

# A STUDY OF HEART RATE VARIABILITY (HRV) IN HEALTHY OFFSPRINGS WITH PARENTAL HISTORY OF TYPE 2 DIABETES MELLITUS

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## ABSTRACT

### Introduction

Type 2 diabetes mellitus (T2DM) is a heterogeneous polygenic metabolic disease condition that is caused by insulin resistance leading to hyperglycemia. Since, T2DM is genetically inherited and autonomic dysfunction is its major complications, healthy offsprings of diabetes parents are highly vulnerable to manifest dysautonomia leading to insulin resistance.

### Objectives

We aimed to assess cardiac autonomic function using heart rate variability (HRV) parameters in healthy offsprings having parental history of T2DM.

### Methodology

A comparative cross-sectional study was carried out in the laboratory of department of Physiology enrolling 30 healthy offsprings of non-diabetic parents (Group 1) and 30 healthy offsprings of diabetic parents (Group 2). Anthropometric, biochemical and cardiovascular variables were assessed using standard procedures. Time domain and frequency domain parameters of HRV spectrum were assessed using photoplethysmography principle.

### Result

HRV findings revealed that markers of sympathetic regulation were significantly higher and those of parasympathetic function were significantly reduced in subject group having parental history of T2DM. LF/HF ratio was significantly increased suggesting sympatho-vagal imbalance in offspring of diabetic parents even in their euglycemic state.

### Conclusion

Alteration of cardiovascular autonomic function is found in healthy offspring of diabetic parents, characterized by reduced vagal activity and pronounced sympathetic regulation. Assessment of cardiac autonomic function would help in timely detection of such dysautonomia and reducing the life-threatening effects on offspring having parental history of T2DM.

## KEYWORDS

Type 2 diabetes mellitus, HRV, dysautonomia, diabetic complications



## INTRODUCTION

Type 2 diabetes mellitus is an inherited metabolic disorder that may be developed due to complex interplay of socioeconomic, demographic, environmental and genetic factors.<sup>1,2</sup> Diabetic patients have higher probability of having one of his/her parents as diabetic.<sup>3</sup> Even being asymptomatic, non-diabetic offspring of diabetic parents may manifest autonomic neuropathy that support an evidence to the evolution of diabetic spectrum through genetic inheritance.<sup>4,5</sup> Diabetics had autonomic nervous system derangement as evidenced by Heart Rate Variability (HRV), which is a well-known risk factor for cardiac events and death.<sup>6-9</sup> Owing to its inheritable nature, the offspring of diabetic parents are genetically prone to develop autonomic imbalance and diabetes. Timely assessment of cardio-autonomic function would be helpful in preventing and reducing the impact of diabetes on global health subserving good quality of life.<sup>10,11</sup> Therefore, we aimed to find out the early changes in cardiac autonomic regulation among healthy offspring of diabetic parents.

## METHODOLOGY

A comparative cross-sectional study was conducted in the laboratory of department of physiology of Birat Medical College & Teaching Hospital. We enrolled a total of sixty healthy subjects of either sex, out of which control group consisted of 30 healthy offspring of non-diabetic parents (Group 1) and targeted group consisted of 30 healthy offspring having parental history of type 2 diabetes mellitus (Group 2). Subjects with known history of chronic illness, on any medications, consuming alcoholic drinks or tobacco, with endocrine disorders or with any diseases that could alter HRV were excluded from the study. Ethical clearance was obtained from the Institutional ethical review committee of the Institute. Detailed information about research procedures was provided and an informed consent was obtained from subjects for voluntarily participation in the study.

Subjects were requested to come 15 minutes earlier before the commencement of test so as to allow them to familiarize properly with the testing environment and attain baseline resting condition. They were requested not to involve in any strenuous physical activity on the day of the test and to avoid heavy meal two hours prior to the test session. Detailed medical and family history were taken and anthropometric variables like height, weight, BMI were measured. The subjects were allowed to rest in supine position for 15 minutes and cardiovascular variables like systolic&diastolic blood pressure and heart rate were measured.

HRV parameters were assessed (at room temperature 20-24°C) by using validated photoplethysmography application, smartphone-based system for real-time pulse-to-pulse (PP) interval time series acquisition by frame-to-frame camera image processing. The developed smartphone application acquires image frames from built-in rear-camera at the maximum available rate (30 Hz) and the smartphone GPU is

used by Renderscript API for high performance frame-by-frame image acquisition and computing in order to obtain photoplethysmography signal and PP interval time series.<sup>[12,13]</sup> Time domain measures [mean RR interval (Mean RR), Standard deviation of normal-to-normal RR intervals (SDNN), root mean square successive difference (RMSSD), the proportion of NN50 to the total number of NN intervals (pNN50)] and frequency domain measures [normalized low-frequency power (LFnu), normalized high-frequency power (HFnu), ratio of LFnu to HFnu (LF-HF ratio) and total power (TP)] were measured. Mean RR, SDNN, RMSSD, pNN50 and HFnu are measures of parasympathetic activity. TP shows overall autonomic activity, LFnu signifies sympathetic activity whereas LF/HF ratio reflects the sympathovagal balance.<sup>12</sup>

## Statistical Analysis

Independent t-test was done to determine the level of significance between the control group and study group using SPSS version 25. The data were expressed in mean  $\pm$  SD. The statistical probability  $p < 0.05$  was considered to be statistically significant.

## RESULTS

Basic subject characteristics, anthropometric, biochemical and cardiovascular parameters of the study group and control group are shown in Table 1.

**Table 1:** Comparison of general characteristics, anthropometric and cardiovascular variable between the study groups.

Parameters	Group 1	Group 2	p-value
Age (yrs)	20.06 $\pm$ 0.90	20.10 $\pm$ 0.95	0.89
Height (meter)	1.66 $\pm$ 0.08	1.61 $\pm$ 0.09	0.94
Weight (kg)	59.63 $\pm$ 3.76	61.76 $\pm$ 4.02	0.038*
Body Mass Index (kg/m <sup>2</sup> )	21.73 $\pm$ 1.9	22.60 $\pm$ 2.79	0.164
Waist Hip Ratio	0.85 $\pm$ 0.01	0.91 $\pm$ 0.6	0.043*
Basal Heart Rate (beats/min)	72.03 $\pm$ 1.82	75.20 $\pm$ 3.04	0.001*
SBP (mm of Hg)	109.20 $\pm$ 2.55	112.20 $\pm$ 5.46	0.009*
DBP (mm of Hg)	71.26 $\pm$ 6.04	73.80 $\pm$ 3.41	0.053
Random Blood Sugar (mg/dl)	79.23 $\pm$ 6.38	78.86 $\pm$ 3.67	0.81

SBP: Systolic blood pressure, DBP: Diastolic blood pressure; \* denotes statistically significant ( $p < 0.05$ )

Table 1 shows that age, height BMI and blood sugar level were comparable between the groups whereas the parameters like weight, waist-hip ratio, heart rate and systolic blood pressure were found to be statistically significant in offspring of diabetic parents when compared to those of non-diabetic parents.

Comparison between frequency and time domain parameters of heart rate variability is shown in Table 2 & 3. The results showed statistically significant difference in the HRV spectral power between the groups. Mean RR, SDNN, RMSSD, pNN50 and HFnu which are the measures of parasympathetic activity were found to be significantly reduced in group 2 reflecting compromised parasympathetic component of cardiovascular autonomic function. Similarly, parameters representing sympathetic component were found to be significantly increased in offspring of diabetic parents.

Significantly increased LF/HF ratio made the result clearer in understanding that the individuals with the parental history of type II diabetes mellitus have deranged sympathovagal balance.

**Table 2:** Comparison of frequency domain parameters of HRV between the study groups

Parameters	Group 1	Group 2	p-value
LFnu	45.89±4.23	48.48±4.70	0.029*
HFnu	57.74±4.49	54.98±4.21	0.017*
LF: HF ratio	0.79±0.078	0.88±0.07	0.001*
TP (m <sup>2</sup> )	1161.32±63.35	1012.77±60.90	0.001*

LFnu: Low-frequency power, HFnu: High-frequency power, TP: Total power; \* denotes statistically significant (p<0.05)

**Table 3:** Comparison of time domain parameters of HRV between the study groups.

Parameters	Group 1	Group 2	p-value
Mean RR (ms)	955.11±59.52	864.28±86.412	0.001*
SDNN (ms)	50.80±6.89	43.58±5.28	0.001*
RMSSD (ms)	33.84±4.31	28.45±4.45	0.001*
pNN50 (%)	15.94±1.86	12.98±1.58	0.001*

SDNN: Standard deviation of normal-to-normal RR intervals, RMSSD: root mean square successive difference, pNN50: the proportion of NN50 to the total number of NN intervals; \* denotes statistically significant (p<0.05)

## DISCUSSION

Many extensive researches are carried out to delineate the effect of family history of T2DM on offspring. Altered cardiovascular autonomic function leading to risk of development of diabetes have been reported among healthy offspring of patients with T2DM.<sup>14,15</sup> Literature suggests that progenies of diabetic parents are more vulnerable to develop diabetes, but early outcome of genetic transmission on such offspring before the symptomatic onset of disease is overlooked.<sup>5,16,17</sup>

In our study, we found out that the parameters like age, height, BMI, diastolic BP, blood sugar level were comparable whereas parameters like weight, waist-hip ratio (WHR), heart rate and systolic BP, despite of being within normal range, were found to be differing significantly between the groups. Contrary to our result, a study done by Praveen EP et al. and Samata Padaki et al. showed significantly higher BMI in normoglycemic healthy offspring of T2DM parents when compared to those of non-diabetic parents.<sup>18,19</sup> However, significantly higher waist to hip ratio was observed in study done by Samata Padaki et al. which was in accordance to our result. Few other studies also have drawn upon inference that central obesity, as measured by the waist to hip ratio, is importantly and independently associated with T2DM.<sup>20,21</sup> WHR being more appropriate predicting parameters than BMI for its association with diabetes, significantly higher WHR in our study reflects the level of vulnerability of offspring having parental history of T2DM towards development of diabetes and cardiovascular disease.<sup>22</sup>

The HRV findings in our study showed extensive differences

in cardiovascular autonomic function in between the two groups. The time and frequency domains of HRV showed that the vagal activity was highly compromised subserving to enhanced sympathetic outflow in subjects having parental history of T2DM. Significantly increased LFnu revealed that sympathetic component is markedly pronounced whereas significantly reduced HFnu, Mean RR, SDNN, RMSSD, pNN50 and TP reflects diminished parasympathetic component deranging overall cardiovascular autonomic features. Higher LF/HF ratio in targeted group project the inference of altered sympathovagal balance even when genetically inherited disease outcome is not manifested. These alterations clearly delineate that subject having family history of T2DM may have underlying autonomic changes predisposing to development of diabetes and cardiovascular autonomic neuropathy. Similar findings like our study were shown by some of the studies, however, F.J Nerves et al. stated that family history of T2DM have no any influence on HRV spectrum.<sup>14,24-26</sup>

Some studies reported that even in the absence of insulin resistance, autonomic disturbance may occur whereas few studies correlated the development of autonomic dysfunction with that of hyperinsulinemia and insulin resistance.<sup>27,28</sup> Central obesity, adiposity and increased free fatty acids level in the body may cause insulin resistance which could lead to hyperinsulinemia predisposing autonomic alteration. Interaction of insulin on hypothalamus leads to activation of sympathetic component and suppress the parasympathetic component decreasing the vagal activity.<sup>29</sup> Hence, from these observations we can deduce that healthy offspring of diabetic parents are at high risk of developing autonomic disorders along with obesity due to genetic inheritance leading to insulin resistance manifesting diabetes mellitus at later stage.

## CONCLUSION

Alteration of cardiovascular autonomic function is found in healthy offspring of diabetic parents, characterized by reduced vagal activity and pronounced sympathetic regulation. Genetic factor may be one of the major causes for the manifestation of such features which might predispose the population to more hazardous complications, even before the symptomatic diagnosis of the disease. Assessment of cardiac autonomic function using modality like HRV would help in early detection of such dysautonomia and reducing the life-threatening effects on offspring having parental history of T2DM.

## LIMITATIONS OF THE STUDY

We have not correlated HRV findings with other biochemical findings.

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## CONFLICT OF INTEREST

The authors would like to declare no conflict of interest.

## FINANCIAL DISCLOSURE

No any support in the form of grants, equipment and drugs has been taken from any organization.

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