RESEARCH

COMPARATIVE STUDY OF HEART RATE VARIABILITY PARAMETERS WITH TYPE 2 DIABETES MELLITUS WITH HEALTHY INDIVIDUALS

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Abstract

Background: Heart sinus node activation on the sympathetic and vagal components of the autonomic nervous system is reflected in heart rate variability, a non-invasive electrocardiographic measure. It expresses the overall variation in sinus depolarization time and instantaneous heart rate. In addition to resting tachycardia, exercise intolerance, orthostatic hypotension, constipation, gastroparesis, erectile dysfunction, and cardiac arrhythmias, diabetic autonomic neuropathy is a critical and frequent consequence of diabetes. Diabetes-related morbidity and mortality are significantly impacted by cardiac autonomic neuropathy. The first goal of this study was to test type 2 DM patients for heart rate variability and, as a result, gauge the severity of diabetic patients' cardiac autonomic neuropathy. 2. Compare the HRV parameters between people with type 2 diabetes and healthy people. **Materials and Methods:** Patients with type 2 Diabetes Mellitus admitted in SNMC and HSK Hospital were included in this study. It is a Case - control study. Healthy controls were compared with type 2 Diabetes Mellitus in terms of age, BMI, gender, body weight and blood pressure. **Result:** Type 2 DM patients had lower RR intervals, lower SDRR, lower RMSSD, lower pRR50, lower total power, lower LF, lower HF compared to controls. All time and frequency domain parameters are lower in diabetic patientsexcept LF/HF ratio. Results of the Spearman correlation coefficient(r) show a negative relationship between the HRV indices and the HbA1c and FBS values. **Conclusion:** It wasn't until the late 1980s, when irregular heart rate variability proved a potent independent predictor of death following myocardial infarction, that the catastrophic ramifications of this condition became clear. In diabetic patients, a prolonged QTc interval and irregular heart rate variability combination are a powerful predictor of cardiovascular disease and death. Consequently, it could serve as a screening tool for diabetic patients.

INTRODUCTION

Heart rate variability is a non-invasive electrocardiographic measure that reflects the activation of sympathetic and vagal autonomic nervous system components on the heart's sinus node. It expresses the overall variation in sinus depolarization time and instantaneous heart rate. The main clinical manifestations of diabetic autonomic neuropathy include resting tachycardia, exercise intolerance, orthostatic hypotension, constipation, gastroparesis, erectile dysfunction, and cardiac arrhythmias. Despite being a serious and frequent complication of diabetes, its implications are not fully understood. Cardiac autonomic neuropathy has received extensive research and is clinically significant. For diabetic individuals, it is a substantial source of morbidity and mortality. Sudden death and high-risk cardiac arrhythmia are linked to cardiac autonomic neuropathy. After a considerable amount of time, clinical autonomic dysfunction symptoms manifest. Within a year following the diagnosis of type 2 diabetes and two years after the diagnosis of type 1 diabetes mellitus,

subclinical cardiac autonomic neuropathy expressed in heart rate variability may be discovered. When it was established in 1980 that aberrant heart rate variability was a significant predictor of death following acute myocardial infarction, the serious consequences of abnormal heart rate variability became clear. Cardiac autonomic neuropathy, which is linked to a range of disorders such cardiac arrhythmias, sudden death, resting tachycardia, exercise intolerance, aberrant blood pressure control, and orthostatic hypotension, constitutes a serious morbidity in diabetes patients, silent myocardial infarction, sudden cardiac death, cardiomyopathy, intraoperative and perioperative cardiovascular instability. Thus a review of this is important for physician to assess diabetes in order to establish safe targets.

Aims and Objectives

1. To screen patients with type 2 DM for Heart Rate Variability and thereby assess Cardiac Autonomic Neuropathy in Diabetic patients.
2. Compare heart rate variability parameters of patients with type 2 Diabetes mellitus patients with normal individuals.

MATERIALS AND METHODS

Study Design

It is a Case-Control Study. Patients with type-2 Diabetes Mellitus for more than 5 years and Age and sex-matched Controls were included.

Ethical Consideration

The Ethical Review Body of SNMC, an institutional ethics committee on human subject research affiliated with RGUHS, Bangalore and accredited by the Medical Council of India, granted approval for the study. Patient confidentiality was maintained. All information gathered during the course of the study was kept private and solely used for this investigation.

For Type 2 diabetes mellitus patients:-

Inclusion Criteria

- Age >30 years (both male and female)
- Admitted patients in the hospital.

Exclusion Criteria

- Pregnancy
- Neurological Disease
- Body mass index (BMI) over 35kgs/sq.m
- Chronic heart, Liver, Renal failure.
- Thyroid disorder
- Treatment that can influence HRV parameter.

For Controls

All controls will be without diabetes mellitus.

Exclusion criteria will be same as for type 2 diabetes mellitus patients.

Sample size is calculated by using open epi version – 2 software we got sample size of n= 47 in each group, drop rate = 5%. Considering drop rate of 5% we got sample size of n=50 in each group.

Patients with Type 2 Diabetes Mellitus and healthy controls were subjected for short term HRV analysis. All subjects were investigated in a quiet room (they were instructed to avoid caffeinated and alcoholic beverages 2 hrs before test). Patients were instructed not to perform strenuous exercise (moderate to heavy) before the test.

Heart rate variability (HRV) will be measured by Power lab AD Instruments. HRV is analyzed by time and frequency domain parameters. This article reviews the mechanisms that generate 24 hr heart rate variability and short-term heart rate variability. There are two types of measures of heart rate variability. The time domain and frequency domain. The time domain measures based on inter beat intervals include SDRR(standard deviation of average of all RR intervals).They reflect both sympathetic and parasympathetic modulation of heart rate. Frequency domain indices: analysis of this domain obtains about the variance of heart rhythm due to heart rate at variable frequency. These frequencies are grouped into 4 bands. The HF band reflects respiratory arrhythmias. HF power measures cardiac vagal activity. The lower frequency power LF/HF ratio is the index of sympathetic activity of heart. Data will be entered in Excel Sheet, then we will calculate Mean and SD for quantitative data. Unpaired t – test is used for different group comparison. Spearman Correlation Coefficient is used to find relation between indices of heart rate and laboratory test.

RESULTS

Patients with type 2 diabetes mellitus of more than 5 years, admitted in SNMC AND HSK Hospital were included. Among 100 patients studied 35 patients belonged to the age group between 55 to 64. 70 patients were male and 30 were female.

Time-domain parameters showed lowered values in diabetic patients than in controls. Frequency domain study results were low in diabetic patients than in controls. Type 2 diabetes mellitus patients had lower RR interval, low SDRR, lower RMSD, lower pRR50 lower total power, lower LF and lower HF compared to controls.

Table 1: Time Domain Parameters – (Unpaired t-test)

	Cases	Controls	P Value	Significance
Average RR(ms)	687 ± 134.47	836.5 ± 155.7	0.0001	HS
Median RR(ms)	690.4 ± 137.54	819.8 ± 197.6	0.0003	HS
SDRR (ms)	20.9 ± 16.04	38.4 ±22.6	<0.0001	HS
SDARR (ms)	8.44 ±9.29	15.84 ±23.89	0.036	S

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SDSD	15.54 ± 17.56	32.9 ±35.8	0.0027	HS
RMSSD	16.37 ± 17.95	32.9 ±35.8	0.004	HS
pRR50	4.5 ± 10.35	61.5 ±335.7	0.23	NS

Unpaired I Test HS=Highly Significant, NS=Not Significant S- Significant

[Table 1] = Shows All Time Domain Parameters are significantly lower in Cases (Diabetic Patients) than in Controls (normal individuals).

Table 2: Frequency Domain Parameters- Unpaired t Test

	Cases	Controls	P Value	Significance
Total (ms2)	407.3 ± 667.4	1894.6 ±2321.0	0.001	HS
VLF (ms2)	268.4 ±450.5	666.8 ± 648.0	0.001	HS
LF (ms2)	139.6 ± 433.1	448.9 ± 590.7	0.001	HS
HF (ms2)	229.6 ± 937.8	709.9 ±1155.1	0.001	HS
LF/HF (%)	2.2 ± 3.1	2.5 ± 3.5	0.725	NS
S = Significant, HS=Highly Significant				

Table 3: Correlation of HbA1c with HRV parameters (Pearson Correlation)

Pearson's correlation - HbAIC			
Variables	**(r) Value**	**p Value**	**Sig**
Time Domain- Average RR, (ms)	-0.309	0.029	Sig
Median RR (ms)	-0.304	0.031	Sig
SDRR (ms)	-0.102	0.48	Not Sig
SDARR (ms)	-0.162	0.261	Not Sig
SDSD (ms)	-0.0842	0.56	Not Sig
RMSSD (ms)	-0.022	0.879	Not Sig
pRR50 (%)	0.0236	0.874	Not Sig
Frequency domain-Total power(ms2)	-0.065	0.653	Not Sig
VLF (ms2)	0.00036	1	Not Sig
LF (ms2)	-0.0092	0.95	Not Sig
HF (ms2)	-0.0177	0.906	Not Sig
LF/HF (%)	0.185	0.19	Not Sig

All HRV parameters are inversely related with HbA1c except LF/HF(%)

Table 4: Correlation of FBS with HRV parameters (Pearson Correlation)

Pearson's correlation - HbAIC			
Variables	**r Value**	**P Value**	**Sig**
Time Domain- Average RR, (ms)	-0.242	0.09	Not Sig
Median RR (ms)	-0.234	0.10	Not Sig
SDRR (ms)	-0.073	0.61	Not Sig
SDARR (ms)	-0.058	0.68	Not Sig
SDSD (ms)	-0.153	0.28	Not Sig
RMSSD (ms)	-0.083	0.56	Not Sig
pRR50 (%)	-0.021	0.88	Not Sig
Frequency domain-Total (ms2)	-0.0062	0.96	Not Sig
VLF (ms2)	0.046	0.75	Not Sig
LF (ms2)	0.021	0.88	Not Sig
HF (ms2)	-0.015	0.91	Not Sig
LF/HF (%)	0.11	0.44	Not Sig

All HRV parameters are inversely related to FBS, except LF/HF (%), VLF, LF.

DISCUSSION

Abnormalities of heart rate variation have been reported in a wide variety of clinical conditions, these include ischemic heart disease, congestive heart failure, hypertension, diabetes and many other conditions. However, it has been established in ischemic heart disease, congestive heart failure and diabetic autonomic neuropathy.[1]

Diabetes mellitus causes autonomic dysfunction in cardiovascular system and our focus of research quantifies both sympathetic and parasympathetic components.

In diabetic patients, cardiac autonomic neuropathy is a substantial cause of morbidity and mortality. It is also linked to a high risk of cardiac arrhythmias and sudden death, which may be caused by silent myocardial ischemia. Significant clinical and prognostic relevance exists there.[2] Thus a review of this topic is both timely and important.

Major clinical trials underline the importance of relation between glycemic control and cardiac risk. Thus a review of heart rate variability measurements is both timelyand important for physician to understand and assess the progress of the complications in disease in patient and timely intervention. Jagmeet P singh et al,[3] studied 1919

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Type 2 DM patients and concluded that heart rate variability is inversely related to plasma glucose levels except LC/HF ratio. This study confirms our results. Patient who were a part of Framingham off spring study and who underwent ambulatory ECG were included. Fasting glucose levels classified as normal <110 mg/dl,110 to 125 mg/dl as impaired fasting glucose, >125mg/dl having diabetes. The Lf power and LF/HF ratio were lower in Type 2 DM subjects with impaired fasting glucose levels. Our result showed all heart rate variability parameters were inversely related to FBS except LF/HF and VLF/LF.

Kudat et al in 2006 compared 30 normal study subjects with 30 Type 2 diabetes mellitus. The heart rate variability results showed decrease in all parameters except LF/HF12.These were the findings in our study. Another study by Thomas Benichou et al, a meta-analysis study showed that type 2 diabetes mellitus patients had significantly lower in time and frequency domain parameters compared to healthy individuals except LF/HF. These findings were confirmed in our study. Laura Poanta et al,[4] study in Acta diabetologica, September 2011,volume 48, issue 3. This study evaluated the impact of diabetes mellitus on left ventricular dysfunction and heart rate variability in diabetic patients without signs of cardiovascular disease. 24hr ECG monitor and ECHO can detect diabetic cardiomyopathy in early stages. This should be performed as routine screening test. Kudat et al study 12 consisted of 30 diabetics and 30 controls, showed that Except for mean R-R interval and LF/HF ratio, all time- and frequency-domain metrics were considerably lower in diabetic patients than in controls. These results were supported by our investigation, which showed that diabetes patients had lower heart rate variability parameters when compared to controls.[5,6]

In a population-based cohort of 6245 people aged 45 to 64 years at baseline band cross-sectional associations among 9940 people, Schroeder E et al,[7] evaluated the impact of diabetes and pre-diabetic metabolic impairments on the 9-year change in heart rate variability (HRV).[8,9]

In relation to baseline HRV, diabetes patients' HRV decreased more quickly over time than non-diabetic subjects'. Our work provides evidence for this. A diabetic subject's autonomic cardiac function progressively deteriorated over the course of nine years, suggesting that cardiac autonomic impairment is already present in the early stages of diabetic metabolic impairment. The correlation between heart rate variability measurements and blood glucose levels was demonstrated by a study by Leon J. Rothberg et al. 31 healthy controls and 32 diabetic patients made up the group. The study showed that HRV parameters are negatively associated with blood glucose levels in diabetic patients. This is confirmed in our study.[10,11,12]

Cardiac Autonomic Neuropathy outperformed the impact of conventional cardiovascular 65 risk factors as the best predictor of mortality throughout a 7-year follow-up in the EURODIAB Prospective Cohort Study10 of 2,787 diabetic individuals. Our work demonstrates that diabetes people have cardiac autonomic neuropathy. The significance of identifying people with Cardiovascular Autonomic Neuropathy (CAN) and potential treatment strategies was reemphasized in a study by Maser RE et al9. Our study helps in the early identification of CAN and thereby initiating proper treatment.[13,14,15]

CONCLUSION

It wasn't until the late 1980s, when irregular heart rate variability proved a potent independent predictor of death following myocardial infarction, that the catastrophic ramifications of this condition became clear. In diabetic patients, a prolonged QTc interval and irregular heart rate variability combination are a powerful predictor of cardiovascular disease and death. Hence it can be a screening test for diabetic patients.

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