## Original Research Article

# A study of cardiac changes in asymptomatic diabetic patients in comparison with normal population

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**ABSTRACT**

**Background:** India is predicted to bear the greatest Coronary artery disease (CAD) burden, according to the estimates from the global burden of disease study. Majority of the time the patient of diabetes presents with complications like Myocardial infarction (MI), heart failure, being end stages of cardiovascular disease associated with other macro and micro-vascular complications.

**Methods:** This study was done in view of screening the asymptomatic diabetic individuals presenting to our hospital for any evidence of early cardio-vascular manifestations. With the aid of non-invasive testing such as electrocardiography (ECG) and 2D echo the early changes were noted and compared with the normal population and the cardiac status thus evaluated. A total of 106 patients (53 were diabetic and 53 non-diabetic controls) were included in the study in order to compare the ECG and 2D echo findings among the population. The main aim of the present study was to observe the ECG manifestations in diabetic patients without overt symptoms of any cardiac disease and to evaluate the ECG changes along with 2D echocardiogram in asymptomatic diabetic patients and compare with normal population.

**Results:** From the study, it was observed that majority among the diabetic population were found to have statistically significant changes in the ECG like PR interval prolongation, T wave inversions and QT interval prolongation. 2D ECHO studied showed the presence of Left ventricular diastolic dysfunction and Regional wall motion abnormalities to be evident among the diabetic population.

**Conclusions:** It was concluded from the study that diabetic patients have a higher risk of cardiovascular morbidities compared to the general population and ECG changes are observed even when they are clinically asymptomatic. This observation has been confirmed by the 2D echo findings. It is essential to screen diabetic patients at an early stage to prevent cardiovascular complications. ECG being a relatively cheap and non-invasive investigation should be utilized to screen diabetics for the same.

**Keywords:** Diabetes Mellitus, ECG changes, Cardiac Manifestations

## INTRODUCTION

The importance of diabetes mellitus, both type 1 and type 2, in the epidemiology of cardiovascular diseases cannot be overemphasized. About one third of acute myocardial infarction patients have diabetes mellitus, the prevalence of which is steadily increasing. In the 1960s, there were 2 million Americans with diabetes mellitus; in the year 2000, their number was 15 million.[1] Statistics have shown that the decrease in cardiac mortality in persons with diabetes mellitus is lagging behind that of the general population. India is predicted to bear the greatest Coronary artery disease (CAD) burden, according to the estimates from the global burden of disease study.[2]

Majority of the time the patient of diabetes presents with complications like MI, heart failure, being end stages of cardiovascular disease associated with other macro and micro vascular complications.[3] If patients are screened at an early stage of diabetes before the onset of symptoms the cardiovascular complications can be delayed and mortality can be reduced.[4] Fibrotic changes, especially in the basal area of the left ventricle, have frequently been observed in diabetic patients, even when cardiac involvement is clinically not yet evident. Even in healthy individuals, hyperinsulinemia- induced hypoglycemia can prolong the QTc interval and decrease T-wave area and amplitude.[5] In the Europe and diabetes (Eurodiab) study on diabetic individuals with a normal QTc at baseline, female sex and higher values of hemoglobin A1C and systolic blood pressure were associated with increased risk of prolonged QTc, whereas physical activity and normal body mass index were protective factors.[6] Correlation was found between the QT duration and the amount of coronary calcium; this association was driven by the QRS and not by QT interval duration.[7] here are only few studies in India done to screen asymptomatic diabetic individuals for cardiovascular complications. This study is done in view of screening the asymptomatic diabetic individuals presenting to our hospital for any evidence of early cardio-vascular manifestations. With the aid of non-invasive testing such as ECG and 2D echo the early changes were noted and compared with the normal population and the cardiac status thus evaluated.

## METHODS

A cross sectional comparative study was conducted on patients attending the outpatient department (OPD) and inpatients admitted in Yenepoya Medical College Hospital, Mangalore, Karnataka, India.

The study was conducted on 50 hypertensive cases and 50 controls. Informed written consent was obtained from cases and controls for participation in the study and for conduction of investigations. The study was conducted between the period of January 2016 and January 2017.

Patients included in the study are those who were detected to be diabetic by ADA guidelines. Controls included are non-diabetic patients. Along with the routine blood investigations Canadian broadcasting corporation (CBC), royal bank of Scotland (RBS), renal function test (RFT), liver function test (LFT), serum electrolytes, HBA1C, FLP, TFT) a resting 12 lead ECG and 2D echo was also done.

The ECG parameters studied include (P-wave, QRS complex, PR interval, T wave, U wave, ST segment, QT interval, QTc, R-R interval, rhythm). The sample size was using independent group t-test, equal sample size was taken. Level of significance5%, power of 80 %, effect size of 0.55. The sample size calculated was 53 cases and 53 controls.

### Inclusion criteria

- The patients of 18 years of age and above of either sex who are willing to participate in the study.
- Patients who have been diagnosed with diabetes by ADA guidelines.

### Exclusion criteria

- The patients previously diagnosed to have other co-morbidities such as systemic hypertension or any coronary artery disease, valvular heart disease, heart failure or thyroid disorders.
- Patients with chronic illness such as chronic liver disease, chronic obstructive pulmonary disease, chronic kidney disease and malignancy.

### Biosafety issues

- Not applicable

### Statistical analysis

Continuous variables are expressed in terms of mean and standard deviation and categorical variables presented in frequency and percentages. Independent t-test is used to compare all the continuous variables between the groups. chi square test is used to find whether there is any association between two categorical variables.

A p-value <0.05 is considered significant. Data visualization is done using appropriate charts. All the analysis is done using SPSS version 22 software and Microsoft excel.

This study was conducted after ethical clearance from the Ethical committee of the university as per standard protocols and guidelines.

## RESULTS

Baseline characteristics including demographics and blood investigations of the cases and controls have been tabulated in Table 1 and 2 shows baseline characteristics of ECG findings noted in cases and controls.

Independent t-test was used to compare the P-wave duration between the two groups. Authors did not observe a significant difference between the P-wave duration of diabetic group (M=79.25, SD=10.349) and the control group (M=80.00, SD= 0.000) as the p value was 0.597 with a mean difference of 0.755.

PR interval between the two groups showed significant difference between the groups with a p value <0.05 (p <0.001). PR interval prolongation was observed in the diabetic group (M=147.92, SD=27.829) compared to the control group (M=120.75, SD=5.494) with a mean difference of -27.170.

**Table 1: Baseline characteristics comparison of controls and diabetics.**

| | GRP | | | | P-value |
|---|---|---|---|---|---|
| | CTRL | | T2DM | | |
| | Mean | SD | Mean | SD | |
| Age | 44.830 | 11.5704 | 53.698 | 11.3096 | <0.001 |
| **Gender** | | | | | |
| Male (N (%)) | 32 (60.4%) | | 29 (54.7%) | | |
| Female | 21 (39.6%) | | 24 (45.3%) | | |
| Pulse rate | 81.000 | 6.4241 | 81.340 | 12.5375 | 0.861 |
| Haemoglobin | 13.975 | 1.6054 | 11.757 | 2.2685 | <0.001 |
| FBS | 104.792 | 14.6240 | 212.302 | 94.7394 | <0.001 |
| PPBS | 115.491 | 17.9268 | 253.321 | 98.8038 | <0.001 |
| HBA1C | 5.409 | .4716 | 9.943 | 2.2700 | <0.001 |
| T. cholesterol | 198.23 | 50.521 | 173.25 | 51.092 | 0.013 |
| Triglycerides | 124.26 | 36.267 | 182.68 | 78.671 | <0.001 |
| HDL | 44.40 | 10.899 | 33.94 | 12.688 | <0.001 |
| LDL | 148.32 | 78.277 | 91.64 | 41.170 | <0.001 |
| VLDL | 29.66 | 13.489 | 37.87 | 19.539 | 0.013 |
| TSH | 1.7687 | .99733 | 2.0155 | 1.02132 | 0.211 |

**Table 2: ECG characteristics comparison of controls and diabetics.**

| | GRP | | | | P-value |
|---|---|---|---|---|---|
| | CTRL | | T2DM | | |
| | Mean | SD | Mean | SD | |
| P wave | 80.00 | 0.000 | 79.25 | 10.349 | 0.597 |
| PR interval | 120.75 | 5.494 | 147.92 | 27.829 | <0.001 |
| QRS complex | 80.75 | 6.751 | 79.25 | 10.349 | 0.376 |
| T wave | 131.70 | 17.291 | 154.72 | 32.380 | <0.001 |
| QTc interval | 409.70 | 35.837 | 449.11 | 48.100 | <0.001 |
| RR interval | 82.75 | 10.446 | 85.45 | 16.086 | 0.308 |
| ST segment* | | | | | |
| Normal | 53 (100%) | | 43 (81.1%) | | <0.001 |
| Depression | 0 (0%) | | 10 (18.9%) | | |

QRS complex duration did not show a significant difference between the groups with a p-value of 0.376. QRS complex duration was more in the control group (M=80.75, SD=6.751) compared to the diabetic group (M=79.25, SD=10.349) with a mean difference of 1.509. T-wave duration authors observed a significant difference between the groups with a p value <0.001.

T wave duration was more in the diabetic group (M=154.72, SD=32.380) compared to control group (M=131.70, SD=17.291) with a mean difference of-23.019.

There was a significant association pertaining to the ST segment between the two groups with a p-value <0.001. Among the diabetic population of 53 patients, 10 patients (18.9%) had ST segment depression compared to none among the controls (all the control subjects had a normal ST segment). Chi-square test was performed on ST segment variable. QTc interval between the two groups. Authors observed a significance difference between the groups with a p value <0.001 QTc interval prolongation was observed in the diabetic group (M=449.11, SD=48.100) compared to the control group (M=409.70, SD=35.837) with a mean difference of -39.415.

RR interval did not observe a significant difference between the groups with a p-value of 0.308. RR interval duration was more in the control group (M=82.75, SD=10.446) compared to the diabetic group (M=85.45, SD=16.086) with a mean difference of -2.698.

There was significant association pertaining to the axis between the two groups with a p-value <0.001. Among the diabetic population of 53 patients, 10 patients (18.9%) had left axis deviation, 4 patients (7.5%) had right axis deviation and 39 patients (73.6%) had a normal axis. Among the controls, all the 53 subjects had a normal axis.

The presence of LVH between the two groups. From chi-square test, authors can say that there is significant association pertaining to the presence of LVH between the two groups with a p-value 0.012. Among the diabetic population of 53 patients, 6 patients (11.3%) had LVH while 47 patients (88.7%) had no evidence of LVH. Among the controls, none of the subjects had any evidence of LVH. Ejection fraction authors observed a significant difference between the groups with a p-value of 0.019. Ejection fraction was better in the control group (M=60.00, SD=0.000) compared to the diabetic group (M=57.64, SD=7.179) with a mean difference of 2.358. Left ventricular diastolic dysfunction in 2D echo between the two groups. From chi-square test, authors can say that there is significant association pertaining to the presence of LVDD between the two groups with a p-value <0.001. Among the diabetic population of 53 patients, 35 patients (66%) had evidence of LVDD while 18 patients (34%) had no evidence of LVDD. Among the controls, none of the subjects had any evidence of LVDD.

## DISCUSSION

The Eurodiab study also showed, a correlation between dyslipidemia (low HDL levels) and QTc prolongation risk and higher mortality risk.[6] Authors did not observe a significant difference between the P-wave duration of diabetic group (M=79.25, SD=10.349) and the control group (M=80.00, SD=0.000) as the p value was 0.597 with a mean difference of 0.755. But regarding the PR interval authors observed a significant difference between the groups with a p value=2mm and a PCA ratio of the T-wave vector >32% in women and >25% in men to be independent predictors of mortality. The most important observation from present study was prolongation of QTc interval. Authors observed a significance difference between the groups with a p value 460msec to be associated with a 2-fold increased cardiovascular and all-cause mortality risk in a 5-year prospective population study in individuals with Type 2 diabetes. Another study done by Nelson MR et al, showed significant correlation between coronary artery calcium measured by coronary artery calcified plaque and QT interval duration.[7] A study done by Zdarska D et al, in 22 type 1 diabetes patients with a mean age of 30 years showed that decreased QRS <120 m sec, QTc ≥450 m sec and increased QT dispersion >70 ms was associated with decreased parasympathetic to sympathetic tone ratio, tachycardia and shortening of the activation time.[8] A study done by Guinti S et al, in 1415 type 1 diabetic patients showed QTc >440 msec to be associated with a progression of cardiovascular disease over a period of 7 years.[9] It was also noticed that among a study population of 3250 type 1 diabetic patients, QTc >440 m sec and QT dispersion was associated with a 3 fold increased risk of left ventricular hypertrophy. In a recent study, MONICA/KORA Augsburg cohort study, during a 9-year follow up period it was observed that reduced heart rate variability and prolonged QTc interval (>440 ms) were independent predictors of a 2-fold and 3-fold increased risk of

mortality, respectively, in the general population (aged 55 up to 74 years) with or without diabetes.[10] In another control study of 682 people with coronary heart disease and diabetes but no history of sudden cardiac death, prolongation of QTc interval was a significant predictor of sudden cardiac death even among individuals with a normal or borderline QTc interval. However, idiopathic abnormal QTc interval prolongation was associated with a higher (5-fold) increased risk of sudden cardiac death.[11] From present study authors observed a significant association pertaining to the axis between the two groups with a p-value 53 patients, 6 patients (11.3%) had LVH while 47 patients (88.7%) had no evidence of LVH. Among the controls, none of the subjects had any evidence of LVH. The presence of LVH was confirmed on 2D Echocardiogram. This finding was in accordance with multiple studies which showed the same. A study done by Marcos GMA et al, in 110 type 2 diabetic patients in the category of 20-80 years had the presence of left ventricular hypertrophy evidenced by the ECG manifestations of increased Cornell voltage and increased QRS duration.[12] A study done by Wiik BP et al, among 9193 diabetic patients showed presence of left ventricular hypertrophy as evidenced by increased Cornell Voltage and Sokolow Lyon voltage product.[13] A study done by Barrios V et al, among 276 diabetic patients showed left ventricular strain pattern as an early manifestation in patients with diabetes.[14] Another study done by Okin PM et al, in 886 diabetic patients also showed the presence of left ventricular strain pattern as an early manifestation of diabetic heart disease.[15] Authors compared the ejection fraction between the two groups and observed a significant difference between the groups with a p-value of 0.019. The ejection fraction was better in the control group (M=60.00, SD=0.000) compared to the diabetic group (M=57.64, SD=7.179) with a mean difference of 2.358. Another observation was the presence of left ventricular diastolic dysfunction in 2D Echo between the two groups. From chi-square test, authors concluded that there was significant association pertaining to the presence of LVDD between the two groups with a p-value <0.001 Among the diabetic population of 53 patients, 35 patients (66%) had evidence of (left ventricular diastolic dysfunction) LVDD while 18 patients (34%) had evidence of LVDD. Among the controls, none of the subjects had any evidence of LVDD.

## CONCLUSION

Present study showed significant changes in the ECG and 2D Echocardiogram of diabetic subjects in comparison to the normal population. There are not many similar studies done in India which observe the early ECG manifestations among diabetic subjects. It was concluded from the study that diabetic patients have a higher risk of cardiovascular morbidities compared to the general population and ECG changes are observed even when they are clinically asymptomatic. This observation has been confirmed by the 2D ECHO findings. It is essential

to screen diabetic patients at an early stage to prevent cardiovascular complications. ECG being a non-invasive test should be utilized in early detection of cardiac changes among diabetics, thereby reducing cardiovascular morbidity and mortality.

## REFERENCES

1. Lackland DT, Roccella EJ, Deutsch AF, Fornage M, George MG, Howard G, et al. Factors influencing the decline in stroke mortality: a statement from the American heart association/American stroke association. Stroke. 2014;45(1):315-3.
2. Labarthe DR. Epidemiology and prevention of cardiovascular diseases: a global challenge. Jones & Bartlett Publishers; 2010:25.
3. Stratton IM, Adler AI, Neil HA, Matthews DR, Manley SE, Cull CA, H et al. Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): prospective observational study. BMJ. 2000;321(7258):405-12.
4. Young LH, Frans JT, Chyun DA, Davey JA, Barrett EJ, Taillefer R, et al. Cardiac outcomes after screening for asymptomatic coronary artery disease in patients with type 2 diabetes: the DIAD study: a randomized controlled trial. JAMA. 2009;301(15):1547-55.
5. Laitinen T, Lyyra-Laitinen T, Huopio H, Vauhkonen I, Halonen T, Hartikainen J, et al. Electrocardiographic alterations during hyperinsulinemic hypoglycemia in healthy subjects. Ann Noninvasive Electrocardiol. 2008;13(2):97-105.
6. Giunti S, Bruno G, Lillaz E, Gruden G, Lolli V, Chaturvedi N, et al. Incidence and risk factors of prolonged QTc interval in type 1 diabetes: the Eurodiab prospective complications study. Diab Care. 2007;30(8):2057-63.
7. Nelson MR, Daniel KR, Carr JJ, Freedman BI, Prineas RJ, Bowden DW et al. Associations between electrocardiographic interval durations and coronary artery calcium scores: the diabetes heart Study. Pacing Clin Electrophysiol. 2008;31:314-21.
8. Žďárská D, Pelíšková P, Charvát J, Slavíček J, Mlček M, Medová E, et al. ECG body surface mapping (BSM) in type 1 diabetic patients. Physiol Res. 2007;56:403-10.
9. Giunti S, Bruno G, Lillaz E, Gruden G, Lolli V, Chaturvedi N, et al. Incidence and risk factors of prolonged QTc interval in type 1 diabetes: the Eurodiab prospective complications study. Diab Care. 2007;30(8):2057-63.
10. Ziegler D, Zentai CP, Perz S, Rathmann W, Haastert B, Döring A, et al. Prediction of mortality using measures of cardiac autonomic dysfunction in the diabetic and nondiabetic population: the MONICA/KORA Augsburg Cohort Study. Diab Care. 2008;31(3):556-61.
11. Chugh SS, Reinier K, Singh T, Uy-Evanado A, Socoteanu C, Peters D, et al. Determinants of prolonged QT interval and their contribution to sudden death risk in coronary artery disease: the oregon sudden unexpected death study. Circulat. 2009;119(5):663-70.
12. Gómez-Marcos MA, Recio-Rodríguez JI, Rodríguez-Sánchez E, Castaño-Sánchez Y, de Cabo-Laso A, Sánchez-Salgado B, et al. Central blood pressure and pulse wave velocity: relationship to target organ damage and cardiovascular morbidity-mortality in diabetic patients or metabolic syndrome. An observational prospective study. Lod-diabetes study protocol. BMC Pub Heal. 2010;10(1):143.
13. Wiik BP, Larstorp AC, Høieggen A, Kjeldsen SE, Olsen MH, Ibsen H, et al. Serum uric acid is associated with new-onset diabetes in hypertensive patients with left ventricular hypertrophy: The life study. Am J Hypertension. 2010;23(8):845-1.
14. Barrios V, Escobar C, Calderón A, Echarri R, Barrios S, Navarro-Cid J. Electrocardiographic left ventricular hypertrophy regression induced by an angiotensin receptor blocker-based regimen in hypertensive patients with diabetes: data from the SARA study. J Renin-Angioten-Aldoster Syst. 2009;10(3):168-73.
15. Okin PM, Devereux RB, Nieminen MS, Jern S, Oikarinen L, Viitasalo M, et al. Life study investigators. Relationship of the electrocardiographic strain pattern to left ventricular structure and function in hypertensive patients: The Life study. J Am Coll Cardiol. 2001;38(2):514-20.