

Impact of Diabetes Type 2 in Adults on Autonomic Modulation at Rest and in Response to the Active Orthostatic Test

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Abstract

Background: Cardiovascular autonomic neuropathy is one of the most common complications of Diabetes Mellitus Type 2 (DM2). Heart rate variability (HRV) is a noninvasive measure of cardiac autonomic modulation. Reduced HRV is an independent cardiovascular risk factor and has been proposed as a marker of increased risk of mortality. Very few studies have measured changes in HRV in DM2 in India.

Objectives: To analyze the autonomic modulation responses in DM2 patients by means of HRV indices.

Methodology: A cross-sectional study of 20 Type 2 Diabetic mellitus from age groups 30-50 years and age and gender matched non-diabetic subjects as controls. Subjects satisfying inclusion and exclusion criteria and gave written informed consent were randomly invited to take part in the study. Initial assessment was done for HTN, hyperlipidemia, smoking, cardiovascular disease, family

H/o DM2, FBS >130 mg/dl, Body mass index (BMI) >25 kg/m², DM2, duration of disease, and Heart rate.

Blood pressure: measured by mercury sphygmomanometer after a 5-min rest. Electrocardiogram was recorded using Power Lab (ADInstruments). The time domain, frequency domain variables, and non-linear parameters were measured from ECG using Lab Chart software.

Results and Conclusion : Time domain variables namely Average RR, SDRR, SDARR, rMSSD and PNN50(%) and Frequency domain variables; High frequency (HF) power, Low frequency (LF) power and Very Low frequency (VLF) power Non-Linear variables; S01 and SD2 were reduced in patients with diabetes Mellitus compared to normal control but was not statistically significant. One of the reasons could be small sample size. Study should be repeated in large sample size.

Key Words : Heart Rate Variability, Autonomic Dysfunction, Type 2 Diabetic Mellitus

Introduction

Diabetes mellitus is one of the most common Non-Communicable Diseases and, as well as the aging process, may influence the autonomic nervous system (ANS), leading to a poor autonomic control of heart

^{1,2}. In subjects with diabetes mellitus, damage to both parasympathetic and sympathetic fibers innervating the cardiovascular system produces the cardiovascular autonomic neuropathy (CAN). CAN clearly entails an increase in mortality and an acceleration of other

micro vascular complications³. Among the most common complications, it is highlighted the diabetic autonomic neuropathy which is poorly recognized and understood despite its significant effects on several organs and systems^{4,5}. Heart-rate variability is a measure of cardiac autonomic function⁶. The heart rate variability (HRV) was proved to be a noninvasive tool as valuable clinical evidence for the prognosis of cardiovascular events and several disorders. Reduced HRV is an independent cardiovascular risk factor^{7,8}. At an early-stage autonomic dysfunction may be asymptomatic or mildly symptomatic. Symptomatic autonomic neuropathy carries worst prognosis, so early diagnosis is essential for maximum benefit more so in Diabetes⁹. Also, very few studies have measured changes in Heart Rate Variability in type 2 diabetes mellitus in India. Thus, analysis of HRV associated with the autonomic active orthostatic test is important in South Indian population. Hence in the present study our aim is to analyze the autonomic modulation responses induced by the implementation of the active orthostatic test, in adults with DM2, and study the autonomic modulation by means of HRV indices.

Objectives

1. To determine HRV in type 2 Diabetics Mellitus.
2. To determine Autonomic modulation responses induced by the implementation of active orthostatic tests in adults with type2 diabetics mellitus.

Material and Methods

A cross sectional study of 20 type 2 Diabetes Mellitus patients from age groups 30-50 years and 20 age and gender matched non-diabetic subjects as controls.

Inclusion criteria

Patients with Diabetes Mellitus type 2 minimum disease duration >2 year with controlled glycemic

status defined as (1) glycosylated hemoglobin (HbA1c) <7 mg % (2) FBS <126 mg% and (3) post prandial blood sugar <180 mg % (ADA guidelines)

- On regular hypoglycemic medication but not insulin
- Patients who are ready to give written informed consent

Exclusion criteria

- Those on irregular treatment, newly diagnosed (<6 months)
- Previous h/o neurological or cardiovascular intervention, on pacemaker, on drugs directly affect ANS, arrhythmia

Initial assessment was done for Hypertension, Hyperlipidemia, Smoking, Cardiovascular disease, family h/o diabetes mellitus, FBS >130mg/dl, BMI >25kg/m², duration of diabetes mellitus and Heart rate.

Assessment of HRV was carried out between 8.30 and 12.00 am in a separate examination room. Patients were requested to avoid coffee, tea, cola drinks, and smoking for 12 h and alcoholic beverages for 24 h before the procedure

Blood pressure was measured by mercury sphygmomanometer after a 5 min rest.

Electrocardiogram was recorded after supine rest for at least 5 min with subject being in supine position and breathing freely using power lab (AD Instruments). The ECG recording from the precordial leads was transferred online to a microcomputer for the analysis of HRV.

Heart rate variability was measured from ECG using Ad instrumentslab chart software

Autonomic Test—Active Orthostatic Test

To perform the active orthostatic test the subjects will be instructed to remain lying at rest for 30 minutes, after which they will stand up (3 to 4s), remaining in a standing position for 10 minutes. The subjects will be monitored throughout the period. The RR interval sequence with greater stability was selected from the initial rest period and during the maneuver for each subject

Statistical Analysis

The statistical significance of differences in the mean distribution of various parameters among various subgroups is done by Mann–Whitney test or unpaired Student’s *t*-test for quantitative data.

Time Domain Variables

- Average RR: Mean RR Interval
- SDRR: Standard deviation of R-R Interval

- SDARR: Standard deviation of average R-R Interval

- rMSSD: Root mean square of successive RR interval differences

- PNN50(%) time domain heart rate variability

Frequency Domain Variables

- High frequency (HF) power
- Low frequency (LF) power
- Very Low frequency (LF) power

Non-Linear Variables

- SD1
- SD2

Results

FIGURE 1



DIAGRAM 1 SHOWING GENDER DISTRIBUTION OF SUBJECTS

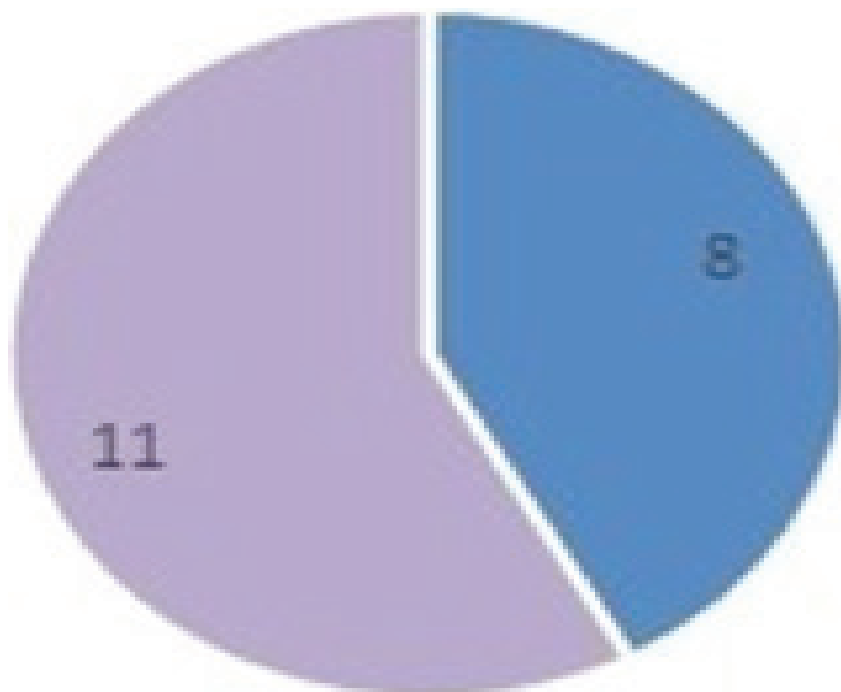


DIAGRAM 2 SHOWING DISTRIBUTION OF SUBJECTS INTO DIABETICS AND NON-DIABETICS

Table-1: Comparison of Time, Frequency Domain and nonlinear variables in diabetic and non-diabetic patient

	Parameters	Diabetic		Non diabetic		P value
		Mean	SD	Mean	SD	
TIME DOMAIN	Average meanRR (ms)	826.41	129.18	774.96	86.15	0.311
	SDRR (ms)	51.87	10.78	71.71	66.06	0.772
	rMSSD(ms)	48.56	18.73	73.68	118.61	0.386
	PNN50(ms)	14.66	11.93	21.17	22.95	0.96
	HF power(ms ²)	39.96	20.40	29.79	19.43	0.26
Frequency Domain	LF power(ms ²)	26.83	11.70	31.07	13.82	0.49
	VLF power(ms ²)	29.71	18.61	36.54	20.04	0.46
	SD1(ms)	35.52	11.82	52.29	83.91	0.30
Nonlinear Domain	SD2(ms)	64.73	14.91	79.30	52.98	0.96

Discussion

Heart rate variability (HRV) asserts the variations of instantaneous HR as well as RR intervals. Decreased HRV is a recognized vital autonomous risk element for greater mortality and sudden cardiac death (SCD) in cardiovascular disease and healthy populations¹⁰. In about half of the patients, diabetes manifests as autonomic neuropathy leading to autonomic imbalance which is a bad prognostic factor^{11,12}. In a latest meta-analysis including 15 researches in diabetic individuals, cardiac autonomic neuropathy established an appreciable association with mortality when abnormal values of two or more indices of HRV expressed autonomic imbalance. Diabetes is known to reduce HR variability. Variations in HRV had been observed in different studies on diabetic patients among different populations based on the variations in their autonomy. In diabetic individuals with associated neuropathy, decreased value of SDNN appears to bear negative prognostic value and herald the manifestation of autonomic neuropathy. The mechanism of diabetic neuropathy is not very comprehensible, although it might be correlated to the disturbance of metabolism and autonomic nerves malnutrition¹³. In our study Non-Linear Variables and SD2 were reduced in patients with diabetes Mellitus compared to normal control but was not statistically significant. The reason could be small sample size. Study should be repeated in large sample size involving various complications like ischemia and foot ulcers to name a few.

Conclusion

TIPNN50 median Variables namely Average RR, SDRR, SDARR, RMSSD and (%) and Frequency domain variables, High frequency (HF) power, Low frequency (LF) power and Very Low frequency (VLF) power

Non-Linear Variables' and SD2 were reduced in patient with diabetes Mellitus compared to normal

control but was not statistically significant. The reason could be small sample size. Study should be repeated in large sample size

Ethical Clearance- Taken from Vydehi Institutional Ethics Committee (VIEC)

Source of Funding- Self

Conflict of Interest - Nil

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