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# Association of Autonomic imbalance with Parental history of Type 2 Diabetes Mellitus

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## ABSTRACT

**Background:** Off springs with a parental history of type 2 diabetes mellitus are genetically susceptible to develop diabetes. In some recent reports it has been shown that these vulnerable population exhibit altered autonomic activity even before the manifestations of disease. Autonomic dysfunction might be the initial cardiac pathology in subclinical type2 diabetes. Till now very few studies have been done to find out the early outcomes of this genetic transmission. Keeping in view of the above facts, the current study was carried out to find out the association between autonomic dysfunction and parental history of diabetes. **Aim and Objectives:** This study was aimed to quantify and compare the difference (if any) of heart rate recovery in response to 3minute step test between the young non diabetic children of non-diabetic and diabetic parents. **Materials and Methods:** Fifty-one non diabetic students were divided into two groups. One group comprised of students with parental history of type2 diabetes mellitus and another group with students without parental history of diabetes. Each student was subjected to 3minute Master step test. Recordings of heart rate were made before and after exercise. Heart arte recovery (HRR) in 1 minute (HRR1) as well as in 2, 3 and 4 minute (HRR2,HRR3, HRR4) were recorded and analyzed. **Results:** The resting (basal) as well as 1$^{st}$minute heart rate recovery (HRR1) was not significantly different between the two groups. Likewise, the 2$^{nd}$ minute HRR (HRR2), 3$^{rd}$ minute HRR (HRR3) and 4$^{th}$ minute HRR (HRR4) respectively were also not significantly different between the two groups. **Conclusion:** This study concludes that there is no difference in the heart rate recovery in response to the exercise stress test between the young non diabetic children of non-diabetic and diabetic parents. Therefore, parental history of diabetes does not have any impact on the cardiovascular autonomic activity before the disease manifestation.

**Key words:** Autonomic dysfunction; Heart rate recovery; Parental history; Type 2 Diabetes mellitus

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## INTRODUCTION

Diabetes Mellitus is a disease of multifactorial origin. This heterogeneous disorder is associated with high mortality rate, specifically from cardiovascular complications.[1-3] These cardiovascular complications frequently results from autonomic neuropathy.[4] Out of the many tools of assessment for cardiac autonomic functions, heart rate recovery is an easy to measure tool to find a reduced parasympathetic activity.[5-6] Attenuated heart rate recovery after a maximal exercise test is an independent predictor of mortality in healthy adults as well as for those who are referred for diagnostic testing.[7] This finding is independent of the workload achieved during exercise test, presence or absence of myocardial perfusion defects and changes in heart rate during the exercise. Some recent studies have reported that fasting plasma glucose is strongly and independently associated with abnormal HRR in non-diabetic levels.[8] Framingham heart study have reported an association between reduced heart rate variability and sympathetic-parasympathetic imbalance in adults with diabetes as well as in adults of impaired fasting glucose.[9-10] The high risk of type 2 diabetes mellitus in the first degree relatives indicates

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that there is an inherited susceptibility to develop this disease.[11] Genetic studies have reported the important roles played by genes in the development of type 2 diabetes mellitus.[12] Recent reports have stated that a significant difference of heart rate recovery exists between the young healthy adults of diabetic and non-diabetic parents.[13] Very few studies have been done so far to find out the early outcomes of cardiac effects in genetically predisposed young healthy adults of diabetic parents. Keeping a view of these above facts, the following study was planned to find the presence of any autonomic dysfunction in non-diabetic healthy adults of diabetic parents by a comparison of heart rate recovery between the young healthy off springs of diabetic and non-diabetic parents.

## MATERIALS AND METHODS

The study was done in the Department of Physiology of COMS, Bharatpur from January to February 2020. The study group comprised of a total 51 healthy students of 19-22year age group from 1st, 2nd MBBS and BDS as well as 1st year Nursing curriculum. The participants were divided into two groups. One group consist of the students having a parental history of diabetes with a single or both parents suffering from diabetes (DP), while another group was having students without a parental history of diabetes (NDP). They were non-diabetic, not having any cardiovascular diseases and not taking any type of over the counter or prescription medication or supplements affecting glucose homeostasis as well as cardiovascular system. On the day of the study participants were instructed to report to the laboratory having abstained from alcohol, caffeine or any type of strenuous activities for the preceding 24 hours. Weight, height and resting heart rate as well as blood pressure were recorded after a 5 minutes of rest. With the help of a metronome, 3 minutes Master step exercise was conducted. The participants were instructed to come out of the exercise maneuver in the events of feeling any types of discomfort. Heart rate was recorded just after the exercise as well as 1, 2, 3 and 4 minutes after exercise in a sitting posture. Heart rate recovery index (HRRI) was calculated by subtracting maximum heart rate achieved just after exercise by the heart rate measured in 1st, 2nd, 3rd, and 4th minute of exercise. The relevant statistical analysis was done with SPSS Statistical Package. All the data were expressed as mean±SD. Pearson's correlation test was performed to determine the association between HRR and study variables. The $p<0.05$ was considered statistically significant.

## RESULT

Statistical analysis was done and analysis were tabulated. Table 1 depicts the demographic and clinical parameters of the study groups. There was no statistically significant ($p>0.05$) differences among the study groups regarding age and BMI. Table 2 shows the comparison of resting pre exercise heart rate and different post exercise heart rates between the two groups. The result showed no significant difference ($p>0.05$) in all types of heart rates between the study groups. For each group when mean heart rate is compared between periods (i.e. within groups) in Table 3, significant difference was present and even after 4th minute post exercise the heart rate was significantly different from resting heart rate. This shows that the heart rate didn't come back to normal even after 4th minute of post exercise in both groups. Comparison of heart rate heart rate recovery index (Table 4) between the two groups also showed no statistical significant difference. This reflects the fact that the pattern of heart rate recovery in both the groups are remaining same.

## DISCUSSION

The role of genetics for predisposition in type 2 diabetes has been suggested by many studies in which first degree relatives

**Table 1: Baseline characteristics of two groups (Mean±SD)**

| Characteristics | DP | NDP | p-value |
|---|---|---|---|
| Age (Years) | 19.89±0.49 | 20±1.08 | 0.643 |
| BMI (kg/m²) | 22.54±5.36 | 20.72±2.3 | 0.138 |
| Gender | | | |
| Male | 5(38.5) | 8(61.5) | 0.168 |
| Female | 213(60.5) | 15(39.5) | |

**Table 2: Pre and post exercise heart rate (Mean±SD) of two groups**

| Periods | Heart rate | DP | NDP | p-value |
|---|---|---|---|---|
| Pre-exercise | RHR | 97.92±14.88 | 98.69±19.34 | 0.877 |
| Post exercise | Peak HR | 162.14±15.35 | 161.3±19.98 | 0.883 |
| | HR1 | 134.78±18.07 | 133.82±21.58 | 0.866 |
| | HR2 | 122±15.69 | 124.08±19.93 | 0.685 |
| | HR3 | 116.64±15.51 | 119.04±18.76 | 0.626 |
| | HR4 | 113.78±15.49 | 114±17.466 | 0.964 |

**Table 3: Comparison between two groups with respect to the mean heart rate between the periods**

| Comparison | DP(p value) | NDP(p value) |
|---|---|---|
| RHR vs Peak HR | <0.001 | <0.001 |
| RHR vs HR1 | <0.001 | <0.001 |
| RHR vs HR2 | <0.001 | <0.001 |
| RHR vs HR3 | <0.001 | <0.001 |
| RHR vs HR4 | <0.001 | <0.001 |
| Peak HR vs HR1 | <0.001 | <0.001 |
| Peak HR vs HR2 | <0.001 | <0.001 |
| Peak HR vs HR3 | <0.001 | <0.001 |
| Peak HR vs HR4 | <0.001 | <0.001 |
| HR 1 vs HR 2 | <0.001 | <0.001 |
| HR 2 vs HR3 | <0.001 | <0.001 |
| HR 3 vs HR 4 | .005 | .002 |

**Table-4: Comparison of Heart Rate Recovery Index between the two groups**

| HRRI (heart rate recovery index) | DP | NDP | p-value |
|---|---|---|---|
| HRRI1 | 27.35+9.72 | 27.56+12.73 | 0.94 |
| HRRI2 | 40.14+14.92 | 37.30+14.81 | 0.5 |
| HRRI3 | 45.5+12.93 | 42.34+14.8 | 0.42 |
| HRRI4 | 48.35+14.35 | 47.39+17.24 | 0.82 |

of type 2 diabetic patients have shown to have enhanced sympathetic flow and an attenuated parasympathetic function.[14,15] Decreased Heart rate recovery after a maximal exercise test is a predictor of mortality in healthy adults and in those referred for diagnostic testing. These findings are independent of workload achieved during the test, presence or absence of myocardial perfusion defects and changes in heart rate during the exercise test. A recent study by Panzer et al reported that fasting plasma glucose is strongly and independently associated with abnormal heart rate recovery even at non diabetic levels.[8] Likewise the Framingham Heart study have shown reduced heart rate variability and sympatho-vagal imbalance in adults with diabetes and impaired fasting glucose.[10,16] Expecting a greater outcome of HRR in patients with diabetes because of known association of diabetes with autonomic dysfunction we took the HRR as our parameter of assessment. In our study, using heart rate recovery we could not find any statistically significant difference in the heart rate at rest as well as at different regular intervals of post exercise duration. There was also no significant difference in the recovery pattern of post exercise heart rates between the healthy young adults of diabetic and non-diabetic parents. Contrary to our findings, in a same type of work Sikarwar et al has found a significant difference of post exercise heart rates between the two groups.[13] The findings of the current work concurs with the reports of Neves et al and Bajaj et al in which by taking the heart rate variability parameter, they have found that family history of type 2 diabetes mellitus, in absence of concomitant metabolic disorders, does not impair the sympatho vagal balance.[17-18] But other studies where again the same heart rate variability parameter was taken for comparison between the two groups, no significant association was found.[14,15]

These contradictory findings of recent studies indicate that there are no predictable changes in cardiovascular autonomic function as measured by HRR or HRV among the euglycemic young adults with a parental history of diabetes. One of the mechanism of autonomic dysfunction in the first degree relatives of type 2 diabetics has been shown as the familial tendency of the hyperinsulinemia with insulin resistance.[19] The insulin resistance state develops under a background environment of higher BMI which predisposes to obesity. Increased adiposity in obesity leads to a higher fatty acids in circulation which leads to the development of insulin resistance indirectly by enhancing sympathetic activity as well as activation of hypothalamo-pituitary adrenal axis.[20] Fiorentini et al has hypothesized from his study that autonomic disturbance in vulnerable population can develop independent of insulin resistance.[21] He also added that this imbalance get more pronounced with the development of insulin resistance. In the above two significant hypotheses, insulin resistance was considered as the background mechanism for development of an overt autonomic imbalance. Since in our study the autonomic imbalance is lacking in the genetically predisposed study group, we infer that our genetically susceptible study group are of normal BMI and insulin resistance is lacking in them for an overt expression of autonomic imbalance.

## CONCLUSION

From the observation of our study, it could be concluded that as such parental history of type 2 diabetes mellitus does not have a significant impact on the cardiovascular autonomic activity. In the genetically susceptible healthy young adults, a background environment of higher BMI is necessary for the autonomic sympatho vagal imbalance. Further since these genetically predisposed population is also prone to develop obesity, follow up study at a later age of life may provide a better understanding of the alterations of cardiovascular autonomic activity.

## LIMITATIONS OF THE STUDY

The major limitation of the present study was the small sample size of the study population. Inclusion of other confounding factors like diet, sodium and carbohydrate intake, physical activity would have given a better conclusion to the study. Similarly, other and more accurate autonomic assessments like estimation of plasma catecholamine and urinary catecholamine metabolites could have been done and compared with to find a more comprehensive and better conclusion.

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**Authors Contribution:**
**SB-** Concept and design of the study, collected data and review of literature, manuscript preparation, critical revision of the manuscript, drafting of manuscript; **HPU-** Statistical analysis, Interpretation of data and review of study.



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