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Association between microalbuminuria and prolonged QT interval in type 2 Diabetes Mellitus

[1]Dr. Prachi Laxman Balani, MBBS, AMC MET Medical College, Ahmedabad

[2]Dr. Utkarsh Balani, Postgraduate Student, Dept. of Gen. Medicine, Sri Aurobindo Medical College & PG Institute-Indore

Corresponding Author: Dr. Prachi Laxman Balani, MBBS, AMC MET Medical College, Ahmedabad

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Abstract

Introduction: Both prolonged QTc interval and QTc dispersion are risk factors for malignant ventricular arrhythmias, affecting patients' mortality, including diabetes mellitus.[1,2]

There are also many studies about the influence of changes in glycemia on the length of QT parameters. Either hypoglycaemia or hyperglycaemia can increase the QT duration and QTd. Coronary artery defects, myocardium, and cardiac electrical propagation cause sudden cardiac death.[3]

Background: ECG Signs in Diabetic Patients-In the epidemiology of cardiovascular diseases, the importance of diabetes mellitus, both type 1 and type 2, cannot be overemphasised. Approximately one-third of patients with acute myocardial infarction have diabetes mellitus, the incidence of which is increasingly increasing: there were two million Americans with diabetes mellitus in the 1960s; the figure was 15 million in 2000. Statistics have shown that the decline in cardiac mortality is lagging behind that of the general population of individuals with diabetes mellitus. Early diagnosis of diabetes mellitus is crucial.[9] by screening techniques using urinary dipsticks.

Material and Methods

Study population: Patients admitted and those attending outpatient units in SAIMS Hospital-Indore (M.P.).

Sampling method: Simple random sampling method.

Inclusion criteria: All type 2 DIABETES MELLITUS who are attending the SAIMS Hospital-Indore (M.P.) for one year.

Exclusion criteria: History of MI/ Angina, Clinical evidence of heart failure Left bundle branch block, Atrial fibrillation Uncontrolled hypertension Febrile illness, Urinary tract infection, History of intake of ACE/ARB.

Results: Most of the patients were in 50 to 70 years of age group. There is a significant association between QTc interval prolongation and microalbuminuria as evidenced by a greater number of cases with microalbuminuria having prolonged QTc interval (67.76% Vs 24.13%, P<0.0001). Male to female ratio is 1.15:1.

Conclusion: There was a significant association between cardiac autonomic neuropathy (i.e. QTc interval prolongation) and microalbuminuria. Microalbuminuria doesn't directly cause QTc interval prolongation, but it can be used as an indicator for

patients who are prone to develop cardiac autonomic neuropathy and hence are at higher risk of having fatal arrhythmias.

Keywords: QTc interval prolongation, Microalbuminuria, Cardiac autonomic neuropathy, Diabetic nephropathy

Introduction

Both prolonged QTc interval and QTc dispersion are risk factors for malignant ventricular arrhythmias, affecting patients' mortality, including diabetes mellitus.[1,2]

There are also many studies about the influence of changes in glycemia on the length of QT parameters. Either hypoglycaemia or hyperglycaemia can increase the QT duration and QTd. Coronary artery defects, myocardium, and cardiac electrical propagation cause sudden cardiac death.[3]

Individuals diagnosed with diabetes reported to have a longer QT interval.[4] Recent studies have concluded that prolonged QT interval is an independent predictor of all- cause and cardiovascular mortalities in type 2 diabetes.[5] Thus, it is of great importance to clarify the patient characteristics that Influence their QT interval for reducing mortality in type 2 diabetes.

One of the most repeated and feared complications of diabetes mellitus is diabetic nephropathy. More and more patients with diabetic nephropathy appear as the incidence of diabetes is rising worldwide.

While both type 1 and type 2 diabetes mellitus (DM) can progress to ESRD, type 2 more commonly seen due to greater prevalence.[6] As WHO has forecasted an increase in the majority of diabetes around the globe with particular importance of increasing obesity, we expect an exceptional rise in diabetic nephropathy worldwide.[7]

Microalbuminuria observed to be a strong predictor of subsequent proteinuria and chronic renal failure in insulin and non-insulin-dependent DM patients since the early 1980s. However, the mortality rate in type 2 DM patients has mainly increased due to cardiovascular diseases.[8] Also noticed that these patients also had concomitant hypertension when they were diagnosed with Microalbuminuria

Aim: To find out the association between microalbuminuria and prolonged QT interval in Type 2 Diabetes Mellitus.

Background

ECG Signs in Diabetic Patients: In the epidemiology of cardiovascular diseases, the importance of diabetes mellitus, type 1 and type 2, cannot be overemphasised. Approximately one-third of patients with acute myocardial infarction have diabetes mellitus, the incidence of which is increasingly increasing: there were two million Americans with diabetes mellitus in the 1960s; the figure was 15 million in 2000. Statistics have shown that the decline in cardiac mortality is lagging behind that of the general population of individuals with diabetes mellitus. Early diagnosis of diabetes mellitus is crucial.[9]

Electrocardiographic Measures of Cardiac Autonomic Neuropathy

Baroreflex dysfunction and disturbed HR variability are the most commonly used methods to assess CAN.[10] showed intensive therapy's protective effect on reducing cardiac complications in patients with type 1 diabetes mellitus.

Prolonged QT interval: Congenitally or by acquired causes, cardiac events and fatal arrhythmias can occur.[11]

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Aetiology: It is possible to divide the causes of QT interval prolongation into congenital or acquired. Mutations in ion channels with more than 15 mutations identified are typically the result of hereditary reasons. In comparison, acquired prolongation of the QT interval may be due to electrolyte defects and medications influencing individual ion channels.[12]

Epidemiology: Estimating the prevalence of congenital causes, also known as Long QT syndrome (LQTS), is difficult, but can be calculated from 1 in 2,500 to 10,000. It is more prevalent in women and is typically present in infancy, adolescence, or early adulthood with cardiac events.

Pathophysiology: The duration of the ventricular action potential positively affects the course of the QT interval. (potassium). Any disruption in these ion channels, which leads intracellularly to an excess of positive ions, will prolong the action potential, leading to protracted QT prolongation.

Treatment/ Management: Prevention of fatal arrhythmias such as torsade de pointes is the priority of management (TdP). The longer the QT interval, the greater the risk is for torsade de points, as mentioned earlier. Non-synchronized electrical defibrillation provided to a hemodynamically unstable patient. Magnesium sulfate is also the first-line therapy, and the benefit shown regardless of the serum level of magnesium.

Pathophysiology of Microalbuminuria: Normal human urine contains only minimal albumin quantities, less than 30 mg of albumin being excreted by healthy adults in 24 hours. A cardinal sign of the glomerular disease is large amounts of albumin in the urine and is not detectable by screening techniques using urinary dipsticks.

Material and Methods

Study population: Patients admitted and those attending outpatient unit in SAIMS Hospital-Indore (M.P.)

Sampling method: Simple random sampling method

Inclusion criteria: All type 2 Diabetes Mellitus who are attending the SAIMS Hospital-Indore (M.P.) for one year.

Exclusion criteria: History of MI/ Angina, Clinical evidence of heart failure Left bundle branch block, Atrial fibrillation Uncontrolled hypertension Febrile illness, Urinary tract infection, History of intake of ACE/ARB.

Method of data collection

Sixty patients with type 2 Diabetes Mellitus attending the outpatient unit in SAIMS Hospital-Indore were selected using a simple random sample method. Informed consent obtained from all the patients. The study subjects are those who adhere to the inclusion and exclusion criteria. The selected patients studied in detail with history and physical examination.

History includes age, sex, age of onset, duration of diabetes, and details regarding presenting complaints. Smoking, alcohol consumption, drug intake noted. A complete clinical examination carried out in each patient with particular reference to complications of diabetes like micro and macrovascular complications.

Result

Table 1: Distribution based on age

Age Distribution	Frequency (%)
50 – 60	24 (40%)
61 – 70	26 (43.3%)
71 – 80	6 (10%)
81 – 90	4 (6.7%)

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Total	60 (100%)
Mean ± SD	63.83 ± 8.48

The mean age of the participants was 63.83 ± 8.48. The majority in the present study belonged to 61 - 70 years age group, i.e. 43.3%, 40% belonged to 50- 60 years age group, 10% in 71 - 80 years age group, 6.7% in 81 - 90 years age group.

Table 2: Distribution based on gender

Gender	Frequency (%)
Male	36 (60%)
Female	24 (40%)
Total	60 (100%)

Table 2 showed distribution based on gender, where 60% were male, and 40% were female in the present study.

Table 3: Distribution based on the duration of diabetes

Duration of Diabetes	Frequency
5 - 10	32 (53.3%)
11 - 15	23 (38.3%)
>16	5 (8.3%)
Total	60 (100%)
Mean ± SD	10.05 ± 3.03

Table 3 shows distribution based on the duration of diabetes where 5 - 10 years duration in 53.3%, 11 - 15 years duration in 38.3%, 8.3% had a period of >16 years in the present study.

The mean duration of diabetes in the present study was 10.05 ± 3.03 years.

Table 4: Distribution based on treatment

Treatment	Frequency (%)
Oral Hypoglycemics	25 (41.7%)
Oral Hypoglycemics + Insulin	22 (36.7%)
Insulin	13 (21.7%)
Total	60 (100%)

Table 4 shows distribution based on treatment where 41.7% of the study population were on Oral Hypoglycemics, 36.7% were on Oral Hypoglycemics and Insulin, 21.7% were on insulin in the present study.

Table 5: Distribution based on Microalbuminuria

Microalbuminuria	Frequency (%)
None	33 (55%)
1 +	8 (13.3%)
2 +	12 (20%)
3 +	7 (11.7%)
Total	60 (100%)

Table 5 shows distribution based on Microalbuminuria, where 20% had 2+, 13.3% had 1+, and 11.7% had 3+ Microalbuminuria in the present study.

Table 6: Distribution based on ECG QTc Prolongation (> 440 msec)

ECG QTcProlongation (>440msec)	Frequency (%)
Yes	22 (36.7%)
No	38 (63.3%)
Total	60 (100%)

Table 6 shows distribution based on QTc prolongation (>440 msec) wherein the present study, the prevalence of QTc prolongation was 36.7%.

Table 7: Association of Prolonged QTc and Age PROLONGED QTc

Age distribution	Yes	No	
50 - 60	11 (18.3%)	13 (21.7%)	24 (40%)
61 - 70	8 (13.3%)	18 (30%)	26 (43.3%)
71 - 80	2 (3.3%)	4 (6.7%)	6 (10%)

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81 - 90	1 (1.7%)	3 (5%)	4 (6.7%)
Total	22 (36.7%)	38 (63.3%)	60 (100%)
Chi Square test= 1.52,p=0.67 (Not significant)			

Table 7 shows distribution based on Age and QTc prolongation, where the majority is seen in 50 - 60 years age group, i.e., 18.3%, followed by 13.3% in 61 - 70 years age group.

There was no significant difference between Age and Prolonged QTc as the p-value calculated to be>0.05.

Table 8: Association of Prolonged QTc and Duration of Diabetes

PROLONGED QTc

Duration of Diabetes in years	Yes	No	
5 - 10	11 (18.3%)	21 (35%)	32 (53.3%)
11 - 15	7 (11.7%)	16 (26.7%)	23 (38.3%)
>16	4 (6.7%)	1 (1.7%)	5 (8.3%)
Total	22 (36.7%)	38 (63.3%)	60 (100%)
Chi Square test = 4.50,p=0.10 (Not Statistically significant)			

There was no significant difference between Duration of Diabetes and Prolonged QTc as the p-value calculated to be>0.05. 18.3% had Prolonged QTc with duration of diabetes in years within 5 – 10 years, 11.7% with prolonged QTc had a course of diabetes within 11-15 years.

Table 9: Association of Prolonged QTc and Microalbuminuria

Microalbuminuria	Prolonged QTc		Total
	Yes	No	
None	6 (10%)	27 (45%)	33 (55%)
1 +	2 (3.3%)	6 (10%)	8 (13.3%)
2+	7 (11.7%)	5 (8.3%)	12 (20%)
3+	7 (11.7%)	0 (0%)	7 (11.7%)
Total	22 (36.7%)	38 (63.3%)	60 (100%)
Chi square test= 19.84,p=0.0002(Statistically significant)			

A significant positive correlation, as observed between Microalbuminuria and Prolonged QTc as the p- value calculated to be <0.05. 11.7% had Prolonged QTc with 3+ and 2+ Microalbuminuria.

Discussion

Diabetes mellitus is a disease of ancient times known to humankind since 2000 years. Ancient Indian Scholars like Charaka and Shushmtha knew about it.

It is a big concern because of the devastating effect of its chronic complications.

In particular, the triad of neuropathy, retinopathy and nephropathy has been alluded to as primary consequences because of the close and relatively specific relationship between the genesis of Tripathy and the metabolic aberrations characteristic of diabetes. In our count", non-insulin-dependent diabetes mellitus compared to insulin- dependent diabetes mellitus afflicts a vast population.

By general consequences, neuropathy is the most common among the complications of diabetes. Yet, it remains the least investigated, and its pathogenesis is most poorly understood. In early diabetic nephropathy, Microalbuminuria is an early marker of glomerular disease that shown to predict injury. There is Microalbuminuria in 25 per cent of type 2 diabetic patients, and it is a good indicator of premature cardiovascular death in them. Diabetic nephropathy is a

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leading cause of mortality and morbidity associated with diabetes. In several studies, a correlation between autonomic neuropathy and diabetic nephropathy has shown in I diabetic patients. QT interval disorders in type I diabetics are consistent with Microalbuminuria. Just a few studies are available on type 2 diabetes. They studied 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 more significant in the microalbuminuric group [mean (SD):450(23) vs 440(20)ms1/2, p=0.046] as was the proportion of patients with QTc max >440ms.

Conclusion

Detailed history related to diabetes and its complications involving neuropathy was asked.

Evidence of CAN like QTc interval prolongation and nephropathy in the form of microalbuminuria was looked for. Most patients were in their $6^{th}$and 7^{th} decade of life and male preponderance was noted. Higher duration of diabetes, higher age groups have increased risk of cardiac autonomic neuropathy. Higher age groups and patients with higher duration of diabetes, have increased risk of cardiac autonomic neuropathy. There is a significant association between prolongation of QTc interval and microalbuminuria in these patients as evidenced by a greater number of cases with microalbuminuria having prolonged QTc interval. There is a significant association between QTc interval prolongation and microalbuminuria as evidenced by ,more number of microalbuminuria cases seen with prolonged QTc interval. As duration of diabetes increases prevalence of microalbuminuria increases. 20% of peripheral neuropathy cases are associated with CAN and 20% of retinopathy are associated with CAN.

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