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RESEARCH ARTICLE

TO FIND ASSOCIATION BETWEEN QTc INTERVAL AND MICROALBUMINURIA IN TYPE-2 DIABETIC PATIENTS

Deep HS, Kumar V, Mahajan D. S, Babbar N.

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Corresponding Author

Deep HS

Abstract

Introduction - Diabetic nephropathy is a leading cause of diabetes related morbidity and mortality. Microalbuminuria is a strong predictor of glomerular injury and premature cardiovascular death in diabetic nephropathy. Diabetic cardiac autonomic neuropathy is a serious and common complication of diabetes. QTc prolongation is a predictor of cardiac autonomic neuropathy.

Aim - The present study was done to find the association between QTc interval and microalbuminuria in type-2 diabetes mellitus.

Material and method - 100 patients of Type-2 diabetes mellitus without nephropathy (group A-50 patients) and with nephropathy (group B-50 patients) were included in this study. All these patients were tested for microalbuminuria by nycocard U-albumin test and QTc interval prolongation in ECG. Study was statistically analysed by student-t test .

Result - The mean microalbuminuria and QTc showed positive relationship in patient of type-2 diabetes mellitus with microalbuminuria.

Conclusion - QTc interval serve as marker of increased cardiovascular mortality and morbidity in Type-2 diabetes mellitus patientswith and without nephropathy and its severity predicted from increasing QTc interval.

INTRODUCTION

Diabetes mellitus is one of the most common chronic diseases in the world affecting about 6.4% of the world population.[1] It comprises a group of common metabolic disorders that share phenotype of hyperglycemia. Many distinct types of diabetes mellitus exist which are caused by complex interactions of genetic, environmental factors and life style. The metabolic dysregulation associated with DM causes secondary pathophysiological changes in multiple organ systems. The vascular complications of DM are retinopathy, neuropathy, nephropathy (microvascular) and coronary heart disease, peripheral arterial disease, cerebrovascular disease (macrovascular).[2]

Diabetic nephropathy is one of the major complication of type 2 diabetes mellitus.[3] The classical definition of diabetic nephropathy is a progressive rise in urine albumin excretion, coupled with increasing blood pressure leading to declining glomerular filtration and eventually end stage kidney disease. These patients generally have diabetic retinopathy also.[4] The pathogenesis of diabetic nephropathy is related to chronic hyperglycemia, the mechanisms though incompletely defined, involve the effects of soluble factors, hemodynamic alterations in the renal microcirculation and structural changes in the glomerulus.[2]

Albuminuria, (independent of cardiovascular risk factors) is an important predictor of cardiovascular morbidity and mortality in patients with NIDDM.[5,6]

Autonomic neuropathy is one of the complications in diabetic patients, which may also involve cardiovascular system. Autonomic neuropathy cause an imbalance between right and left sympathetic innervation and a marker of electrical instability possibly leading to life threatening ventricular arrhythmias.[7]

ECG is the primary tool in arrhythmia analysis.[8] In the normal 12 lead ECG, QT interval is the measure of time between the beginning of Q wave and end of T wave.[9] The QT interval is the most used parameter in the electrocardiographic assessment of repolarization and its prolongation which is associated with increased risk of

arrhythmogenesis.[10] QT interval represents the electrical depolarization and repolarization of right and left ventricles.[9] The QT interval is dependent on the heart rate. Faster the heart rate, shorter the QT interval. QT interval can be adjusted according to the heart rate by Bazett's Formula which is used for calculating the heart rate-Corrected QT interval (QTc).

$$QTc = \frac{QT}{\sqrt{RR}}$$

(Here QT measured in milliseconds)

RR is the interval from one QRS complex to the next. (measured in seconds).(9)

The normal range of QTc is 0.35 sec to 0.43 sec.

Prolonged QT interval on ECG is indicative of an imbalance between right and left sympathetic innervation and is thought to increase the risk of arrhythmias.[11] QT prolongation or QT dispersion have shown to be independent predictor of mortality (total and cardiac mortality).[12]

Studies have shown that prolonged QTc is taken as a direct evidence and stands favourable to standard autonomic function tests in cardiac autonomic neuropathy.[13,14]

QT prolongatoion and microalbuminuriaare common determinant in Type-2 diabetes mellitus also. So patients of Type-2 diabetes mellitus with microalbuminuria showing QT prolongation may contribute to increased mortality.[12]

MATERIAL AND METHODS

In this study 100 individual with type-2 diabetes mellitus admitted in medical ward of Sri Guru Ram Das Institute of Medical Science and Research, Amritsar included.These patients were divided into two groups.

Group A - Diabetes mellitus Type-2 with Normoalbuminuria(50 patients)

Group B - Diabetes mellitus Type-2 with Microalbuminuria (50 patients)

Microalbuminuria was measured by Nycocard U-Albumin test. Informed consent was taken from every patient. All the patients were subjected to routine biochemistery test. Patients of ischemic heart disease, cerebrovascular accidents, organophosphoruspoisioning, psychotropic drugs overdosage and antiarrhythmic drugs which are known to prolong QT interval was excluded from the study.

Normoalbuminuria-defined as urine albumin concentration < 20mg/L.

Microalbuminuria-defined as urine albumin concentration20-200mg/L.[24]

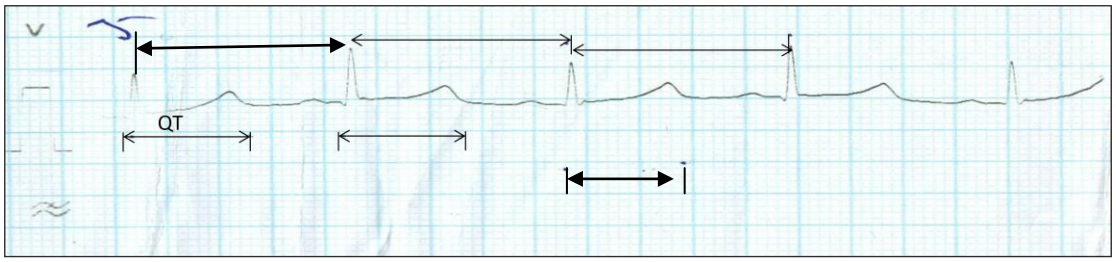
Microalbuminuria is present when the urine albumin excretion is persistently elevated to 30-300mg/24 hours, giving a urine albumin concentration of 20-200 mg/L with a normal urine volume by Nycocard U-Albumin test.

ELECTROCARDIOGRAPHY

A standard 12 lead E.C.G. was recorded at a speed of 25 mm/s. QT interval measured from onset of QRS complex to end of T wave. Where U waves were present QT Interval was measured to Nadir of curve between T and U wave. Three consecutive cycles were measured wherever possible in each of standard 12 leads and their mean was taken. If end of T wave were not reliably determined or when T waves were isoelectric or very low amplitude these leads were excluded from analysis. QTc interval was calculated by using Bazett's Formula.

Result

In the present study, The mean QTc was 376.3 $\pm$ 19.9 in group A and in group B was 449.9 $\pm$ 28.1 with p value of <0.001,which was highly significant. The results of the present study are in concordance with the study by **Rutter MK et al**[16] whoproved a link between microalbuminuria and premature death in Type-2 diabetic patients which could not be fully explained by conventional cardiovascular risk factors. They studied asymptomatic patients with Type-2 diabetes mellitus with no clinical evidence of coronary disease (43 patients with microalbuminuria matched with 43 normoalbuminuric patients). Rate corrected maximum QT interval was greater in the microalbuminuric group [mean (SD):450(23) vs 440(20)$ms^{1/2}$, p=0.046] as was the proportion of patients with QTc max >440ms. QT prolongation may contribute to the increased mortality observed in microalbuminuric patients with Type-2 diabetes mellitus.

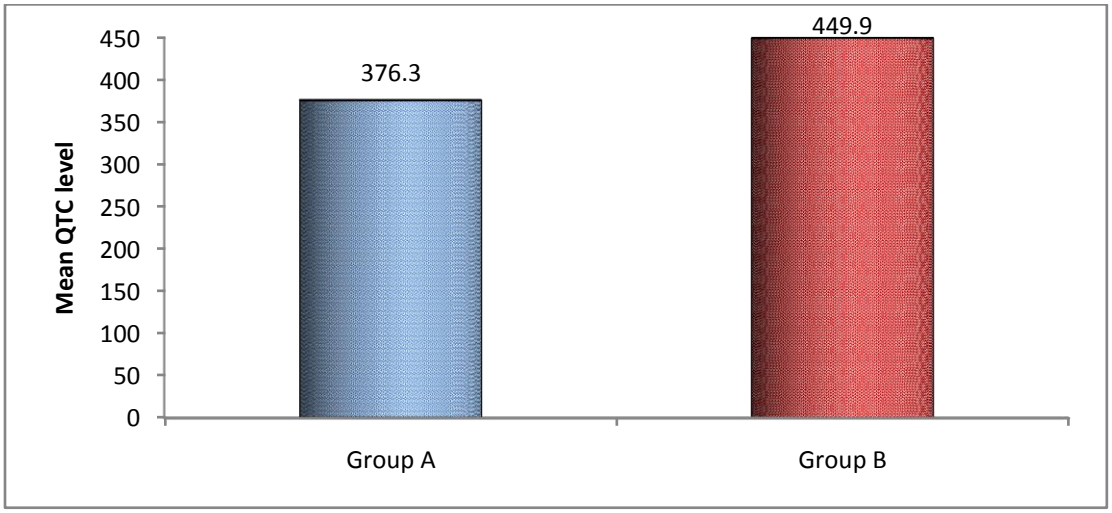


$$QTc = \frac{QT}{\sqrt{RR}} = \frac{12}{\sqrt{21}} = \frac{11}{\sqrt{20}} = \frac{11}{\sqrt{21}}$$

$$\frac{480}{\sqrt{0.84}} + \frac{440}{\sqrt{0.80}} + \frac{440}{\sqrt{0.84}} = \frac{1495.6}{3} = 498.5 \text{ SEC}$$

TABLE – 1
SHOWING MEAN QTC LEVEL IN BOTH GROUPS

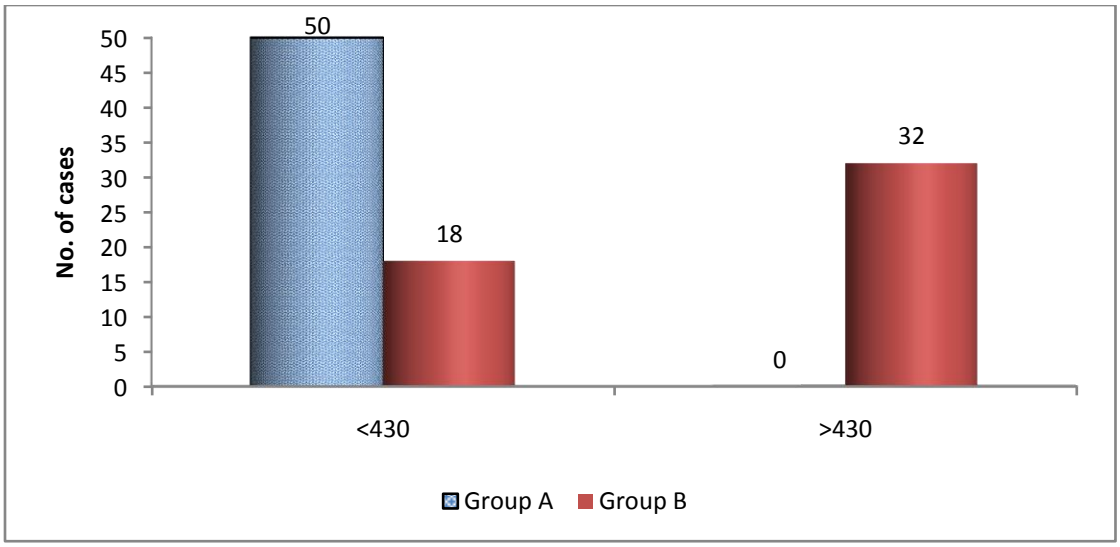
Group	Mean ± S.D.	'p' value
A	376.3 ± 19.9	0.001 (HS)
B	449.9 ± 28.1	



The mean QTc was 376.3 ± 19.9 in group A and in group B (449.9 ± 28.1). The p value is <0.001 which is highly significant.

TABLE - 2
PREVALENCE OF INCREASED QTC IN BOTH GROUPS

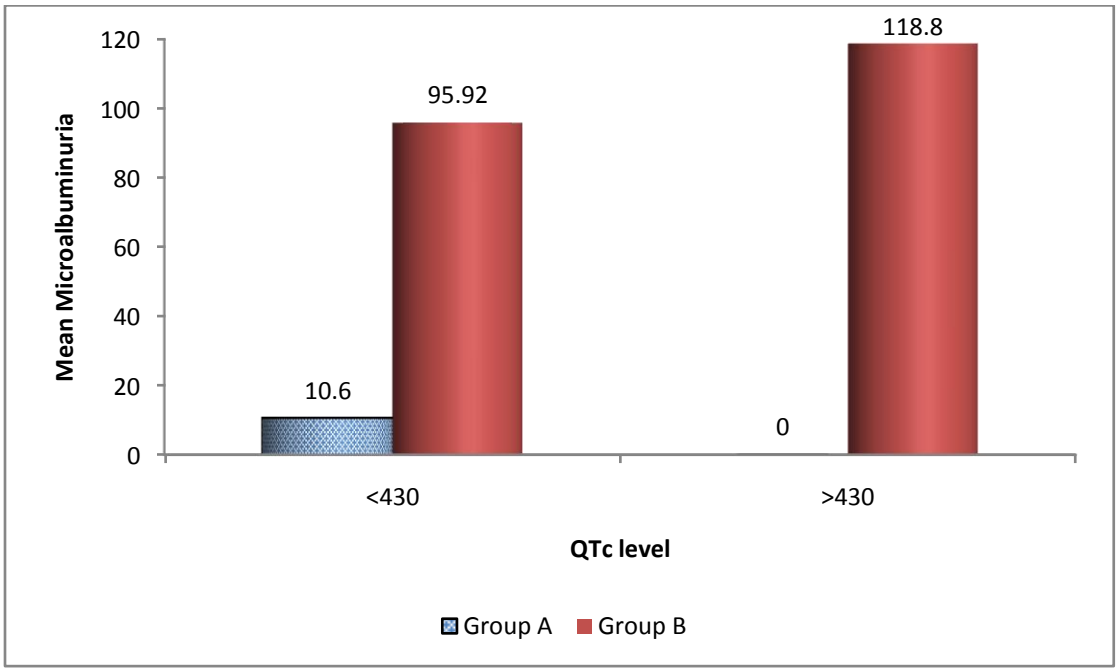
	Group A		Group B	
	No. of cases	**%age**	**No. of cases**	**%age**
<430	50	100.0	18	36.00
>430	0	0	32	64.00
Total	**50**	**100.00**	**50**	**100.00**



The prevalence of prolonged QTc was higher in group B as compared to group A, which was 64 % in patients of type 2 diabetes mellitus with nephropathy. The QTc was normal in patient of type 2 diabetes mellitus without nephropathy.

TABLE 3
RELATIONSHIP BETWEEN QTc AND MICROALBUMINURIA

QTc level	Group A	Group B
<430	**10.6 ± 5.1**	**95.92 ± 5.82**
>430	**-**	**118.8 ± 5.98**
'p' value	**-**	**0.20 (NS)**



The mean microalbuminuria and QTc- showed positive relationship in group B and negative relationship in group A. The QTc was increased in patients of type 2 diabetes mellitus with nephropathy. The p value is 0.20.

DISCUSSION

The present study was conducted on 100 cases of Diabetes mellitus Type-2 with and without nephropathy to find association between QTc and Microalbuminuria.

The present study showed the following results :

- **The prevalence of prolonged QTc was higher in group B as compared to group A, which was 64 % in patients of type 2 diabetes mellitus with nephropathy. The QTc was normal in patient of type 2 diabetes mellitus without nephropathy.**
- **The mean QTc was 376.3 ± 19.9 in group A and in group B (449.9 ± 28.1). The p value is <0.001 which is highly significant.**
- **The mean microalbuminuria and QTc showed positive relationship in group B and negative relationship in group A. The QTc was increased in patients of type 2 diabetes mellitus with nephropathy. The p value is 0.20.**

Conclusion

This study has shown that prevalence of prolonged QTc in type 2 diabetes mellitus is higher as compared to non-diabetics. QTc was increased in diabetic nephropathy. QTcinterval serve as marker of increased cardiovascular mortality and morbidity in Type-2 diabetes mellitus patients with and without nephropathy.

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