Section: General Medicine

Original Research Article

ASSOCIATION BETWEEN PROLONGED QTC INTERVAL AND MICROALBUMINURIA IN PATIENTS WITH TYPE 2 DIABETES MELLITUS: A CROSS-SECTIONAL STUDY

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Received *: 16/02/2026*
Received in revised form *: 04/04/2026*
Accepted *: 21/04/2026*

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DOI: 10.70034/ijmedph.2026.2.169

Source of Support: Nil,
Conflict of Interest: None declared

Int J Med Pub Health
2026; 16 (2); 994-999

ABSTRACT

Background: Type 2 diabetes mellitus (T2DM) is associated with multiple microvascular complications, including cardiac autonomic neuropathy (CAN) and diabetic nephropathy. Prolonged QTc interval is a non-invasive marker of CAN, while microalbuminuria reflects early renal involvement and endothelial dysfunction. The aim is to assess the association between prolonged QTc interval and microalbuminuria in patients with T2DM.

Materials and Methods: This analytical cross-sectional study was conducted at Alluri Sitarama Raju Academy of Medical Sciences (ASRAM), Eluru, India, over 18 months. A total of 100 T2DM patients aged 50–79 years with microalbuminuria were included. QTc interval was measured using a 12-lead electrocardiogram and corrected using the modified Bazett's formula. Microalbuminuria was assessed using the urine albumin-to-creatinine ratio (ACR) and categorized into Grade I and Grade II. Statistical analysis was performed using IBM SPSS version 26, with Chi-square test applied for associations.

Results: The mean age of participants was 63.47 ± 8.50 years, with a male predominance (57%). QTc prolongation was observed in 68% of patients. Grade II microalbuminuria was present in 56% of cases. A highly significant association was found between QTc prolongation and microalbuminuria severity ($\chi^2 = 26.50$, $p < 0.0001$). QTc prolongation also showed a significant association with duration of diabetes ($\chi^2 = 8.730$, $p = 0.015$), with increasing prevalence in patients with longer disease duration. No significant gender association was observed.

Conclusion: In T2DM patients, a prolonged QTc interval is strongly linked to microalbuminuria and the length of diabetes, suggesting a strong connection between cardiac autonomic dysfunction and early diabetic nephropathy. Early identification and risk stratification can be facilitated by routine ECG and microalbuminuria monitoring.

Keywords: Type 2 diabetes mellitus, QTc prolongation, microalbuminuria, cardiac autonomic neuropathy, diabetic nephropathy.

INTRODUCTION

Diabetes mellitus is a chronic metabolic disorder characterized by persistent hyperglycemia resulting from defects in insulin secretion, insulin action, or both. The dramatic increase in the prevalence of type 2 diabetes mellitus (T2DM) over the past few decades has made it a serious worldwide health concern. India has a disproportionately high prevalence of diabetes and is referred to as the "diabetes capital of the world".[1] As the prevalence of type 2 diabetes rises, so do the microvascular and macrovascular effects, which dramatically raise morbidity and mortality.

Two of the most clinically important long-term effects of diabetes are diabetic nephropathy and cardiac autonomic neuropathy (CAN). CAN is a critical but often undiagnosed outcome caused by damage to the autonomic nerve fibers innervating the heart and blood vessels. It is associated with orthostatic hypotension, exercise intolerance, resting tachycardia, and an increased risk of silent myocardial ischemia and sudden cardiac death.[2] One of the first and most reliable indicators of CAN is the prolongation of the corrected QT (QTc) interval on electrocardiography (ECG), which indicates delayed ventricular repolarization.

In individuals with type 2 diabetes, a prolonged QTc interval has been extensively studied as a predictor of cardiovascular mortality. Numerous investigations have shown that QTc prolongation is independently associated with an increased risk of arrhythmias and sudden cardiac death.[3] The pathophysiological reasons of QTc prolongation in diabetes include myocardial ischemia, metabolic abnormalities, and autonomic imbalance, notably reduced parasympathetic activity and raised sympathetic tone.[4] As a result, QTc prolongation detection can be a simple, non-invasive way to spot cardiac autonomic dysfunction early on.

Diabetic nephropathy, another important microvascular consequence, is the leading cause of end-stage renal disease worldwide. Microalbuminuria, defined as an elevated albumin-to-creatinine ratio (ACR) or an albumin excretion rate of 30–300 mg/day, is an early and curable stage of diabetic nephropathy.[5] In addition to renal involvement, it is an indication of extensive endothelial dysfunction and increased cardiovascular risk. Early detection of microalbuminuria is crucial for timely treatment and to halt the progression of the illness. New research suggests a link between cardiac autonomic dysfunction and diabetic nephropathy. Both conditions share pathogenic mechanisms, including oxidative stress, inflammation, endothelial dysfunction, and chronic hyperglycemia.[6] Research on type 1 diabetes has demonstrated a strong association between microalbuminuria and CAN; however, data on type 2 diabetes is currently limited and inconsistent.[7] Understanding this connection is essential for identifying high-risk people and supporting early intervention strategies. Furthermore, it has been shown that the duration of diabetes has a major role in the development of CAN and nephropathy. Longer duration is associated with a higher risk of microvascular damage and cumulative exposure to hyperglycemia.[8] Although the findings are still ambiguous, the prevalence of these issues has also been investigated in connection to gender.

Given the increasing incidence of type 2 diabetes and its accompanying complications, easy-to-use, reasonably priced screening techniques are needed to identify early organ involvement. Measuring the QTc interval with a traditional ECG is a practical option for routine clinical use since it is easily available and moderately priced. Similarly, measuring microalbuminuria by urine ACR is a reliable indicator of early renal damage. This is why the current investigation was carried out to evaluate the connection between a prolonged QTc interval and microalbuminuria in T2DM patients. The study also aimed to assess the incidence of QTc prolongation and its correlation with gender and duration of diabetes in order to better understand the interaction between cardiac autonomic neuropathy and diabetic nephropathy.

MATERIALS AND METHODS

Study Design: This study was designed as an analytical cross-sectional study to evaluate the association between QTc interval prolongation and microalbuminuria in patients with Type 2 Diabetes Mellitus (T2DM).

Study Setting: The study was conducted at the Department of General Medicine, Alluri Sitarama Raju Academy of Medical Sciences (ASRAM), Eluru, India. Patients were recruited from both outpatient and inpatient departments.

Study Duration: The total study duration was 18 months (November 2022 to April 2024), with data collection carried out over 12 months.

Study Population and Sample Size: A total of 100 patients diagnosed with T2DM and microalbuminuria were included in the study. A convenience sampling technique was used.

Inclusion Criteria

- Patients with confirmed Type 2 Diabetes Mellitus
- Presence of microalbuminuria (urine spot ACR: 30–300 mg/g)
- Age group 50–79 years
- Patients willing to provide informed consent

Exclusion Criteria

- History of myocardial infarction or overt cardiovascular disease
- Patients with hypertension
- Urinary tract infection
- Poor glycemic control
- Smokers
- Patients on drugs affecting QT interval (e.g., antiarrhythmics, ACE inhibitors)
- Electrolyte imbalance

Data Collection Procedure: After obtaining ethical clearance and informed consent, all eligible patients were enrolled. A detailed clinical history and physical examination were performed. The following data were recorded:

- Age and gender
- Duration of diabetes
- Clinical history and complications

Assessment of Microalbuminuria

Microalbuminuria was assessed using the spot urine albumin-to-creatinine ratio (ACR) and categorized as:

- Grade I: 30–100 mg/g
- Grade II: 101–300 mg/g

Measurement of QTc Interval

- A standard 12-lead ECG was recorded for all participants
- QT interval was measured and corrected using the modified Bazett's formula:

QTc=QT+0.00175×(ventricular" " rate-60)

- QTc prolongation was defined as >440 ms

Laboratory Investigations

The following investigations were performed:

- Complete blood count (CBC)
- Fasting blood sugar (FBS)
- Postprandial blood sugar (PPBS)
- Serum creatinine
- Urine routine examination
- Urine ACR

Statistical Analysis: Data were entered into Microsoft Excel and subsequently analyzed using IBM SPSS version 26. Continuous variables were expressed as mean ± standard deviation, while categorical variables were summarized as frequencies and percentages. The chi-square test was employed to assess associations between categorical variables. A p-value of less than 0.05 was considered statistically significant.

Ethical Considerations: Ethical approval was obtained from the Institutional Ethics Committee of ASRAM.

Written informed consent was obtained from all participants prior to enrolment.

RESULTS

Table 1: Age Distribution of Study Participants (N = 100)

Age Group (Years)	Frequency (n)	Percentage (%)
50–59	28	28.0
60–69	47	47.0
70–79	25	25.0
Total	100	100.0

Mean age: 63.47 ± 8.50 years

The study included 100 patients with Type 2 Diabetes Mellitus (T2DM), with the majority belonging to the 60–69 years age group (47%), followed by 50–59 years (28%) and 70–79 years (25%). The mean age was 63.47 ± 8.50 years, indicating that most participants were elderly, reflecting the higher prevalence of chronic diabetic complications in this age group.

Table 2: Gender Distribution (N = 100)

Gender	Frequency (n)	Percentage (%)
Male	57	57.0
Female	43	43.0
Total	100	100.0

Male: Female = 1.32 : 1

Among the study participants, males constituted 57% (n = 57) and females 43% (n = 43), with a male-to-female ratio of 1.32:1. This suggests a slight male predominance in the study population.

Table 3: Duration of Diabetes (N = 100)

Duration (Years)	Frequency (n)	Percentage (%)
5–10	45	45.0
10–15	27	27.0
15–20	28	28.0
Total	100	100.0

Mean duration: 10.90 ± 4.12 years

The duration of diabetes ranged from 5 to 20 years. The majority of patients (45%) had diabetes for 5–10 years, followed by 15–20 years (28%) and 10–15 years (27%). The mean duration was 10.90 ± 4.12 years, indicating a relatively long-standing disease in most patients.

Table 4: Distribution of QTc Prolongation (N = 100)

QTc Status	Frequency (n)	Percentage (%)
Prolonged QTc	68	68.0
Normal QTc	32	32.0
Total	100	100.0

QTc prolongation was observed in 68% of patients, while 32% had normal QTc intervals. This high prevalence suggests a significant burden of cardiac autonomic neuropathy (CAN) among T2DM patients.

Table 5: Distribution of Microalbuminuria Grades (N = 100)

Microalbuminuria Grade	Frequency (n)	Percentage (%)
Grade I (30–100 mg/g)	44	44.0
Grade II (101–300 mg/g)	56	56.0
Total	100	100.0

Regarding microalbuminuria severity, 56% of patients had Grade II microalbuminuria, while 44% had Grade I. This indicates that a majority of patients had more advanced early nephropathy.

Table 6: Association Between QTc Prolongation and Microalbuminuria (N = 100)

Microalbuminuria Grade	QTc Prolonged (n)	QTc Normal (n)	Total
Grade I	20	24	44
Grade II	48	8	56
Total	68	32	100

Chi-square = 26.50, $p < 0.0001$ (Highly Significant)

A strong association was observed between QTc prolongation and microalbuminuria severity. Among patients with Grade II microalbuminuria, 48 out of 56 (85.7%) had prolonged QTc, compared to 20 out of 44 (45.5%) in Grade I. This association was found to be highly statistically significant (Chi-square = 26.50, $p < 0.0001$), indicating that higher microalbuminuria levels are strongly associated with QTc prolongation.

Table 7: Association Between QTc Prolongation and Duration of Diabetes (N = 100)

Duration (Years)	QTc Prolonged (n)	QTc Normal (n)	Total
5–10	27	18	45
10–15	17	10	27
15–20	24	4	28
Total	68	32	100

Chi-square = 8.730, $p = 0.015$ (Significant)

QTc prolongation increased with longer duration of diabetes. It was observed in 60% of patients with 5–10 years duration, 63% with 10–15 years, and 85.7% with 15–20 years duration. This association was statistically significant (Chi-square = 8.730, $p = 0.015$), suggesting that longer duration of diabetes is linked to higher risk of cardiac autonomic dysfunction.

DISCUSSION

The present study evaluated the association between prolonged QTc interval and microalbuminuria in patients with Type 2 Diabetes Mellitus (T2DM), highlighting the interplay between cardiac autonomic neuropathy (CAN) and diabetic nephropathy. The findings indicate a significant frequency of QTc prolongation and a robust relationship between the duration of diabetes and the degree of microalbuminuria. The majority of patients in this study were between the ages of 60 and 69, with a mean age of 63.47 years. This is consistent with previous studies showing that cumulative metabolic stress and prolonged exposure to hyperglycemia enhanced the incidence of diabetic complications in older adults.[9] Aging is associated with vascular stiffness, endothelial failure, and diminished autonomic regulation, all of which can worsen renal impairment and QTc prolongation.

There was a little male preponderance (57%) in the current investigation. Similar gender distributions have been identified in other studies, despite the fact that the role of gender in the development of diabetic complications is still up for debate.[10] The current study found no statistically significant gender link with QTc prolongation, suggesting that men and women are equally susceptible to cardiac autonomic dysfunction in type 2 diabetes.

With an average duration of 11 years, over half of the patients in this study had diabetes for five to 10 years. The duration of diabetes is one recognized risk factor for both diabetic nephropathy and CAN. The accumulation of advanced glycation end products (AGEs), oxidative stress, microvascular damage, and autonomic nerve dysfunction are all consequences of chronic hyperglycemia.[6]

One important finding of this study is the high frequency of QTc prolongation (68%), which suggests a substantial burden of cardiac autonomic neuropathy in T2DM patients. QTc prolongation is well recognized as a surrogate measure of CAN and has been associated with an increased risk of arrhythmias and abrupt cardiac death.[2] Prolonged QTc interval is an independent predictor of cardiovascular mortality in diabetics, according to earlier research by Veglio et al. and Maser et al.[3,4]

More than half of the patients (56%) had Grade II microalbuminuria, indicating the progression of early diabetic nephropathy. Microalbuminuria is a marker of extensive endothelial dysfunction and elevated cardiovascular risk in addition to renal impairment.[5] The co-occurrence of QTc prolongation with microalbuminuria suggests a shared pathophysiological mechanism involving vascular and autonomic dysfunction.

The most significant finding of the study is the strong connection ($p < 0.0001$) between QTc prolongation and microalbuminuria. Patients with higher grades of microalbuminuria had a considerably higher incidence of QTc prolongation. This supports the hypothesis that cardiac autonomic neuropathy and diabetic nephropathy are related diabetes sequelae. Endothelial dysfunction, oxidative stress, inflammation, and chronic hyperglycemia are common causes of both conditions.[11] Previous studies have shown similar outcomes, particularly in type 1 diabetes, where autonomic dysfunction was closely linked to microvascular issues.[7]

Another significant observation is the high connection ($p = 0.015$) between QTc prolongation and the duration of diabetes. The incidence of QTc prolongation increased gradually throughout the course of the illness, reaching 85.7% in people with 15–20 years of diabetes. This outcome is consistent with other studies that shown a direct link between the duration of diabetes and the degree of autonomic neuropathy.[10] Increased nerve damage and diminished autonomic control brought on by extended exposure to hyperglycemia are the causes of QTc prolongation.

These discoveries have important clinical ramifications. A straightforward, non-invasive, and affordable method for the early diagnosis of cardiac autonomic neuropathy is the measurement of the QTc interval using a routine ECG. Similarly, early detection of diabetic nephropathy is made possible by screening for microalbuminuria. Patients with microalbuminuria should be frequently assessed for QTc prolongation and vice versa, according to the substantial correlation between these two measures.

Early detection of patients at high risk allows These findings have significant clinical implications. Measuring the QTc interval with a standard ECG is a simple, non-invasive, and cost-effective way to identify cardiac autonomic neuropathy early. Similarly, screening for microalbuminuria allows for the early diagnosis of diabetic nephropathy. Given the strong link between these two metrics, patients with microalbuminuria should be regularly evaluated for QTc prolongation and vice versa.

Early detection of high-risk individuals enables timely intervention, such as strict glycemic control, lifestyle modification, and pharmaceutical therapy like ACE inhibitors or beta-blockers, which have been shown to improve autonomic function and lower cardiovascular risk.[13] Additionally, routine monitoring can prevent the onset of overt nephropathy and reduce the risk of cardiovascular events. Prompt intervention includes strict glycemic control, lifestyle modifications, and medications such as beta-blockers or ACE inhibitors, which have been shown to improve autonomic function and reduce cardiovascular risk.[13] Additionally, routine monitoring can prevent the onset of overt nephropathy and reduce the risk of cardiovascular events. However, proving causality is more challenging due to the cross-sectional form of this study. Longitudinal studies are needed to further understand the temporal relationship between QTc prolongation and microalbuminuria.

CONCLUSION

The present study demonstrates a significant association between prolonged QTc interval and microalbuminuria in patients with Type 2 Diabetes Mellitus, highlighting the interrelationship between cardiac autonomic neuropathy and diabetic nephropathy. The high incidence of QTc prolongation (68%) in this population indicates a considerable burden of subclinical cardiac autonomic dysfunction. Patients with increasing grades of microalbuminuria had significantly higher rates of QTc prolongation, suggesting a connection between autonomic dysfunction and worsening renal involvement. Additionally, a significant positive correlation between the duration of diabetes and QTc prolongation was found, underscoring the cumulative impacts of chronic hyperglycemia on the circulatory and neurological systems. These findings lend credence to the theory that common pathophysiological mechanisms including endothelial dysfunction, oxidative stress, and chronic inflammation connect diabetes-related microvascular issues. It is implied that patients of both sexes are equally vulnerable to these issues because there is no visible gender difference. Clinically speaking, assessing microalbuminuria and measuring the QTc interval with a simple ECG might be helpful, cost-effective screening techniques for early identification of high-risk individuals. Early identification enables timely management, including strict glucose control, lifestyle modifications, and appropriate medication, which may help prevent the onset of overt cardiovascular disease and end-stage renal disease. Therefore, frequent assessment of the QTc interval and microalbuminuria should be part of the standard therapy of patients with Type 2 Diabetes Mellitus in order to improve long-term outcomes and reduce morbidity and death.

Limitations of the study

1. **Cross-sectional design:** The study design limits the ability to establish a causal relationship between QTc prolongation and microalbuminuria.
2. **Single-center study:** Being conducted at a single tertiary care center, the findings may not be generalizable to the broader population.
3. **Small sample size:** The study included only 100 participants, which may limit the statistical power and external validity.
4. **Selection bias:** Convenience sampling may have introduced selection bias, affecting the representativeness of the study population.
5. **Exclusion of comorbid conditions:** Patients with hypertension and cardiovascular diseases were excluded, which may limit applicability to

real-world diabetic populations where such comorbidities are common.

6. **Lack of longitudinal follow-up:** The study did not assess progression over time, limiting insights into the temporal relationship between QTc prolongation and nephropathy.
7. **Limited assessment of confounders:** Factors such as glycemic control (HbA1c), lipid profile, and medication adherence were not analyzed in detail, which could influence outcomes.

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