

## Original Article

## Comparison of Left Ventricular Mass Index and Prolonged QT Interval in Type 2 Diabetic Patients

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### Abstract

**Objective:** To compare left ventricular mass index and QT interval in type 2 diabetic and non-diabetic patients.

**Methods:** 108 patients with 54 in each group were inducted. Group A (case) were diabetic type 2 and group B (control) were non-diabetic. The study was conducted in the medicine department of Lahore General hospital.

**Results:** In this study, the mean age in diabetic and non-diabetic subjects was  $47.54 \pm 9.25$  and  $44.53 \pm 10.53$  respectively with no significant difference,  $p$ -value = 0.199. In the diabetic group, there were 29 (53.70%) males and 25 (46.30%) females while in the non-diabetic group there were 27 (50%) male and 27 (50%) female patients. The mean LVMI in diabetic patients was significantly higher ( $129.48 \pm 30.72$ ) as compared to control (49.30) with  $p$ -value < 0.001. The mean QT in diabetic and non-diabetic was 431.65ms and 387.33ms while corrected QT interval was 468.31ms and 413.37ms respectively.

**Conclusion:** The results of this study suggest that both LVMI and QT interval are higher in diabetic population when compared to non-diabetic subjects. Early screening and proper diagnosis must be adopted in type 2 diabetic patients as they are very prone to develop higher left ventricular mass and deranged QT interval can further lead to significant cardiovascular risk because left ventricular hypertrophy and deranged QT interval are absolute risk factors for ventricular arrhythmia, infarction of myocardium, coronary artery disease, cardiac failure and sudden mortality.

**Keywords:** Congestive heart failure, hypertension and diabetes.

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### Introduction

Metabolic disorder leading to Diabetes mellitus (DM) is an inappropriate hyperglycemia insulin resistance or an inadequate insulin secretion. It is approximated that 366 million people will have DM by 2030.<sup>1</sup> According to a study performed in 2004 there are 5.2 million people suffering from diabetes mellitus in Pakistan.<sup>2</sup> A cross-sectional study was organized in the major villages and towns of all the four provinces of Pakistan. In towns, new onset diabetes was 5.1% in male population and 6.8% in female population and in villages; it was 5.0% in male population and 4.8% in female population.<sup>3</sup> The prevalence of cardiovascular disease (CVD) is greater in type 2 diabetic patients as compared to the non-diabetic patients. The Framingham Heart Study concluded that the cumulative mortality in the male and female population with diabetes was 3.5 to 4 times

greater as compared to a group of non-diabetic individuals.<sup>4</sup> Other studies have shown a correlation between the high risk of coronary heart disease events and period of diabetes, apparently as a result of the consequences of long term hyperglycemia.<sup>5</sup> The Framingham study showed that incidence rate of congestive heart failure (CHF) is higher in diabetic men (2.4:1) and women (5:1) irrespective of age, hypertension, increased BMI, coronary artery diseases (CAD) and dyslipidemias.<sup>6</sup> Moreover, the prospective studies also demonstrated that patients with type 2 diabetes have a notably higher long term risk of developing CHF<sup>7,8</sup>, and raised probability of death due to both Q-wave and non-Q-wave myocardial infarction.<sup>9,10</sup> There is also an important association among idiopathic cardiomyopathy and diabetes as demonstrated in a study by Bertoni.<sup>11</sup>

Diabetes mellitus is interlinked with a greater incidence

of cardiovascular mortality even in a population with low cardiovascular risk.<sup>12</sup> Electrocardiogram (ECG) is one of the most extensively used noninvasive diagnostic tool for stratification of cardiovascular risk. It is renowned that QT interval or corrected QT interval (QTc) prolongation and greater QT dispersion are repolarization abnormalities which are interlinked with greater risk of malignant arrhythmias of ventricular origin and sudden cardiac death in high-risk populations such as cardiomyopathy and myocardial infarction. Additionally, majority of the studies revealed that both in patients with and without diabetes mellitus, QTc prolongation and greater QT dispersion are prognosticators of cardiovascular mortality.<sup>13</sup> Moreover, left ventricular hypertrophy (LVH), is one of the dangerous predictors and distinct cardiovascular risk factor which can occur in patients with type 2 diabetes mellitus.<sup>12</sup> The prevalence of prolonged QT interval is as high as 26% in type 2 diabetic patients (T2DM).<sup>14</sup>

Another study reported that type 2 diabetics have higher left ventricular mass index (LVMI) and left ventricular hypertrophy than in patients without diabetes mellitus.<sup>15</sup> Nevertheless, newly diagnosed diabetics and without apparent cardiac complications have been observed to have a prolonged QTc interval in comparison with general population<sup>16-19</sup>. Since the QT interval is influenced by cardiac disease and diabetic complications, mainly autonomic neuropathy, it is likely to predict the prolonged QT interval in newly diagnosed patients or those that might have previously undetermined neuropathy or congestive cardiac failure.<sup>20</sup>

## Methods

This case control study was undertaken at the Department of Medicine, Lahore General Hospital, Lahore. Non-probability, purposive sampling was done to target the patients in the age group 18-60 years, both males and females diagnosed with T2DM, on oral or injectable anti-diabetic therapy with known duration of diabetes from 0 to 30 years. An informed consent was taken from all the patients. The demographic data like name, age, sex and address were documented. Proper history and clinical examination were carried out.

Echocardiography was done on Esaote My lab 50 X vision Cardiovascular with Phased array transducer PA-240 with frequency range of 1-4MHz and 3 harmonic frequencies. All Doppler measurements are automated in above unit having compound imaging and speckle reduction technology; PW, CW and Tissue Doppler Imaging are in standard configuration. By using parasternal view, LV dimensions were calculated either at the point of the papillary muscle or at the tip of mitral leaflet from M-mode echocardiogram of left ventricle. The thickness of the ventricular septum and the posterior wall of left ventricle were also estimated. With the help of these measured values, left ventricular mass (LVM) was measured. Furthermore, LVMI was measured by subdividing this calculated LVM with the body surface area.

During echographic studies, three measurements were recorded for each parameter and average were used for calculations and data analysis. Operator was not less than the rank of Assistant Professor and the researcher had worked as assistant and facilitator of the operator for data collection and analysis.

On resting ECG, QT interval was measured manually from starting of QRS complex to the end of T wave mostly in lead II. As QT interval varies with the heart rate, corrected QT interval was calculated via dividing measured QT interval by square root of the cycle length. The formula used was  $QTc = QT / (RR)^{1/2}$ . QT interval is prolonged when the QTc interval  $>0.44$  s.

## Results

The average BMI in diabetic patients was significantly higher ( $28.60 \pm 4.38$ ) when compared with non-diabetic ( $26.37 \pm 4.02$ ), p-value = 0.007. The mean body surface area in diabetic and non-diabetic was  $1.62 \pm 0.40$  and  $1.70 \pm 0.14$  respectively, p-value 0.155; the difference was insignificant.

The mean LVMI in diabetic was significantly higher ( $129.48 \pm 30.72$ ) when compared with controls ( $49.30 \pm 48.5$ ), p-value  $<0.001$ . The mean QT interval in diabetic and non-diabetic was  $431.65 \pm 16.29$ ms and  $387.33 \pm 30.14$ ms respectively with significant difference, p-value  $<0.001$ . The mean QT interval corrected was

**Table 1:** Comparison of anthropometric parameters in both study groups.

		Mean	Std. Deviation	Minimum	Maximum	p-value
<b>LVM/Height</b>	with T2DM	145.06	36.57	82.19	253.16	$<0.001$
	non-T2DM	88.53	16.31	58.82	121.95	
	Overall	116.79	40.01	58.82	253.16	
<b>LVM Height 2.7 (g/m<sup>2.7</sup>)</b>	with T2DM	68.94	23.12	42.10	139.70	$<0.001$
	non-T2DM	38.61	8.28	24.40	54.19	
	Overall	53.78	23.04	24.40	139.70	
<b>Heart rate</b>	with T2DM	71.13	4.66	62.00	82.00	0.002
	non-T2DM	68.80	5.59	61.00	86.00	
	Overall	69.96	5.26	61.00	86.00	

**Table 2:** Comparison of LVMI and QT interval in both study groups

		Mean	Std. Deviation	Minimum	Maximum	P value
LVMI	with T2DM	129.48	30.72	71.42	216.20	<0.001
	non-T2DM	49.30	48.57	1.43	111.73	
	Overall	89.39	57.08	1.43	216.20	
QT INT(ms)	with T2DM	431.65	16.29	400.00	460.00	<0.001
	non-T2DM	387.33	30.14	310.00	440.00	
	Overall	409.49	32.82	310.00	460.00	
QT interval (corrected)	with T2DM	468.31	9.18	441.00	485.00	<0.001
	non-T2DM	413.37	23.33	358.00	458.00	
	Overall	440.84	32.76	358.00	485.00	

468.31 ± 9.18ms in diabetic and 413 ± 23.33ms in non-diabetic subjects, the mean QT in diabetic patients was significantly greater in comparison with non-diabetics, p-value < 0.001.

### Discussion

Among metabolic disorders diabetes mellitus shares the phenotype of hyperglycemia. Its prevalence is increasing worldwide and would be 366 million people with DM by the year 2030.<sup>1</sup>

In diabetic patients, the causes of morbidity and mortality are cardiovascular complications. Diabetic cardiomyopathy is associated with structural and functional alteration in myocardium finally causing left ventricular hypertrophy along with systolic and diastolic dysfunction or both. These myocardial changes are not due to increased blood pressure or coronary artery disease though the diabetic patients are at high risk of ischemic heart disease. The pathogenesis of diabetic cardiomyopathy is suggested as myocardial structural changes, calcium and sodium signaling and metabolism with decrease in potassium level.<sup>21</sup> In a study conducted in the USA, the prevalence of diabetes mellitus is in increasing trend even though the modifiable cardiovascular hazards like as smoking, dyslipidemia and uncontrolled hypertension are in decreasing trend.<sup>22</sup>

Diabetes mellitus is strongly associated with cardiac arrhythmias, myocardial ischemia, cardiac failure and sudden death for which left ventricular hypertrophy is an absolute hazardous factor in patients with diabetes mellitus and prolonged QT interval is associated with autonomic neuropathy which may lead to sudden cardiac death. Various studies revealed that though, presence of diabetes mellitus is independent of atherosclerosis, it may be associated with structural and functional abnormalities of the left ventricle.<sup>23,24</sup> Recently, various studies have shown that the QT interval is an important prognostic factor in determining the total mortality in both diabetic and non-diabetic population. Further over, many studies have highlighted the strong and significant association of prolonged QT interval with the probability of cardiovascular disease. Hence, to stratify the risk of cardiovascular disease in diabetic patients, QT interval can be used.<sup>14</sup>

A study revealed that in post-myocardial infarction diabetics, patients have increased QTc max, QTd and QTcd in comparison with non-diabetic patients, (P-value < 0.05). Ventricular arrhythmias were significantly associated with QTc max, QTd and QTcd (all p values < 0.05). Therefore, the study had shown that non-ST segment elevation myocardial infarction with diabetes have increased QTc max, QTd, and QTcd which further lead to the poor cardiac outcomes and worst prognosis.<sup>26</sup>

In the current study we also found that mean QT interval (ms) in diabetic and non-diabetic patients was 431.65 ± 16.29 and 387.33 ± 30.14 respectively with significant difference, p-value < 0.001. Similar findings are reported in another study in which they found that the prevalence of QTc interval prolongation was 34.6% in type 2 diabetic patients. Thus, the study concluded that prolonged QTc interval identified in type 2 diabetic patients have significant probability of cardiovascular events.<sup>27</sup> In the current study we also found that mean LVMI in diabetics was significantly higher (129.48 ± 30.72) when compared with controls (49.30 ± 48.5), p-value < 0.001. Moreover, in the Northern Manhattan Study (NOMAS), the results showed that patients with type 2 diabetes had higher LVM (189 ± 60 vs. 174 ± 59g; p < 0.0001), systolic blood pressure and body mass index as compared with the non-diabetic people, whereas age and sex distribution showed no difference among both the groups. Type 2 diabetes mellitus was separately inter-linked with higher LV mass (P = 0.03) as shown by multi component analysis. Similarly, type 2 diabetes mellitus was significantly related with higher probability of left ventricular hypertrophy (P = 0.004).

Further in 2003, a Framingham Study was conducted, enrolling 2623 people including 1514 women of mean age 53 years without any cardiac disease, infarction of myocardium and cardiac failure to look for association of glucose tolerance status with the LV measurements in echocardiography. Mass of left ventricle was measured by adjusting for height, age, heart rate and systolic blood pressure and found to be inversely proportional to the glucose tolerance. The left ventricular mass was increased with worsening of glucose intolerance in women (P < 0.001) as compared to men (P = 0.054). Hence, this

community-based study concluded that the LV mass and wall thickness is higher when the glucose intolerance worsens in females as compared with males. In the women with obesity, increased LV mass was interlinked with insulin resistance.<sup>28</sup>

In a study of type 2 diabetic patients with hypertension, it was shown that greater LV mass and increased concentric LV geometry was seen in type 2 diabetic patients irrespective of age, gender, body size and blood pressure. Type 2 diabetic patients had greater LV wall thicknesses and left ventricular mass as compared to non-diabetic patients. Hence, the study concluded that the probability of LV hypertrophy is significantly greater in type 2 diabetics than in the non-diabetic population.<sup>16</sup> Bella et al conducted a Strong Heart Study including a total of 1,025 American Indian participants in which 642 were with diabetes mellitus alone, 614 had systemic hypertension alone, and 874 had both diabetes mellitus and systemic hypertension. After adjusting variables for age, body mass index and heart rate, the analysis revealed that increased left ventricular (LV) wall thicknesses is strongly interlinked with both diabetes mellitus and systemic hypertension, with a significant effect of diabetes mellitus on left ventricular thickness and influence of both diabetes mellitus and systemic hypertension on left ventricular mass (both  $p < 0.001$ ). Hence, the study revealed that in patients with diabetes mellitus and systemic hypertension, there is a significant adverse impact on LV function and LV geometry, either alone or both.<sup>16</sup>

For analyzing left ventricular mass (LVM) index in diabetic patients, a study conducted by Rutter et al revealed that LVM ( $P=0.04$ ) and LVH prevalence were higher in diabetic patients. Therefore, left ventricular hypertrophy is significantly prevalent in patients with type 2 diabetes mellitus.<sup>28</sup>

### Conclusion

So, the results of this study suggest that both LVMI and QT interval are higher in diabetic population when compared to non-diabetic subjects. Moreover, these parameters are higher in the male and obese population as well. Early screening and proper diagnosis must be adopted in type 2 diabetic patients as they are prone to develop higher left ventricular mass and deranged QT interval can further lead to significant cardiovascular risk because left ventricular hypertrophy and deranged QT interval are absolute risk factors for ventricular arrhythmia, infarction of myocardium, coronary artery disease, cardiac failure and sudden mortality.

**Ethical Approval:** The IRB/EC approved this study via letter no. null issue by PGMI/LGH Lahore.

**Conflict of Interest:** None

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