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Original Research Article

Comparison of microalbuminuria and heart rate variability in prediction of cardiovascular complications in diabetic population: a pilot study

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ABSTRACT

Background: Microalbuminuria is considered as an early marker and strongly associated with risk of cardiovascular complications in diabetic patients. Autonomic imbalance due to micro vascular damage to parasympathetic and sympathetic fibers results in reduced heart rate variability; also predicts increased risk for cardiovascular events in diabetics. Hence it is necessary to identify an early and effective predictor of diabetic micro vascular complications. Objective of the study was to compare heart rate variability of controls with type 2 diabetes with and without microalbuminuria.
Methods: This comparative study was conducted among individuals without diabetes, hypertension and dyslipidemia (controls) and Type II diabetics with and without microalbuminuria (cases). Cases and controls were subjected to general clinical examination; microalbuminuria and HbA1C were noted. heart rate variability was assessed using digital physiograph. Frequency (HF, LF, LF/HF ratio) domain readings were noted.
Results: Mann Whitney U test was employed to analyze nonparametric data. Diabetics with microalbuminuria when compared with controls showed statistically significant (p-value=0.015) reduction in vagal activity. When compared with diabetics without microalbuminuria (180.4±151.7) they showed reduction in HF with no statistical significance. When diabetic group without microalbuminuria (0.56±0.31) was compared with controls they showed alternation in LF/HF ratio which has no statistical significance. Diabetics with microalbuminuria when compared with controls showed a statistically significant (p-value=0.009) alternation in LF /HF ratio implying an autonomic imbalance.
Conclusions: This study shows there is significant vagal inhibition and autonomic imbalance in diabetic patients with microalbuminuria compared to controls. To ascertain the role of HRV as an early predictor of cardiovascular complications we propose to conduct study with a larger sample size in future.

Keywords: Autonomic imbalance, Diabetes mellitus, Heart rate variability, Microalbuminuria

INTRODUCTION

The magnitude of non-communicable diseases (cardiovascular diseases, diabetes, malignancies and chronic respiratory diseases) has brought about a negative socioeconomic impact and sufferings to the mankind.[1] 36 million deaths have been reported every year due to diabetes and its complications. Moreover, 9 million people succumb to death prematurely.[2] Improved and effective medications have increased the lifespan of diabetic population. Hence there is a need to identify and intervene at the earliest in order to prevent complications and provide them a better quality of living. Microalbuminuria is considered as an early marker. It

causes endothelial dysfunction and predisposes atherosclerotic coronary artery disease, stroke, peripheral vascular disease, and cardiovascular mortality among diabetic population.[3,4] It was stated in heart outcomes prevention evaluation study, that diabetic patients with microalbuminuria are more prone for cardiovascular complications thus periodic screening for microalbuminuria could allow early identification of vascular disease.[5] Moreover, microvascular damage to parasympathetic and sympathetic fibers cause autonomic imbalance also predicts increased risks for cardiovascular arrhythmias, sudden death, and myocardial infarction in adults with diabetes.[6] HRV rate variability is a non-invasive indicator of cardiac autonomic function that predicts mortality and morbidity.[7]

However, the studies available till date give no conclusive answer to the concurrent association between lower cardio vascular autonomic function and microalbuminuria. Our objective was to compare heart rate variability of normal individuals with type 2 diabetics with and without microalbuminuria.

METHODS

This comparative study was conducted after obtaining clearance from institutional human ethics committee and informed consent from study participants. Individuals without diabetes, hypertension and dyslipidemia were recruited as controls (n=14). Type II diabetics with and without microalbuminuria of both sexes with age ranging from 45-65 years were included as cases (n=14). Patients with hypertension, coronary artery disease, cerebrovascular accident, family history of young MI, hyper or hypothyroidism, and beta blocker treatment were excluded. Cases and controls were subjected to general clinical examination. Presence of microalbuminuria and HbA1C values were noted from their clinical records.

Heart rate variability

Cases and controls were instructed to refrain from smoking, caffeine intake for 2 hours and alcohol intake for 36 hours. It was ensured they had adequate rest, got at least 8 hours of uninterrupted sleep on the night before the assessment of HRV and had normal breakfast on the day of assessment. They were made to lie quietly in a couch in supine position for five minutes to alleviate the anxiety in a sound attenuated room with dim lighting and the temperature ranging from 20 to 25°Celsius.

After explaining the procedure to the subject, heart rate variability, a quantitative marker of the autonomic activity was assessed using an ambulatory ECG system (INCO digital NIVIQURE, Bangalore, India) in lead II for 5 minutes. It is a multi-channel digital data acquisition system which enables to acquire, analyze and store ECG data. ECG data was obtained at a sampling rate of 1024 Hz in standard lead II configuration. The interface RS232C-compatible module was used to transfer data from the recording unit to the computer. The transferred data was analyzed using inbuilt software system. The series of RR intervals obtained was subjected to frequency domain analysis.

Frequency domain variables low frequency (LF) and high frequency (HF) power of HRV spectrum in normalized units and LF/HF ratio were measured. Descriptive statistics and Mann Whitney U test was employed to analyze nonparametric data.

RESULTS

42 individuals participated in the study, out of which 14 were non-diabetics, who acted as controls and the remaining 28 diabetics acted as cases. Out of 28 diabetics, 14 were presented without microalbuminuria and 14 with microalbuminuria. Results were expressed in mean±standard deviation. The mean age of the control group was found to be 45.78±6.8 and that of cases without microalbuminuria was 53.07±10.9 and with microalbuminuria was found to be 53±10.8.

When the diabetic group was compared with the non-diabetics HF showed statistically significant reduction (p=0.041) and the LF/HF ratio showed a significant alteration (p=0.015) (Table 1).

Table 1: Comparison between diabetics and non-diabetics.

Variables	Mean±standard deviation		P-value
	Non - diabetics N=14	Diabetics N=28	
HBA1C	5.71±0 .23	8.55±2.57	0.000*
HF	281±262	136.7±123.5	0.041*
LF	82.8±64.8	74.8±43.5	0.883
LF/HF	0.47±0.3	0.73±0.35	0.053

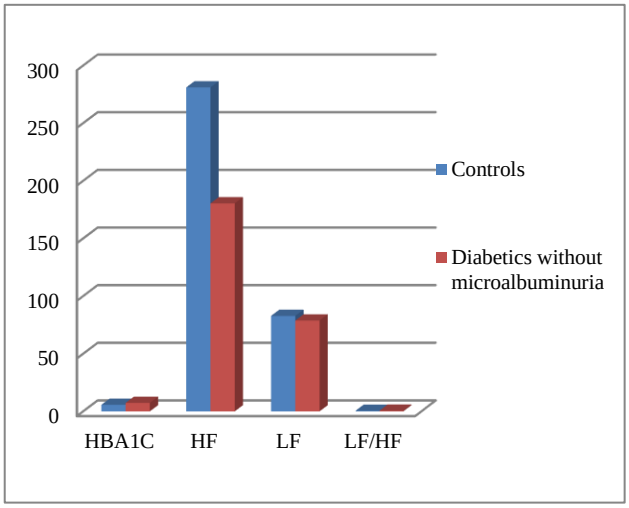

Figure 1: Comparison between the controls and diabetics without microalbuminuria.

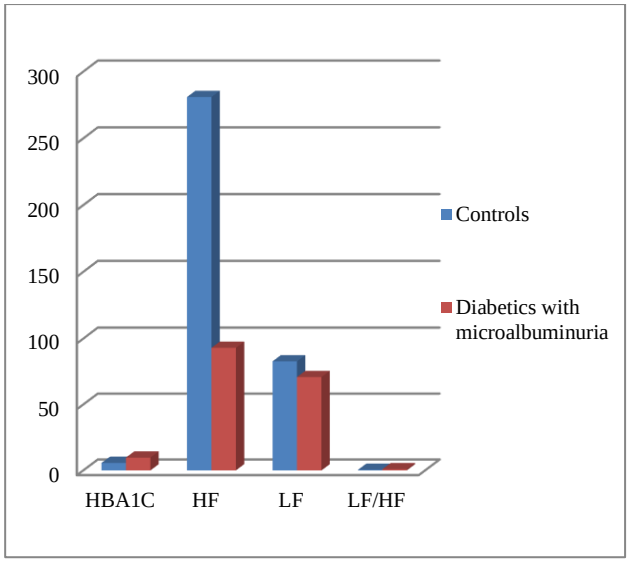

Figure 2: Comparison between the controls and diabetics with microalbuminuria.

On analysis of short term HRV, the mean HF was found to be 281±262 in controls. When the diabetic group without microalbuminuria (180.4±151.7) was compared with the controls reduction in HF was observed with no statistical significance (Figure 1). However, the diabetic group with microalbuminuria (93.05±67.6) when compared with controls showed statistically significant (p=0.015) reduction in HF (Figure 2).

LF/HF ratio was found to be 0.47±0.3 in controls. When diabetic group without microalbuminuria (0.56±0.31) was compared with controls they showed an alteration which has no statistical significance. However when the diabetic group with microalbuminuria was compared with controls they showed a statistically significant (p=0.009) alteration in LF/HF ratio (Table 2).

DISCUSSION

Microalbuminuria and heart rate variability are considered as the early predictors and prognostic markers of impending microvascular complications in diabetic population.[8,9] Increased prevalence of microalbuminuria (10 to 40%) was found to be reported in diabetic population when compared normal healthy individuals (5 to 7%).[10] This finding substantiates the presence of microalbuminuria as an early marker for diabetic complications.

Table 2: Comparison between diabetics with and without microalbuminuria.

Variables	Mean±standard deviation		p-value
	Diabetics without microalbuminuria n=14	Diabetics with microalbuminuria n=14	
HBA1C	7.37±1.25	9.72±3.02	0.021*
HF	180.42±151.71	93.05±67.6	0.08
LF	78.79±35.83	70.86±51.06	0.38
LF/HF	0.56±0.31	0.89±0.32	0.004*

HRV analysis is a noninvasive method to assess cardiac autonomic function. It is quantified in time and frequency domains. Time domain is based on statistical operation on R-R intervals and frequency domain is based on spectral analysis of an array of R-R intervals. Frequency domain measures are considered to be more sensitive according to the suggestion of Task force of the European society of Cardiology.[11] This suggestion led to the usage of frequency domain measures in our study.

The frequency domain measures such as LF indicates sympathetic activity, HF assesses cardiovagal activity and the LF/HF reflects the sympathovagal balance. In present study we observed that the frequency domain parameters (HF, LF and HF/LF) which assess the autonomic balance showed an alteration suggesting autonomic dysfunction in diabetic patients with and without microalbuminuria.

Many researchers have reported that there is 2 to 4 times increased risk for cardiac dysautonomia in a diabetic population when compared to controls.[12] In accordance with this study, our findings report a significant reduction in HF (136.7±123.5) and an alteration in LF/HF (0.73±0.35) which suggests a significant cardiovagal inhibition and sympathovagal imbalance in the diabetic group when compared with the nondiabetic population. In a comparative study conducted among diabetics and controls, Mirza M observed both sympathetic and parasympathetic dysfunction with parasympathetic dominance in diabetic group[13,14]

Furthermore, present study also revealed a nonsignificant decrease in HF among the diabetics without microalbuminuria whereas a statistically significant decrease among the diabetics with microalbuminuria. This finding proved that there exists a significant cardiovagal inhibition in the diabetics with microalbuminuria. This observation is in line with the

other studies which report a decrease in time and frequency domain parameters of HRV before the clinical evidence of autonomic neuropathy in diabetic patients.[15] Carnethon et al, in their study found out that reduced HRV leads to complications and found to be independent prognostic marker in patients with type 2 diabetes.[16]

In our study LF/HF ratio was found to be altered in diabetics without microalbuminuria with no statistical significance. However, the diabetic group with microalbuminuria showed a statistically significant alternation implying an autonomic imbalance. In another study conducted by Colhoun et al among type 1 diabetic patients power spectral analysis of HRV was found to be reduced and was associated with cardiovascular risk factors such as increased HbA1c, dyslipidemia, higher BMI hypertension and albuminuria.[17]

It was observed in previous studies that there was a higher incidence of myocardial Ischemia in Type 1 diabetes patients with microalbuminuria.[18] However, several studies confirmed the association of microalbuminuria and alteration in vascular tone are the results of endothelial dysfunction which predicts cardiovascular events in diabetic population.[19] The results of a study which employed heart rate reserve and rating of perceived exertion in prescribing intensity of exercise also strongly support the proposed role of reduced heart rate variability along with microalbuminuria as a sensitive marker in predicting cardiovascular complications.[20]

Prevention plays a key role in quality health care delivery so it is necessary to identify early, noninvasive, feasible and effective tool to predict cardiovascular complications in diabetic population. Our pilot study is in favor of the positive role of short term HRV as a tool which fulfils all the aforementioned criteria in predicting cardiovascular complications

CONCLUSION

This study shows there is significant vagal inhibition and autonomic imbalance in diabetic patients with microalbuminuria when compared to controls. To ascertain the role of HRV as an early predictor of cardiovascular complications we propose to conduct the study with a larger sample size in future.

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Ethical approval: The study was approved by the institutional ethics committee

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