulfilling the inclusion criteria were included. For the purpose of study two groups were formed.

Group I (Study group): with parental history of diabetes mellitus

Group II (Control group): without parental history of diabetes mellitus.

Following inclusion and exclusion criteria was used to select the study subjects.

Inclusion Criteria

- Students with parental history of diabetes mellitus
- General good health as determined by history and routine physical examination.
- Both males and females in the age group 18-25 years were included.
- Individuals who did not have any abnormal findings on his/her history and clinical examination and who did not complain of any symptoms were included.

Exclusion Criteria

- Individuals suffering with diabetes mellitus, hypertension, known cardiovascular disease, or any other known endocrine or known systemic disorders.
- Individuals with acute illness such as respiratory tract infection, gastroenteritis.
- Individuals under any pharmacological treatment, drugs, hormones, alcohol ingestion.

Same inclusion and exclusion criteria were used except students without parental history of diabetes mellitus were enrolled. Thus by using above mentioned inclusion and exclusion criteria total 70 subjects were selected for study and control group each. Proper consent was obtained from the volunteer individuals before the procedure. History taking, general examination and systemic examination were done before the procedure. And the findings were entered in the prestructured profrorma. All the participants were asked to take rest for 10 minutes in supine position then pulse rate and blood pressure was measured by using standard protocol. Three readings were taken and the average of the three was taken as the resting use rate and blood pressure. The cardiovascular tests to measure cardiovascular Sympathetic autonomic response were performed. These tests were explained and demonstrated to the participants before performing on them.

Tests Done For Assessing Sympathetic Activity

1. Blood pressure response to standing (Orthostasis):
2. Hand grip test:
3. QTc interval:

After performing the tests, the results were calculated by measuring the R-R intervals directly from the electrocardiogram record. Then the data was entered using Microsoft Excel (2007). Statistical analysis was done using SPSS version 10.

RESULTS

Table 1: Age and sex distribution in study and control group

Variable		Study group	Control group	Significance
Age		19.29 ± 1.49	19.29 ± 1.36	Not significant
Sex	Male	40(57.1%)	45(64.3%)	Not significant
	Female	30(42.3%)	25(35.7%)	

In the present study it was observed that mean age of the participants was 19.29 years in both the group. In control group 64.30% were males and 35.70% were females whereas in study group 57.10% were males and 42.30% were female and difference was not statistically significant (p>0.05).

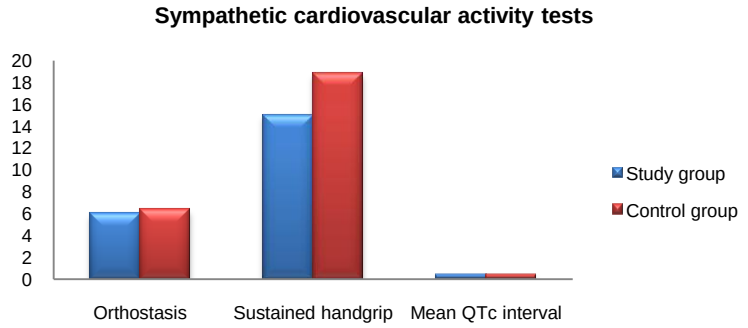
Table 2: Distribution according to cardiovascular parameter

	Study group	Control group	t value	P value	Significance
mean resting pulse	78.87 ± 3.83	77.80 ± 4.20	1.575	0.1175	Not significant
Mean SBP	111.86 ±7.61	110.26 ±7.92	1.22	0.2245	Not significant
Mean DBP	75.66 ± 05.05	74.66 ± 04.32	1.2590	0.2102	Not significant

The mean resting pulse rate was 77.80 beats per minute among control group, which was comparable with 78.87 beats per minute among study group and the difference was statistically insignificant (p >0.05). The mean SBP among study group was 111.86 ± 7.61 mm of Hg, whereas among control group was 110.26 ±7.92 mm of Hg and the difference was statistically not significant (p> 0.05). The mean DBP of study and control group was 75.66 ± 05.05 mm of Hg and 74.66 ± 04.32 mm of Hg respectively and difference observed in these groups was statistically not significant (>0.05).

Table 3: Distribution according to Sympathetic cardiovascular activity tests

Test	Study group	Control group	t value	P value	Significance
Orthostasis	6.00 ± 2.75	6.37 ± 2.95	0.7676	0.444	Not significant
Sustained handgrip	15.01 ± 4.46	18.81 ± 5.08	4.7031	0.000	Significant
Mean QTc interval	0.38 ± 0.01	0.38 ± 0.02	0	1.0	Not significant



Effect of Orthostasis i.e. blood pressure response to standing was within normal range (10 mm of Hg). Mean blood pressure response to standing (orthostasis) was 6.00 ± 2.75 mm of Hg among study group whereas 6.37 ± 2.95 mm of Hg among control group and the difference was statistically not significant (p>0.05). It was observed that mean blood pressure in response to sustained handgrip was 15.01 ± 4.46 mm of Hg among study group whereas 18.81 ± 5.08 mm of Hg among control group. The difference in the mean blood pressure in response to sustained handgrip between both the groups was statistically significant (p<0.05). Mean QTc interval was 0.38 sec among both stud and control group which was within normal range (0.35-0.43 sec). The difference in mean QTc interval between these groups was statistically not significant (p>0.05).

DISCUSSION

Diabetes Mellitus type 2 is a chronic heterogeneous disorder characterized by chronic hyperglycemia owing to combination of insulin resistance and changed insulin secretion[6]. It is a complex disorder that develops as a result of interplay between the genetic and environmental factors and prognosis depends on the genetic load and relevant environmental exposure specific to each

individual[7]. On e of the important risk factor cardiovascular autonomic neuropathy is diabetes mellitus which is presented by resting tachycardia and beat to beat variation even at rest. The present study was conducted to evaluate cardiovascular autonomic response in non diabetic off springs of diabetic parents and to compare it with non diabetic off springs of non diabetic parents. For this purpose 70 subjects were selected in subject and control group each. In the study participants in both control and study group were having same mean age (yrs.) i.e.19.29±1.36 and 19.26±1.49 respectively. Male participants were 64.3% in control group and 57.1% in study group. Female participants were 35.7% in control group and 42.3% in study group. The difference in these factors among the two groups was statistically not significant (P>0.05). Age and gender are the important factors influencing sympathetic autonomic nervous system activity[8]. Thus the age and sex were matched in the present study to prevent the confounding effect. Mean blood pressure in response to standing (orthostasis) was 6.00 ± 2.75 mm of Hg among study group whereas 6.37 ± 2.95 mm of Hg among control group and the difference was statistically not significant (p>0.05). On standing peripheral pooling of the blood in the legs causes a fall in blood pressure, which is normally rapidly corrected by peripheral vasoconstriction. In the patients with sympathetic autonomic dysfunction the blood pressure falls on standing and remains lower than in the lying position. A difference of systolic blood pressure (SBP) more than 30 mm Hg between the standing and lying position is considered positive for autonomic involvement [9]. In the present study both groups showed normal responses to this test, also it is said that this test becomes abnormal only with severe autonomic dysfunction[10,11,12]. It was seen that there was significant difference (p<0.05) in the handgrip response between control and subject group. The mean blood pressure in response to sustained handgrip was 15.01 ± 4.46 mm of Hg among study group whereas 18.81 ± 5.08 mm of Hg among control group. In control group during sustained handgrip exercise, a mean rise in blood pressure was ≥16 mm Hg. However in the study group rise in blood pressure was found to be significantly reduced as compared to control group. During handgrip exercise test, sustained muscle contraction causes a sharp rise in blood pressure ≥16 mm of Hg. due to heart rate dependent increase in cardiac output with unchanged peripheral vascular resistance. This rise in blood pressure is caused by a reflex arc from the exercising muscle to central command and back along efferent fibers. The efferent fibers innervate the heart and muscle, resulting in increased cardiac output, blood pressure, and heart rate. Thus it suggests that the handgrip response, a measure of cardiac sympathetic function is reduced in the study group. Previous studies done Ewing DJ *et al*[13], Kashara Y *et al*[14] and Khatoon N *et al*[15] on diabetic patients have shown reduced blood pressure response to sustained handgrip similar to present study findings. Mean QTc interval was 0.38 sec among both stud and control group which was within normal range (0.35-0.43 sec). The difference in mean QTc interval between these groups was statistically not significant (p>0.05). QTc interval may be prolonged in conditions like Hypocalcaemia, Acute MI, Hypertrophic cardiomyopathy, Hypothermia, cerebral injury, advanced AV block, side effect of certain drugs like Quinidine, Procainamide, Tricyclic antidepressants and in certain congenital diseases like Jarvell- Lange Neilson syndrome etc[16]. Previous studies have also observed that there is an association between an abnormal QTc interval and sudden cardiac death in diabetic patients with severe autonomic neuropathy; it may be because of sympathetic imbalance, as left efferent cardiac sympathetic fibers influence QT interval[17,18,19,20,21]. But in present study as the participants were in general good health on examination and history taking, QTc interval in both the groups was found to be within normal range. As only one test out of the total three tests used to study the sympathetic cardiovascular Function has abnormal finding. According to Ewing and Clarke [(15)] the results of the above tests can be inferred as mildly abnormal. Findings of our study are comparable with the previous studies where they found a higher prevalence of cardiac autonomic neuropathy in the nondiabetic subjects with parental type2 diabetes compared with those without parental diabetes[22,23,24,25,26]. Various studies have shown that poor control of diabetes associated with the progression of sympathetic and parasympathetic autonomic neuropathy in a negative way[27,28]. But in our study, long term hyperglycemia is not a plausible cause of autonomic neuropathy as subjects participated in the study were in good health on examination. The differences in mean values of the cardiovascular reflex tests between nondiabetic children with parental diabetes and control are significant even with two groups having same mean age. Thus subclinical autonomic neuropathy may develop without the presence of long term hyperglycemia in family members of type 2 diabetic subjects and it is not simply a complication of the hyperglycemia in these subjects. The possible reason behind is that the inherit susceptibility genes for sympathetic and parasympathetic autonomic neuropathy, and that these genes could be expressed before or may be even without the subject developing diabetes[24]. Studies done on genes associated with retinopathy and nephropathy identified different loci on chromosomes that could affect susceptibility to these complications.

Results from studies have shown inherited trait in non diabetic family members of patients with type 2 diabetes[29,30]. These results suggest that genetic factors could play a role in the pathogenesis of the features known as complications of type 2 diabetes, and they also suggest that these features can be present without diabetes[24]. Previous studies have also found out that acute hyperinsulinemia caused statistically significant changes in HRV only in offspring of diabetic patients with the insulin resistance phenotype but not in the offspring of diabetic patients with the deficient insulin secretion phenotype or in the control subject. Thus, insulin–resistant state itself could be associated with sensitization of the sympathetic autonomic nervous system to insulin[31,32]. In parallel to our findings it could also be suggested that subclinical autonomic neuropathy may be part of a genetic syndrome that includes augmented risk for developing cardiovascular disease (CVD), type 2 diabetes, symptomatic sympathetic autonomic neuropathy and hypertension. Whether such development takes place could depend on exogenous factors such as nutrition, smoking and physical activity[24].

CONCLUSION

Thus from the above results and discussion we conclude that early subclinical sympathetic autonomic neuropathy may develop in children of type 2 diabetic parents without the presence of long term hyperglycemia. It could be due to inherited susceptibility genes for sympathetic autonomic neuropathy which could be expressed before or even without development of diabetes mellitus.

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