

Original Research Article

## **The Study of Autonomic Functions in Young Nondiabetic Offsprings of Type 2 Diabetes Mellitus Parents by Time Domain Analysis of Heart Rate Variability**

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**Abstract:** Children with parental history of diabetes have inherited susceptibility to develop diabetes. It has been shown that patients with Diabetes Mellitus exhibit altered autonomic activity of cardiovascular system. The present study aimed to determine the early changes in cardiac autonomic modulation by measuring the time domain analysis of heart rate variability among healthy subjects with parental history of type 2 diabetes and to compare it with the age and sex matched controls. The study of Cardiovascular Autonomic Functions was carried out in 50 healthy offsprings of Type 2 Diabetic Parents (Case group) and 50 healthy offsprings of Nondiabetic Parents (Control group) in the age range of 18 - 25 years randomly selected among MBBS students of J.L.N. Medical College Ajmer. Statistical Analysis is done by student t-test. Probability P value <0.05 was considered statistically significant. In offsprings of type 2 diabetic patients significantly lower SDNN (ms), RMSSD (ms), p NN50% were observed as compared to control group. The present study reveals that shift in the sympathovagal imbalance was due to vagal withdrawal in offspring of type 2 Diabetes Mellitus patients. Impairment in autonomic function is associated with increased risk of future diabetes. Early detection of diabetes can be used for risk stratification at early stages of life and serious consequences can be reduced.

**Keywords:** Autonomic Function Test, Diabetes Mellitus, Heart Rate Variability

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### **INTRODUCTION**

Type 2 DM is characterized by hyperinsulinemia and hyper glycaemia due to insulin resistance and relative insulin deficiency, and a slow, progressive loss of beta-cell function. Type 2 DM has a strong genetic component. 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. Type 2 diabetes mellitus (T2DM) are marked by abnormal metabolic profiles [1]. The autonomic nervous system (ANS) has a role in the regulation of long- and short-term energy balance and ANS dysregulation is implicated in the pathogenesis of obesity and T2DM[2]. In developed countries, diabetes is the most common cause of autonomic neuropathy. The most studied form of diabetic autonomic neuropathy is cardiovascular autonomic neuropathy. It is defined as impairment of autonomic control of the cardiovascular system in the setting of diabetes and after exclusion of other possible

cause. HRV refers to the phenomenon of continuous oscillation in the intervals between consecutive heartbeats. Quantification of HRV from short- and long-term ECG recordings is a non-invasive method widely used in the assessment of cardiovascular autonomic regulation and it measures the working of the heart, including autonomic nerve functioning [3-5]. Short-term recordings are usually 1- to 10-min ECG recordings obtained in stationary laboratory conditions. Analysis of 5 minutes measurements of heart rate variability (HRV) has been shown to be a good predictor of physiological distress and mortality, especially for cardiovascular disease [6-11]. Variations in heart rate may be evaluated by a number of methods. Perhaps the simplest to perform are the time domain measures. In a continuous electrocardiographic (ECG) record, each QRS complex is detected, and the so-called normal-to-normal (NN) intervals (that is all intervals between adjacent QRS complexes resulting from sinus

node depolarizations), or the instantaneous heart rate is determined.

The aim of present study was to evaluate cardiac autonomic functions of non-diabetic offsprings of type 2diabetic parents (cases) comparing them with healthy subjects who do not have family history of diabetes (controls) using time domain analysis of heart rate variability.

**MATERIAL AND METHODS**

The study was performed in department of Physiology, J.L.N. Medical College, and Ajmer. In this comparative study, 100 healthy subjects including both males and females, in the age group of 18-25 years were recruited from M.B.B.S. students of J.L.N. Medical College, Ajmer. The study group consisted of 50 volunteers with parental history of Type 2 DM and control group included 50 volunteers without parental history of diabetes. Known case of diabetes, hypertension and congenital heart disease and with any history of smoking, alcohol or substance abuse and on long term medication that may influence cardiovascular and respiratory system were excluded from the study. Ethical clearance was obtained from Ethics committee of J.L.N. Medical College, Ajmer. The study protocol was explained and informed written consent was taken from the volunteers. Detailed personal, medical and family history including history of parental DM was taken. Anthropometrical parameters like height, weight, BMI were taken. The study was carried out between 9.30 am-12.30 pm after emptying bladder, consuming a light breakfast 1-2 hr before arrival. Subjects were asked to abstain from use of caffeine and other stimulants 12 hrs before the study and strenuous exercise 24 hr before study. The random blood sugar level [Using Dr More pen Gluco One blood glucose

monitoring system] was measured. Blood Pressure and Autonomic function of subjects by HRV analysis was recorded after making them comfortable by resting in supine posture for 15 minutes. Blood Pressure and Heart Rate Variability were recorded by RMS Polyrite D Version 2.4. Simple time-domain variables that can be calculated from direct measurements of the NN intervals or from the differences between NN intervals. These variables may be derived from analysis of the total electrocardiographic recording. The simplest variable to calculate is the standard deviation of the NN interval (SDNN), i.e. the square root of variance. ng. Other commonly used measures derived from interval differences include RMSSD, the square root of the mean squared differences of successive NN intervals, NN50, the number of interval differences of successive NN intervals greater than 50 ms, and pNN50 the proportion derived by dividing NN50 by the total number of NN intervals. Statistical analysis was performed with the SPSS, Trial version 23 for Windows statistical software package (SPSS Inc., Chicago, IL, USA) and Primer. The Groups were compared for quantitative data were presented as mean and standard deviation (Mean ± SD) and were compared using by student t-test. Probability P value <0.05 was considered statistically significant.

**RESULTS**

The Groups were compared for anthropometric measures. Table 1 shows Subject characteristics and anthropometric measures of study population in two groups. It was shown that age, height, weight, BMI, Systolic and Diastolic blood pressure were comparable and there were no significant differences between cases and controls in subject characteristics and anthropometric measures.

**Table 1 shows Subject characteristics and anthropometric measures of study population in two groups**

Variables	Cases(N=50)	Control (N=50)	P value
Age (yrs)	19.42±1.727	19.88±1.923	0.21 NS
Height (meters)	1.67±8.22	1.69±7.97	0.25 NS
Weight (kg)	62.38±14.20	61.32±8.77	0.65 NS
Body Mass Index (kg/m2)	22.04±4.15	21.44±2.32	0.36 NS
Systolic BP (mm of Hg)	112.86±8.29	113.60±6.77	0.62 NS
Diastolic BP (mm of Hg)	70.4±9.65	68.66±8.08	0.62 NS

Data expressed as Mean ±SD

Cases = healthy subjects with parental history of type 2 DM

Controls = healthy subjects without parental history of Diabetes

S = statistically significant

NS= statistically non-significant

Table 2 provides Time Domain analysis of HRV between study groups. The results of present study showed that global HRV was significantly lower among

the cases was seen as evidenced by reduced SDNN and RMSSD and pNN50% than did healthy control subjects.

**Table 2: Time Domain analysis of HRV between study groups**

Parameters	Cases	Controls	P value
SDNN(ms)	44.42±13.04	51.32±19.01	0.037S
RMSSD(ms)	31.17±16.32	40.00±21.49	0.023S
pNN50%	10.58±12.99	15.89±13.29	0.046S

Data expressed as Mean ±SD

Cases = healthy subjects with parental history of type 2 DM

Controls = healthy subjects without parental history of Diabetes

S = statistically significant

NS= statistically non-significant

**DISCUSSION**

Autonomic dysfunction as primary pathological factor has been associated as a risk factor for developing diabetes in future. Currently HRV analysis is recommended as test of choice for clinical evaluation of autonomic nervous functions. The present study attempted to assess the changes in cardiac autonomic activity in healthy offspring's of normal parents and healthy of type 2 diabetic parents by analysing the time domain indices of HRV. In present study, physiological factors like Age, Gender, BMI, SBP and DBP in two study groups were matched. In time-domain analysis of HRV, significantly lower global HRV among the cases was seen as evidenced by reduced SDNN and RMSSD and pNN 50% than did healthy control subjects. Time-domain indices represent parasympathetic modulation of cardiac activity. Among HRV indices, RMSSD exclusively reflects vagal modulation of HR on a short-term basis and is considered as an important indicator of parasympathetic tone. Significantly decreased RMSSD in the study group confirms poor cardiac vagal control in offspring of diabetic patients. These findings are consistent with that of Fiorentini A *et al.*; in 2005 [12]and Pal GK *et al.*; in 2014 [14] showing that offsprings of Type 2 Diabetic subjects exhibited autonomic imbalance which was expressed by higher weight of sympathetic and lower weight of parasympathetic component. Pal GK *et al.*; in 2014 [14] assessed CV and autonomic functions in FDR of diabetic patients by HRV analysis. . All the time domain indices (RMSSD, SDNN, NN50, and pNN50) were significantly less (P< 0.0001) in test group subjects compared to that of the control group subjects.

Fiorentini A *et al.*; in 2005[12] conducted study to evaluate, by heart rate variability (HRV) with 24-hours ECG Holter (HRV), the circadian autonomic

activity in offspring of type 2diabetic subjects and the relation with insulin-resistance. In time domain analysis of HRV, a significant reduction of the total autonomic system activity in both groups, expressed by progressive decrease of SDNN value from Non-insulin resistant to Insulin resistant groups. However Neves F *et al.*; in 2008 [13] have reported that HRV is preserved in offsprings of type 2 diabetic patients in the absence of concomitant metabolic disorders.

The present study reveals that shift in the sympathovagal imbalance was due to vagal withdrawal Time-domain indices represent parasympathetic modulation of cardiac activity. Though the cause of sympathovagal imbalance cannot be elucidated from the present study but it could be attributed to raised insulin levels as various studies have shown that subjects with family history of diabetes have raised insulin level [15, 16] and hyperinsulinemia is known to enhance sympathetic outflow [17] via effects in the hypothalamus [18] and also contribute to decrease in vagal tone. As impairment in autonomic function is associated with increased risk of future diabetes hence early detection can be used for risk stratification and intervention may be carried out at early stages of life to reduce the serious consequences.

The limitation of present study is that we did not quantify the exact physical activity or the exercise capacity of the participants. Also, we have not estimated the plasma insulin, and not assessed insulin resistance, dyslipidemia and oxidative stress that could contribute to SVI in of springs of diabetic's patients. Future studies should assess if restoration of sympathovagal homeostasis attained by non-pharmacological means such as yoga-relaxation would reduce the CV risks in the subjects, as practice of such

techniques has been reported to restore sympathovagal balance.

### CONCLUSION

Present study reveals that nondiabetic offspring of Type 2 Diabetic patients have Sympathovagal imbalance with decreased Parasympathetic activity. This can be used to take measures to establish sympathovagal homeostasis attained by non-pharmacological means such as yoga that would reduce future cardiovascular risk in the subjects.

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