

Cardiac autonomic dysfunction and ECG abnormalities in patients with type 2 diabetes mellitus—a comparative cross-sectional study

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ABSTRACT

Background: Globally, diabetes mellitus has now emerged as a major public health problem, especially in India. Diabetic neuropathy may occur in nearly half of the patients with long-standing diabetes mellitus. In diabetes mellitus, the determinants of cardiac autonomic dysfunction were duration of diabetes, extent of glycemic control, age, and gender. **Aims and Objective:** To study the various ECG abnormalities in type 2 diabetes mellitus patients when compared with control subjects. **Materials and Methods:** The study was carried out as a hospital-based cross-sectional study among 50 diabetic patients and 50 age- and sex-matched control subjects. Resting ECG was recorded among study and control groups and compared. SPSS, version 20.0, was used for statistical analysis; unpaired *t* test was used to test the statistical difference in comparison of means, and a *p* value of <0.05 was considered statistically significant. **Result:** The study results showed that certain ECG changes such as resting heart rate, RR interval, PR interval, QRS axis, and QTc interval significantly varied between study and control groups. Abnormal heart rate response to deep breathing and postural hypotension were observed at higher frequency among patients with diabetes mellitus. **Conclusion:** Evaluation of various cardiovascular reflexes and ECG in type 2 diabetic patients may serve as a feasible technique to determine the presence of cardiac dysautonomia.

KEY WORDS: Diabetes Mellitus; Cardiac Autonomic Dysfunction; ECG Changes

INTRODUCTION

Globally, diabetes mellitus has now emerged as a major public health problem, especially in India. Diabetes is a chronic metabolic disorder characterized by prolonged hyperglycemia. Diabetes mellitus is classified into two broad categories: type I and type II, of which type II makes up for 90% of the overall

cases. As on 2014, 387 million people worldwide are living with diabetes, and 205 million are expected to be added on to this existing number by the year 2035. Nearly 46% of the individuals with diabetes remain undiagnosed, and 77% of them live in low- and middle-income countries. It was estimated that there are around 75 million diabetic patients in southeast Asian region of which 66 million people were in India, with a prevalence rate of 8.3%.^[1] Diabetic neuropathy may occur in nearly half of the patients with long-standing diabetes mellitus.^[2] The pathogenic mechanism and clinical presentation of diabetic neuropathies are multifactorial in nature. Hyperglycemia exhibits a governing role in the pathogenesis of diabetic neuropathy. Diabetic neuropathy manifests as poly/mononeuropathy and/or autonomic neuropathy. Diabetic autonomic neuropathy can involve multiple systems including cardiovascular, gastrointestinal and genitourinary systems. One-third to half of the patients die within 10 years of

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developing overt symptoms of autonomic neuropathy mostly owing to cardiac arrest.^[3] In diabetes mellitus, the determinants of cardiac autonomic dysfunction were duration of diabetes, extent of glycemic control, age, and gender.^[4,5] Mostly, cardiac autonomic dysfunction in diabetes mellitus remains asymptomatic in the early stages of the disease; hence, identifying the diseases early may be crucial in the treatment and prevention of complications. The features of cardiac autonomic neuropathy include exercise intolerance, postural hypotension, resting tachycardia, fixed heart rate, and painless (or) silent myocardial infarction. Mortality associated with autonomic neuropathy after clinical diagnosis has been reported to be as high as 50% in 3 years, and its presence has been suggested to serve as a poor prognostic indicator. Electrocardiogram (ECG) records the electrical activity of the heart and can serve as a potential tool in diagnosis the abnormalities in electrical activity of the heart in patients with diabetes mellitus. Diagnosis of autonomic dysfunction in patients with diabetes mellitus early can serve vital in reducing the morbidity and mortality owing to autonomic dysfunction. It is important to study various ECG abnormalities in patients with diabetes mellitus that are possible owing to autonomic dysfunction. This study aims to study the various ECG abnormalities in type 2 diabetes mellitus patients when compared with control subjects.

MATERIALS AND METHODS

The study was conducted as a hospital-based cross-sectional study in a tertiary-care hospital in Puducherry, a union territory in south India. The study was conducted during January 2012 to August 2013 among 100 adult participants (50 in study group and 50 in control group) aged 20 years or more. Eligible participants were recruited from the outpatient department (OPD) based on the inclusion and exclusion criteria. Study group consisted of patients with diabetes mellitus and control group of patients without diabetes mellitus. For each participant in study group, age- and gender-matched eligible individual who visited next in the OPD was recruited as a control subject.

Inclusion Criteria

Individuals with diabetes for at least 2 years of duration were only included in the study group.

Exclusion Criteria

Elderly patients (aged > 60 years), who are already a known case of coronary artery disease/ischemic heart disease, a known case of valvular heart disease or congenital heart disease, known case of systemic hypertension, patients with uremia, patients with features of hypo- or hyperthyroidism, patients on any drug that alters the sinus node impulse generation and AV conduction, patients with fever and features suggestive of infections, patients with chronic obstructive pulmonary disease and other chronic lung disorders, patients with parkinsonism and other

movement disorders, and patients with dyselectrolytemia were excluded. For exclusion and selection of participants from patients attending OPD; patients were initially examined by the authors VPC and DS. Later, necessary investigations were carried using standard procedures. Autonomic dysfunction was assessed by the following maneuvers: parasympathetic function by tachycardia in resting ECG and heart rate response to deep breathing (HRBD); and sympathetic function by blood pressure response to standing and QTc prolongation.

Procedure

Resting ECG was taken twice at 15-min interval for all the participants in the study and control groups using a 12-leaded PHILIPS Page Writer Trim I Cardiograph, using standard procedures by the authors. The subjects were made to lie down quietly and asked to take deep breath and evenly at a rate of six breaths per minute, i.e., 5 s for inspiration and 5 s for expiration. A continuous ECG was recorded for 1 min. The maximum and minimum RR intervals during each breathing cycle were measured and converted into beats/minute. The result was then expressed as the mean of the difference between maximum and minimum heart rates for the six measured cycles in beats/minute; <10 beats variation is taken as abnormal. RR and QTc intervals were measured with a meter on the resting ECG tracing. The lead considered here is lead V2. The QT interval was measured from the beginning of QRS complex to the down slope of the T wave (crossing the isoelectric line). When a U wave was present, the QT interval was measured to the nadir of T wave and U wave. A QTc > 460 ms is considered abnormally prolonged.

Statistical Analysis

SPSS version 20.0 was used for statistical analysis; unpaired *t* test was used to test the statistical difference in comparison of means, and a *p* value of <0.05 was considered statistically significant. Informed written consent was obtained from all the study participants after explaining the benefits and implications of the study in the local language. Institute ethical committee certificate was obtained for conducting the study before the study was started.

RESULTS

Study participants in both study and control groups were equally distributed as matching was done at the time of recruitment. Majority of the participants in the study group revealed diabetes mellitus for a period of 2 to 10 years duration. Nearly, half of the study group participants showed diabetes mellitus for a duration of 2 to 5 years.

The study results showed that certain ECG changes such as resting heart rate, RR interval, PR interval, QRS axis, and QTc interval significantly varied between study and control groups. Mean resting heart rate was significantly high among the

study group (84.2 ± 12.86) when compared with control group (75.2 ± 10.65); similar higher values were observed in PR interval also. Mean RR interval of study group (725.4 ± 121.49) participants were significantly low when compared with control group (815.4 ± 114.4). QTc interval remained high among the study group while QRS axis was comparatively less among the study group. There was no statistically significant change observed in QRS duration between study and control groups (Table 1).

Although clinically significant number of patients in study group presented with ECG changes suggestive of ischemia or infarction, this difference was not found to be statistically significant. ECG evidence of ischemia was found in 26% of the

study group participants, while it was 12% in control group; similarly, ECG evidence of ischemia was present in 10% of study group participants when compared with 6% cases of control group participants, although this difference was not statistically significant. Abnormal HRBD was observed in 28% of participants in study group; it was only 10% in control group (Table 2). Among the patients who presented with ECG changes suggestive of ischemia or infarction, five (27.78%) were asymptomatic (not presented in table).

DISCUSSION

This study compared ECG changes among 50 participants with diabetes mellitus and 50 participants without diabetes mellitus, by using conventional ECG parameters. Ziegler et al.^[6] in a study reported cardiac autonomic diabetic neuropathy among 22.1% of the patients with type II diabetes mellitus. In our study, ECG changes were observed among 36% of the study group participants with type II diabetes mellitus. Kahn et al.^[7] found that patients with cardiac dysautonomia have higher resting heart rates and lower maximal heart rates during exercise than diabetic patients without autonomic neuropathy. Similar results were observed in our study also. The measurement of PR interval that reflects the AV conduction showed that mean PR interval was 162.4 ± 31.72 in diabetic patients as against 138.2 ± 16.986 in nondiabetic population, which was statistically significant. A similar difference was also observed by a study done by

Table 1: Distribution of ECG changes in study and control group (n = 100)

ECG parameters	Study group (n = 50), mean $\pm$ SD	Control Group (n = 50), mean $\pm$ SD	P*
Resting heart rate(bpm)	84.2 $\pm$ 12.86	75.2 $\pm$ 10.65	0.0001
RR interval (ms)	725.4 $\pm$ 121.49	815.4 $\pm$ 114.4	0.0002
PR interval (ms)	162.4 $\pm$ 11.67	138.2 $\pm$ 16.99	0.0001
QRS duration (ms)	68.4 $\pm$ 11.67	65 $\pm$ 8.69	0.1016
QRS axis (°)	26.4 $\pm$ 30.54	67.6 $\pm$ 27.82	0.0001
QTc interval (ms)	405.16 $\pm$ 40.38	365.38 $\pm$ 25.3	0.0001

*Fischer's exact test.

Table 2: Distribution of study participants based on various other ECG changes in study and control groups (n = 100)

Various abnormalities in ECG and cardiac reflexes	Study group, n (%)	Control group, n (%)	P*	Odds ratio (95 % CI)
ECG evidence of ischemia/infarction				
Present	18 (36)	9 (18)	0.07	2.56 (1.01-6.45)
Absent	32 (64)	41 (82)		
Evidence of ischemia				
Present	13 (26)	6 (12)	0.12	2.58 (0.89-7.45)
Absent	37 (74)	44 (88)		
Evidence of infarction				
Present	5 (10)	3 (6)	0.71	1.74 (0.39-7.71)
Absent	45 (90)	47 (94)		
Intraventricular conduction blocks				
Present	4 (8)	1 (2)	0.36	4.26 (0.46-39.55)
Absent	46 (92)	49 (98)		
HRBD ^a				
Abnormal	14 (28)	5 (10)	0.03	3.5 (1.15-10.63)
Normal	36 (72)	45 (90)		
Postural drop of SBP ^b				
Present	3 (6)	0 (0)	0.24	NA
Absent	47 (94)	50 (100)		

^aHeart rate response to deep breathing.

^bPostural fall of > 30 mm Hg was considered significant.

*Fischer's exact test.

Mustonen et al.^[8] in their 4-year follow-up in middle-aged diabetic and nondiabetic subjects. Prolonged QTc interval was significantly higher in the diabetic group in comparison with the nondiabetic group, 8% and 2%, respectively. The QTc interval in diabetic patients (405.16 ± 40.375) was significantly ($p < 0.05$) prolonged when compared with that of nondiabetic patients (365.38 ± 25.3) in our study also. Similar results were also seen in yet another study by Mathur and Gupta.^[9] It is well established in various studies^[10,11] of the past regarding the cardiovascular complications of diabetes mellitus leading to ischemic heart disease. In our study, silent ischemic heart disease was observed in 27.78% of the patients with diabetes mellitus when compared with 22% in a study done by Negrusz-Kawecka et al.^[11] This was important as sudden unexpected deaths are reported to occur in patients with cardiac autonomic neuropathy, and this was attributed to asymptomatic ischemic heart disease.^[12] The HRBD is abnormal in diabetic patients, indicating parasympathetic damage. It was positive in 28% of diabetic patients in our study. A similar proportion of abnormal HRBD among diabetic patients was observed in a study by Domuschiev.^[13] Overall, cardiac autonomic dysfunction was found to occur more frequently in patients with diabetes when compared with nondiabetic individuals. The strengths of this study include that standard procedures and investigations were followed in selecting the patients as controls and subjects carefully. Interobserver and instrumental bias was minimized as the procedures were carried out by one investigator using one instrument throughout. Possible limitation of this study could be that no temporal association between duration of diabetes mellitus and cardiac autonomic neuropathy could be established. Additional large-scale studies may be required to establish the possible pathogenesis behind the occurrence of cardiac autonomic dysfunction and feasibility of using various cardiovascular reflexes as a screening procedure.

CONCLUSION

ECG changes suggestive of subclinical or clinical autonomic cardiac neuropathy occur more frequently in patients with diabetes mellitus when compared with nondiabetic control subjects. Evaluation of various cardiovascular reflexes and ECG in type 2 diabetic patients may serve as feasible technique to determine the presence of cardiac dysautonomia.

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