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QTc Interval, "A Harbinger of Fatal Cardiac Events"

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Abstract: ***Diabetes Mellitus is a common metabolic disorder. It is associated with pathophysiologic changes in multiple organ systems. Of primary concern is the cardiovascular disorders associated with diabetes mellitus. Even early in the course of diabetes, ECG alterations in the rhythm starting from simple sinus tachycardia and moving on to different ECG parameters like the prolongation of the classical QTc interval, or the QT dispersion, ST-segment and T-wave changes, alterations in heart rate variability, and presence of left ventricular hypertrophy, may be observed.The study was conducted on patients attending the outpatient department (OPD) and inpatients admitted in Yenepoya medical college Hospital. The study was conducted on 50 cases and 50 controls. Informed written consent was obtained from cases and controls for participation in the study and for conduct of investigations.A total of 106 subjects participated in the study, of which 53 were diabetic patients and remaining 53 non-diabetics.We did not observe a statistically significant pertaining to pulse rate among our two groups.Independent t-test was used to compare the QTc INTERVAL between the two groups. We observed a significant 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.An important observation among our diabetic subjects was prolongation of the QTc interval. There are not many similar studies done in India which observe the early ECG manifestations among diabetic subjects. ECG being a non-invasive test should be utilized in early detection of cardiac changes among diabetics, thereby reducing cardiovascular morbidity and mortality.***

Keywords:

1. Introduction

Diabetes mellitus (DM) refers to a group of common metabolic disorders that share the phenotype of hyperglycemia. Several distinct types of DM are caused by a complex interaction of genetics and environmental factors. Depending on the etiology of the DM, factors contributing to hyperglycemia include reduced insulin secretion, decreased glucose utilization, and increased glucose production. The metabolic dysregulation associated with DM causes secondary pathophysiologic changes in multiple organ systems that impose a tremendous burden on the individual with diabetes and on the health care system. In the United States, DM is the leading cause of end-stage renal disease (ESRD), nontraumatic lower extremity amputations, and adult blindness. It also predisposes to cardiovascular diseases. With an increasing incidence worldwide, DM will be a leading cause of morbidity and mortality for the foreseeable future[1].

Diabetes can be classified into the following general categories:

1) Type 1 diabetes (due to autoimmune b-cell destruction, usually leading to absolute insulin deficiency).
2) Type 2 diabetes (due to a progressive loss of b-cell insulin secretion frequently on the background of insulin resistance).
3) Gestational diabetes mellitus (GDM) (diabetes diagnosed in the second or third trimester of pregnancy that was not clearly overt diabetes prior to gestation).
4) Specific types of diabetes due to other causes, e.g., monogenic diabetes syndromes (such as neonatal diabetes and maturity-onset diabetes of the young [MODY]), diseases of the exocrine pancreas (such as cystic fibrosis), and drug- or chemical-induced diabetes (such as with glucocorticoid use, in the treatment of HIV/AIDS, or after organ transplantation.[2]

India is predicted to bear the greatest CAD burden, according to the estimates from the Global Burden of Disease Study. Out of the 9 million deaths due to CAD in 1990 in developing countries, 2.4 million (25%) occurred in India. In the same year, mortality rates in India due to acute myocardial infarction (MI) were 141 per 100,000 in males and 136 per 100,000 in females, which was much higher than in China (66 per 100,000 in males and 69 per 100,000 in females) and Latin American countries (81 per 100,000 in males and 76 per 100,000 in females). A matter of serious concern is that 52% of the CAD deaths in India occurred in people aged below 70 years, while the same was just 22% in developed countries.[3,4,5] 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 microvascular complications.[6] 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.[7]

Even early in the course of diabetes, ECG alterations in the rhythm starting from simple sinus tachycardia and moving on to different ECG parameters like the prolongation of the classical QTc interval, or the QT dispersion, ST-segment and T-wave changes, alterations in heart rate variability, and presence of left ventricular hypertrophy, may be observed.

ECG variations help diagnose cardiac autonomic neuropathy and detect signs of silent myocardial ischemia even in clinically asymptomatic patients with diabetes.

QTc Interval

QTC interval measures the duration of electrical activation and recovery of the ventricular myocardium and varies inversely with the cardiac rate. It is measured from the beginning of QRS complex to the end of T wave. It is rate dependent and must be corrected for heart rate (QTC). QTC interval is determined using modified Bazett's formula by Hodges and coworkers.

It corrects more completely for high and low rates.[8]
QTC = QT + 0.00175 (Heart rate – 60).

The upper limit of the duration of QTC interval is approximately 0.46 seconds (460 m sec).

2. Methodology

The study was conducted on patients attending the outpatient department (OPD) and inpatients admitted in Yenepoya medical college Hospital. The study was conducted on 50 cases and 50 controls. Informed written consent was obtained from cases and controls for participation in the study and for conduct 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, 18 years of age or older of either gender excluding pregnant women. Controls included are non-diabetic patients. Along with the routine blood investigationsa resting 12 lead ECG (12 channel ECG machine by BPL) was also done and parameters evaluated.

3. Results

A total of 106 subjects participated in the study, of which 53 were diabetic patients and remaining 53 non-diabetics.The mean age among the diabetic subjects were 53.69 years, while among the control subjects it was 44.83 years.Among the diabetics, 29 (54.7%)were males and 24 (45.3%) were females. In the control group 32 (60.4%) were males and 21 (39.6%) were females.

We did not observe a statistically significant pertaining to pulse rate among our two groups.

Independent t-test was used to compare the QTc INTERVAL between the two groups. We observed a significant 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.

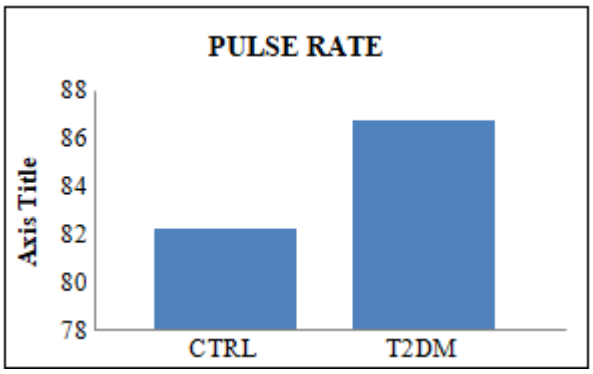

Figure 1: Pulse rate in controls and subjects

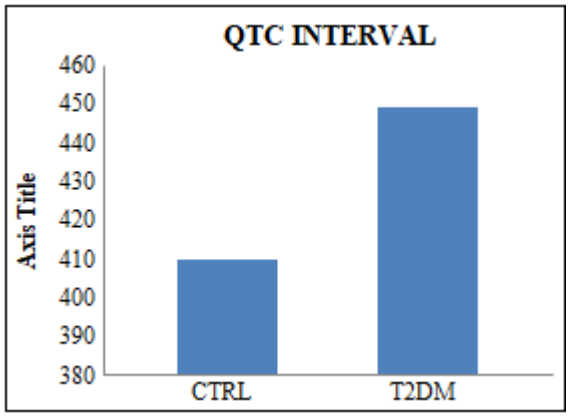

Figure 2: QTc interval in controls and subjects

Table 1: Group Statistics

	Grp				*t (df)-statistic*	*p*-value
	CTRL		T2DM			
	Mean	Std. Deviation	Mean	Std. Deviation		
Pulse Rate	82.23	10.192	86.74	17.247	-1.639	.104
QT Interval	352.08	15.733	375.89	26.831	-5.573	<0.001
QTc Interval	409.70	35.837	449.11	48.100	-4.784	<0.001

Table 2: Independent Samples Test

	t-test for Equality of Means						
						95% Confidence Interval of the Difference	
	t	df	p-value	Mean Difference	Std. Error Difference	Lower	Upper
Pulse Rate	-1.639	104	.104	-4.509	2.752	-9.966	.947
QT Interval	-5.573	104	.000	-23.811	4.272	-32.284	-15.339
QTc Interval	-4.784	104	.000	-39.415	8.239	-55.754	-23.076

4. Discussion

Diabetes mellitus (Type 1 and Type 2) is a disease which has a potential for a wide variety of systemic manifestations. It has an important contributory role in the epidemiology of cardiovascular diseases. About one-third of acute myocardial infarction patients have diabetes and the prevalence of this co-morbidity is steadily increasing.[9]

Even early in the course of diabetes mellitus, ECG alterations such as sinus tachycardia, long QTc, QT dispersion, changes in heart rate variability, ST-T changes, and left ventricular hypertrophy may be observed. ECG alterations help evaluate cardiac autonomic neuropathy and detect signs of myocardial ischemia even in asymptomatic patients.

The most important observation from our study was prolongation of QTc INTERVAL.We observed a significant 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. This was in accordance with multiple studies which showed significant correlation between QT prolongation and cardiovascular mortality risk.

A study done by Okin et al[10] showed QTc>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 et al[11]showed significant correlation between coronary artery calcium measured by coronary artery calcified plaque and QT interval duration.

A study done by Zdarska et al[12] in 22 Type 1 diabetes patients with a mean age of 30 years showed that decreased QRS < 120msec, QTc ≥450msec and increased QT dispersion >70ms was associated with decreased parasympathetic to sympathetic tone ratio, tachycardia and shortening of the activation time.

A study done by Guinti et al[13] in 1415 Type 1 diabetic patients showed QTc>440msec to be associated with a progression of cardiovascular disease over a period of 7 years. It was also noticed that among a study population of 3250 Type 1 diabetic patients, QTc>440 msec and QT dispersion was associated with a 3 fold increased risk of left ventricular hypertrophy.

This study was conducted to observe the ECG manifestations in diabetic patients without any overt symptoms of cardiac disease and to evaluate the ECG changes and compare it with the normal population, thereby assisting in the early detection of cardiovascular changes so as to initiate appropriate intervention with the aim to reduce the complications.

There are multiple studies which show associations between diabetes and early cardiovascular manifestations in the form of ECG changes, and ECG being an easily accessible, relatively cheap and non-invasive modality of testing can be readily used. From our studies we could observe multiple ECG changes among the diabetics which could probably assist in early detection of diabetic cardiomyopathy.

5. Conclusion

An important observation among our diabetic subjects was prolongation of the QTc interval. This observation is supported by ample evidence from multiple trials which quote QTc interval as an important predictor of cardiac and cerebrovascular mortality as well as being an important prognosticator in diabetic heart disease.There are not many similar studies done in India which observe the early ECG manifestations among diabetic subjects. ECG being a non-invasive test should be utilized in early detection of cardiac changes among diabetics, thereby reducing cardiovascular morbidity and mortality. To confirm the same large scale observational studies are the need of the hour

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