A STUDY OF GLYCEMIC STATUS AND PARASYMPATHETIC FUNCTIONS IN NONDIABETIC OFFSPRINGS OF TYPE 2 DIABETES MELLITUS

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Abstract
Objective: Diabetes Mellitus is a group of common metabolic disorders that share the phenotype of hyperglycemia. Several distinct types of Diabetes Mellitus exist and are caused by interaction of genetics and environmental factors. Individuals with Diabetes Mellitus may develop signs of autonomic dysfunction involving cholinergic, noradrenergic and peptidergic systems. Type 2 Diabetes Mellitus has a strong genetic component. Individuals with a parent with Type 2 Diabetes Mellitus have an increased risk of Diabetes. If both parents have Type 2 Diabetes Mellitus, the risk approaches to 40%. Thus this study is designed to evaluate glycemic status and autonomic functions in nondiabetic offsprings of Type 2 diabetic parents.
Method: The cross-sectional study of Glycemic status and Cardiovascular Autonomic Functions was carried out in 30 healthy offsprings of Type 2 Diabetic Parents (Study group) and 30 healthy offsprings of Nondiabetic Parents (Control group) in the age range of 18 - 21 years randomly selected among 1st MBBS students. Statistical Analysis is done by 'Z' test.
Results: There is insignificant decrease in parasympathetic functions and insignificant increase in Fasting and Postload Blood Glucose in Study Group compared to Control Group.
Conclusion: Our observations indicate that subclinical autonomic dysfunction may develop without the presence of long-term hyperglycemia in family members of type 2 diabetic subjects; thus, it is not simply a complication of the hyperglycemia in these patients. An explanation could be that it is possible to inherit susceptibility genes for autonomic neuropathy, and that these genes could be expressed before or maybe even without the subjects developing diabetes. Different factors (including hyperglycemia) could subsequently affect the expression of the genes and influence the progression of neuropathy.
Keywords: Parasympathetic Functions, Nondiabetic Offsprings ,Glycemic Status

1. Introduction

Diabetes Mellitus is a group of common metabolic disorders that share the phenotype of hyperglycemia. Several distinct types of Diabetes Mellitus exist and are caused by a interaction of genetics and environmental factors[1]. Individuals with Diabetes Mellitus may develop signs of autonomic dysfunction involving cholinergic, noradrenergic and peptidergic systems. Autonomic neuropathies affecting cardiovascular system cause a resting tachycardia and orthostatic hypotension. Reports of sudden death have also been attributed to autonomic neuropathy[1]. Type 2 Diabetes Mellitus has a strong genetic component. The concordance of Type 2 Diabetes Mellitus in identical twins is between 70% to 90%.

Individuals with a parent with Type 2 Diabetes Mellitus have an increased risk of Diabetes. If both parents have Type 2 Diabetes Mellitus, the risk approaches to 40%. Now a day Type 2 Diabetes Mellitus is being diagnosed more frequently in children and young adults, particularly in obese adolescents[1].The possibility of early alterations in neural cardiovascular regulation in healthy offspring of diabetic patients has been addressed recently[2-5].

Aim of this study was to assess glycemic status and Cardiovascular Autonomic Functions in the offsprings of Type 2 Diabetic Parents & compare them with that offsprings of Nondiabetic parents.

2. Materials and Methods.

The cross-sectional study was carried out in 30 healthy offsprings of Type 2 Diabetic Parents (Study group) and 30 healthy offsprings of Nondiabetic Parents (Control group) in the age range of 18 - 21 years randomly selected among 1st MBBS students of BLDEU's Shri B M Patil Medical College, Bijapur. The ethical clearance for the study was obtained from ethical committee.

2.1 Method of Collection of Data:

Study group: This group consists of 30 normal healthy male medical students (Offsprings of Type 2 Diabetic Parents) of BLDEU'S Shri B.M.Patil Medical College, Bijapur.

Control group: This group consists of 30 age matched normal healthy male medical students (Offsprings of Nondiabetic Parents) of BLDEU'S Shri B.M.Patil Medical College, Bijapur. Each subject taking part was explained about the procedure to be adapted in the research. All the subjects after thoroughly understanding the procedures to be adopted signed an informed consent form provided to them. All subjects underwent thorough clinical examination.

Inclusion criteria: Only healthy subjects of Indian origin were included in the study. The subjects without signs of cardiovascular, endocrinological, neurological, hematological &inflammatory diseases were selected for the study. The apparent health status of the subject was determined through clinical examination and history taking.

Exclusion criteria: The subjects with any of following findings were excluded from study.

1) Evidence of hypertension (systolic blood pressure more than 150 and diastolic blood pressure more than 90 mm Hg).
2) Subjects having diabetes mellitus, bronchial asthma, giddiness on standing, syncopal spells, visual disturbances, nocturnal diarrhea.
3) Subjects receiving drugs that are known to interfere with cardiac function or respiratory functions such as beta blockers, sympathomimetic drugs, vasodilators and diuretics.
4) Associated disease or conditions known to affect autonomic function like Guillean Barre syndrome, Poliomyelitis,Diphtheria, Tuberculosis,Syphilis, Amyloidosis, Chronic renal failure.
5) Subjects with history of alcohol intake/ tobacco consumption in any form.
6) Any disease condition affecting the autonomic nervous system.

Following parameters were recorded in each subject:

A. Record of Physical Anthropometry of subjects: Height(in centimeters), Weight (in kilograms), Body Surface area & Body Mass Index were measured.

B. Record of Physiological parameters: Pulse rate (beats per minute), Blood Pressure (SBP and DBP in mmHg), Respiratory Rate (Cycles/Minute) were recorded.

C. Record of Autonomic Function Parameters: The subject was informed about the procedure. Consent from each subject was taken before recording. For each parameter, three readings were taken. Mean of three readings was taken for calculation.

The following parasympathetic function parameters were recorded using Computerised 4 channel Physiopac performed as per methods described by Sir Roger Bannister[10].

I.Heart Rate response to Valsalva Maneuver

II.Heart rate response to deep breathing.

III.Immediate heart rate response to standing

D. Glycemic status of an individual is determined by Oral Glucose Tolerance Test[7].

1. Fasting blood glucose. 2. Two hours After Glucose Load (Consisting of 75g glucose anhydrate in 300ml of water ingested over the course of 5 minutes

2.2 Statistical analysis: All values are presented as Mean ± Standard Deviation (Mean ± SD). Comparison of mean values of parameters between Control and Study group is done by Z test. Correlation between various autonomic function parameters & glycemic status is done by correlation. A p value of 0.05 or less was considered as statistically significant.

3. Results:

3.1. Heart Rate response to Valsalva maneuver:

Mean VR ± SD of Control Group- 1.33 ± 0.20
Mean VR± SD of Study Group - 1.29 ± 0.24.
There is insignificant (p=0.222) decrease in the Valsalva ratio (VR) of subjects in Study Group compared to Control Group.

3.2 Heart rate variation (HRV) during Deep Breathing.

Mean HRV ± SD of Control Group- 28.56 ± 7.44
Mean HRV ± SD of Study Group- 26.25 ± 8.47
There is insignificant (p=0.132) decrease in the heart rate variation during deep breathing in Study Group compared to Control Group.

3.3 Immediate heart rate response to standing (30:15 ratio)

Mean Ratio ± SD of Control Group- 1.34 ± 0.20
Mean Ratio ± SD of Study Group- 1.31 ± 0.20
There is insignificant (p=0.335) decrease in the immediate heart rate response to standing in Study Group compared to Control Group.

3.4 Fasting Blood Glucose (mg/dl):

Mean FBG + SD of Control Group 85.03±7.81

Mean FBG ± SD of Study Group 85.56 ±7.03
There is insignificant (p=0.395) increase in the Fasting Blood Glucose in Study Group compared to Control Group.

3.5 Postload Blood Glucose (mg/dl):
Mean PLBG ± SD of Control Group 96.56±12.55
Mean PLBG ± SD of Study Group 99.20 ±14.92
There is insignificant (p=0.234) increase in the Postload Blood Glucose in Study Group compared to Control Group.

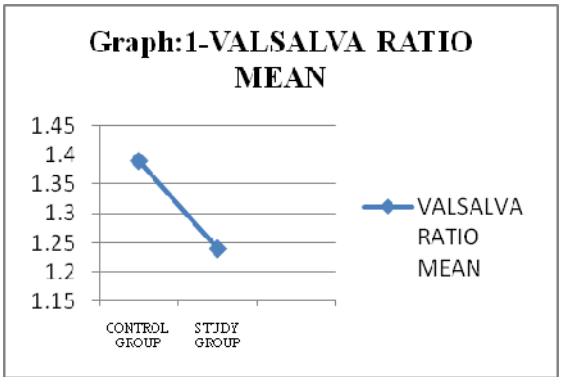

Table 1: Anthropometric & Physiological Parameters (Mean ± SD) of Control and Study Group:

Parameters	Control Group	Study Group	Level of significance
Age (Years)	18.86 ± 1.04	19.0 ± 0.78	0.293
Height (cms)	170.16± 5.14	172.73± 6.51	0.04*
Weight (Kg)	65.2 ± 10.82	70.16 ± 11.01	0. 04*
BMI (kg/m^2)	22.52 ± 3.55	23.51 ± 3.33	0.13
BSA (Sq m)	1.76 ± 0.13	1.83 ± 0.15	0. 01**
Resting SBP (mm of Hg)	119.53± 11.9	124.13± 12.80	0.07
Resting DBP (mm of Hg)	77.06± 5.29	77.66± 6.74	0.35

*p <0.05: Significant, ** p <0.01: Highly significant, *** p <0.001: Very highly significant.

Table 2: Parasympathetic function parameters of subjects in Study and Control Groups

Parasympathetic function parameters	Control Group	Study Group	Level of significance
Valsalva Ratio	1.33 ± 0.20	1.29 ± 0.24	0.222
HR variation to deep breathing	28.56 ± 7.44	26.25 ± 8.47	0.132
Immediate HR response to standing (30:15)	1.34 ± 0.20	1.31 ± 0.20	0.335

*p <0.05: Significant, ** p <0.01: Highly significant, *** p <0.001: Very highly significant

Table 3: Fasting and Postload Blood Glucose in Control and Study Group.

Parameters	Control Group	Study Group	Level of significance
Fasting Blood Glucose(mg/dl)	85.03± 7.81	85.56 ±7.03	0.395
Postload Blood Glucose(mg/dl)	96.56± 12.55	99.20 ±14.92	0.234

*p <0.05: Significant, ** p <0.01: Highly significant, *** p <0.001: Very highly

4. Discussion

The cross-sectional study is carried in 60 normal healthy medical students (Offsprings of Type 2 Diabetic Parents n=30; and Nondiabetic Parents n=30) in the age group of 18-21years. In our study we have recorded various physical & physiological parameters in both Control and Study groups. Parasympathetic function is assessed by heart rate response to Valsalva maneuver, heart rate response to deep breathing, immediate heart rate response to standing. Glycemic status was assessed by Oral Glucose Tolerance Test.

4.1: Heart rate response to Valsalva maneuver: Our study showed insignificant decrease ((p=0.222)) in mean valsalva ratio in study group compared to control group. Our findings are in accordance with earlier studies done by C. Hauerslev Foss et al[8] , Frontoni S et al[5]. Heart rate response to Valsalva maneuver appears to be more sensitive parameters to detect autonomic dysfunction amongst the three Parasympathetic function tests.

4.2: Heart rate response to deep breathing: There is insignificant (p=0.132) decrease in the heart rate variation during deep breathing in Study Group compared to Control Group. Our study is in accordance with studies done by C. Hauerslev Foss et al[8], Frontoni S *et al*[5].

4.3: Heart rate response to Standing (30: 15 Ratios): Heart rate response to standing in normal subjects consists of tachycardia maximum around 15th beat followed by relative bradycardia

around 30th beat after standing. These hemodynamic responses are mediated by baroreceptors. In our study we found a insignificant (p=0.335) decrease in the immediate heart rate response to standing in Study Group compared to Control Group. Our study is in accordance with studies done by C. Hauerslev Foss et al[8].

4.4: Glycemic Status: There is insignificant increase in the Fasting Blood Glucose and Postload Blood Glucose in Study Group compared to Control Group. Our study is in accordance with studies done by I.N.Migdalis et al[9], Frontoni S et al[5].Our results are not in agreement with C. Hauerslev Foss *et al*[8].

5. Conclusion:

This cross sectional study shows that offsprings of Type 2 diabetic parents have increased prevalence of cardiac autonomic neuropathy compared with offsprings of nondiabetic parents. The results indicate that early autonomic neuropathy may be present without the influence of long-term hyperglycemia and we suggest that autonomic neuropathy may be part of a genetic syndrome rather than a secondary complication of diabetes. In future studies on family members of Type 2 diabetic subjects, we will presumably gain important knowledge by following the trait of autonomic neuropathy as well as the diabetes trait itself.

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