ORIGINAL ARTICLE

IMPACT OF DIABETES ON HEART RATE VARIABILITY IN PATIENTS WITH ACUTE MYOCARDIAL INFARCTION

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Background: Diabetes is a well-known cause of sudden mortality. Due to autonomic imbalance, those patients who are suffering from ischemic heart disease and diabetes concurrently are at a greater risk of manifesting arrhythmias. Heart rate variability (HRV) can be utilised for assessment of autonomic nervous system. The purpose of this study was to identify the values of HRV in diabetic and non-diabetic patients with acute myocardial infarction (AMI). **Methods:** This non-interventional descriptive study was carried out at Armed Forces Institute of Cardiology over a period of 6 months. A total of 50 healthy volunteers and 50 patients with myocardial infarction (MI) were Holter monitored for 24 hours and HRV was analysed in time and frequency domains. **Results:** The time domain indices; SDNN (non diabetics=78±30 ms vs diabetics=58±20 ms; p=0.01), SDANN (non diabetics=68±28 ms vs diabetics=49±19 ms; p=0.23), SDNNi (non diabetics=36±13 ms vs diabetics=26±14 ms; p=0.02), RMSSD (non diabetics=29±11 ms vs diabetics=23±15 ms; p=0.16) and pNN50 (non diabetics=7±10 ms vs diabetics=4±12 ms; p=0.43) were declined in diabetic patients with acute myocardial infarction when compared with non diabetic patients inflicted with infarction. Frequency domain indices, Total power (non diabetics=1479±12 ms^2 vs diabetics=759±6 ms^2, p=0.01), VLF (non diabetics=997±9 ms^2 vs diabetics=495±5 ms^2, p=0.04), LF (non diabetics=292±2 ms^2 vs diabetics=123±1 ms^2, p=0.01) and HF (non diabetics=121±1 ms^2 vs diabetics=54±5 ms^2, p=0.01) showed attenuated HRV in diabetic patients with acute myocardial infarction. Comparison of diabetic and non diabetic infracted patients with healthy volunteers revealed decreased HRV in patients with myocardial infarction but gets even worse in diabetic patients with myocardial infarction. **Conclusions:** Heart rate variability is attenuated in diabetic patients with acute myocardial infarction. It reflects sympatho-vagal imbalance in coronary patients with co-existent diabetes mellitus.

Keywords: Autonomic nervous system, diabetes mellitus, ambulatory electrocardiography

INTRODUCTION

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 populations.[1] Cardiac autonomic impairment in diabetic individuals can be identified before conventional cardiovascular autonomic function tests by means of HRV. Diabetic patients with ischemia have a progressive and hasty course as a product of combined effect of increased glycaemic conditions and multiple other risk factors associated with heart diseases, like dyslipidemia, obesity, smoking and hypertension.[2] In about half of the patients, diabetes manifests as autonomic neuropathy leading to autonomic imbalance which is a bad prognostic factor.[3,4] Virtually half of the diabetic population after coronary artery disease suffers from cardiac autonomic neuropathy which may induce both diastolic and systolic dysfunction. Increased oxidative stress produced by hyperglycaemia depicts a significant association between diabetes and vascular events.[5]

Kudet *et al*[6] reported that patients with diabetes had attenuated HRV parameters than healthy individuals, and among patients suffering diabetes those with micro-vascular complications had the lowest HRV indices. Diabetes is known to reduce HR variability. Casolo *et al*[7] performed a study on acute myocardial infarction patients and found that in six of eight diabetic patients surviving AMI HR variability increased considerably over time therefore it was unlikely that diabetes could have influenced their results significantly. A study done on the subjects of southern Serbia demonstrated that time domain indices of HRV were appreciably reduced in diabetic individuals with infarction; it was the foremost report recognising attenuated HRV in patients with type II diabetes to be a risk factor for sudden cardiac death. Their results depicted that individuals suffering with type II diabetes have reduced HRV and the mortality risk from cardiac death is increased two times than the patients with greater HRV. In their study no relationship was established amid SCD and HRV in borderline cases of diabetes.[8] Another study revealed decrease in time domain measures of HRV in diabetic individuals with AMI.[9]

Variations in HRV had been observed in different studies on diabetic patients among different

populations based on the variations in their autonomy. There is only limited data regarding effect of diabetes on HRV in coronary patients and none that compares time and frequency domain indices of HRV in diabetics and non diabetics after MI. We planned a study to evaluate the HRV in patients with acute MI to look for the synergistic effects of diabetes and infarction on autonomic nervous system of our study population and to compare the results with heart rate variability of healthy volunteers.

MATERIAL AND METHODS

Fifty healthy volunteers and 50 (male and female) patients with acute MI were included in the study. Patients with history of myocardial infarction, non compliant patient or patients reluctant to grant written informed consent were excluded. Apparently and electrocardiographically normal individuals were taken as controls. The study was conducted after approval by Medical Ethics Committee, Army Medical College, Pakistan.

Standard ECG was performed on all the subjects. For evaluating heart rhythm ten cycles of ECG were recorded. For HRV analysis 'DMS 300-3A Serials Holter Recorder' and 'DMS Serials Holter Software Premier 11' were used. Artefacts were excluded during editing of the data.

Time and frequency domains of HRV were analysed according to the recommendations of Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology (NASPE).[10] Parameters analysed for time domain included SDNN, SDANN, SDNNi, RMSSD and pNN50, and indices analysed for frequency domain included total power, Very Low Frequency (VLF), Low Frequency (LF) and High Frequency (HF).

Data were analysed using SPSS. Variables were expressed as Mean±SD. Student's *t*-test was applied for comparing the groups and $p<0.05$ was considered significant. ANOVA test was applied to compare the heart rate variability amongst healthy volunteers, non diabetic patients and diabetic patients with acute myocardial infarction and $p<0.05$ was considered significant.

RESULTS

The values of time domain indices of HRV in diabetic and non diabetic patients with AMI are presented in Table-1. SDNN in non diabetic patients was 78±30 ms while in diabetic patients was 58±20 ms. SDANN in non diabetic and diabetic patients was 68±28 ms and 49±19 ms respectively. SDNNi was 36±13 ms and 26±14 ms in non diabetic and diabetic study group respectively. RMSSD was recorded as 29±11 ms in non diabetics and 23±15 ms in diabetics with AMI. pNN50 was 7±10% and 4±12% in non diabetic and diabetic group of the study population.

When the HRV in non diabetic and diabetic individuals was compared, it was found that heart rate variability indices were attenuated in diabetic group in comparison with the non diabetic group. The difference in values of SDNN, SDANN, and SDNNi was statistically significant ($p<0.05$) between non diabetic and diabetic subjects with AMI whereas the difference between RMSSD and pNN50 was not significant statistically (Table-1).

Table-1: Time Domain Indices in diabetic and non diabetic patients with acute myocardial infarction (Mean±SD)

Time domain parameters	Non Diabetics	Diabetics	*p*
SDNN(ms)	78±30	58±20	0.01
SDANN(ms)	68±28	49±19	0.01
SDNNi(ms)	36±13	26±14	0.02
RMSSD(ms)	29±11	23±15	0.16
pNN50(%)	7±10	4±12	0.43

The values of frequency domain indices of non diabetic and diabetic study population are presented in Table-2. Total power in non diabetics was found as 1479±12 ms^2, and in diabetics it was 759±6 ms^2. Likewise, the frequency band including VLF, LF, and HF exhibited mean values of 997±9 ms^2, 292±2 ms^2, and 121±1 ms^2 in non diabetic patients with AMI; and mean values of 495±5 ms^2, 123±1 ms^2 and 54±5 ms^2 in diabetic group of patients respectively.

Similarly, the frequency domain indices like total power spectral component, VLF, LF and HF were found attenuated in diabetic individuals with AMI as compared to the non diabetic individuals and the difference was found statistically significant ($p<0.05$) (Table-2).

Table-2: Frequency Domain Indices in diabetic and non diabetic patients with acute myocardial infarction (Mean±SD)

Frequency domain parameters (ms^2)	Non diabetics	Diabetics	*p*
Total power	1479±12	759±6	0.01
VLF	997±9	495±5	0.04
LF	292±2	123±1	0.01
HF	121±1	54±5	0.01

The comparison of time and frequency domain parameters of heart rate variability after acute myocardial infarction amongst healthy volunteers and diabetic and non diabetic patients after acute myocardial infarction is depicted in table. The results show a decrease in heart rate variability after acute myocardial infarction when compared with normal healthy volunteers. Both time and frequency domain parameters are attenuated in patients with acute myocardial infarction and the indices are even worse in patients with co existent myocardial infarction and diabetes (Table-3).

Table 3: Comparison of Time and Frequency Domain Indices in healthy individuals, diabetic and non diabetic patients with acute myocardial infarction (Mean±SD)

Parameters	Healthy volunteers	Non diabetics With MI	Diabetics with MI	*p*
Time domain parameters				
SDNN (ms)	133±44	78±30	58±20	<0.01
SDANN (ms)	59±4	68±28	49±19	<0.01
SDNNi (ms)	118±7	36±13	26±14	<0.01
RMSSD (ms)	40±5	29±11	23±15	<0.01
pNN50 (%)	13±8	7±10	4±12	<0.01
Frequency domain Parameters				
Power (ms²)	3525±09	1479±12	759±6	<0.01
LF (ms²)	695±55	997±9	495±5	<0.01
VLF (ms²)	2485±07	292±2	123±1	<0.01
HF (ms²)	315±91	121±1	54±5	<0.01

DISCUSSION

Diabetes is a well-known cause of sudden mortality. In the Honolulu Heart Program, which included Japanese-American men as study subjects, RR interval in case of sudden death was appreciably increased in diabetic group than non diabetic group after modifying risk factors for coronary heart disease.[11] The Paris prospective study also established analogous outcome, in which cardiovascular disease triggered 55.2% of sudden deaths.[12] Kuller *et al*[13] similarly illustrated likewise results. Possibility of ischemic cardiovascular events is aggravated two to four times in type II diabetic patients in contrast to subjects without diabetes, and the threat is principally less affected by the associated hyperlipidemia, hypertension and smoking. When the risk factors of ischemic heart disease in patients suffering type II diabetes, are controlled, the mortality rate due to cardiovascular ailments is twofold greater in males and fourfold increased in females.[10]

Infracted patients with diabetes have 1.5–2 times greater mortality rates than patients without diabetes. This augmented mortality rate is triggered by different mechanisms that influence integrity of myocardium and compromise blood supply owing to increased tendency of thrombosis in individuals with diabetes.

Autonomic nervous system dysfunction with attenuated parasympathetic activity or aggravated sympathetic activity, exhibited by decreased HRV, triggers ventricular arrhythmias and sudden cardiac death and symbolize an autonomous risk factor for mortality in patients with AMI.[14]

HRV analysis is presently being applied in clinically, with reduction in HRV; a proven index of risk of mortality after AMI and risk of autonomic neuropathy of diabetes mellitus.[15] After myocardial infarction reduced heart rate variability might be an indication of attenuated parasympathetic activity and sympathetic mechanisms dominance which leads to cardiac electrical instability. The underlying mechanism of decreased HRV after myocardial infarction producing neural response as a consequence, has not yet been defined, but it probably implies derangement in the autonomic nerve activity of cardiac origin. 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 malnutrition.[16]

Casolo's study did not reveal significant changes in HRV in diabetic patients with AMI.[7] Another study revealed significant changes in HRV in diabetic patients with AMI.[8] 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.[17] None of the studies reported the changes in the frequency domain measures of HRV in diabetic patients suffered AMI. Our study reveals significant changes in time and frequency domain indices of HRV in diabetic individuals after AMI. That justifies severe autonomic imbalance in diabetic individuals suffering from AMI.

Follow up studies with a larger sample size may help identify the risk of sudden cardiac death in diabetic patients with AMI.

CONCLUSION

HRV is attenuated in diabetic patients with AMI. It reflects sympathetic imbalance in coronary patients with diabetes.

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