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QT PROLONGATION IN TYPE 2 DIABETES MELLITUS

Medicine

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KEYWORDS

INTRODUCTION AND NEED FOR THE STUDY:

The QT interval in the surface electrocardiogram (ECG) reflects the total duration of depolarization and repolarization of the ventricles. QT dispersion (QTd) represents non uniformity of regional myocardial ventricular repolarization and is reflected by differences of the QT interval duration between ECG leads. Both prolonged QT interval and increased QTd are predisposing factors to develop malignant ventricular arrhythmias .Prolonged QT interval is associated with cardiac arrhythmias and sudden death. Studies show that prolonged QT interval and increased QT dispersion are predictors of cardiovascular mortality and all-cause mortality in patients with type 1 and 2 Diabetes Mellitus[1,2] and in the population of apparently healthy individuals .[3]

REVIEW OF LITERATURE:

A study done in Italy among diabetics showed prevalence of prolonged corrected QT (QTc) duration and increased QT dispersion(QTd) to be 25.8% (95% CI 23.5–28.3) and 33.1% (95% CI 30.6–35.7), with no sex differences[4].

Similarly a study done in Helsinki showed the prevalence of QT prolongation (440 ms) to be relatively high (44.1 %), but the prevalence of high-risk QT prolongation(>500 ms), and increased QT dispersion (80 ms) in patients with type 2 diabetes is low (2 and 3.6 % respectively)[5].

Another study done in 2003 showed that maximum QTc interval prolongation was highly significant ($p<0.01$) in diabetics and hence concluded that the prolongation of the maximum QTc-interval could be a expression of an increased arrythmogenic and cardiovascular risk in diabetes .[6]

A population based study done in Europe showed a considerably high prevalence of increased QTc and QTd in type 2 diabetic patients and their association with coronary heart disease. These findings have both epidemiological and clinical relevance, as they might be implicated in the excess mortality risk of type 2 diabetic patients.[7]

QTc prolongation , but not increased QT dispersion , was found to be an independent marker of increased mortality in patients with type 1 diabetes mellitus .[8] A study done in 2000 showed that whereas QT-dispersion was not a predictor , QTc was an independent predictor of cardiovascular mortality . It also showed a high prevalence of QTc and QTd abnormalities and indicated that QTc but not QT-dispersion was a independent predictor of all cause and cardiovascular mortality in patients with type 2 diabetes mellitus .[9]

A study done in Hungary, however, concluded that the hypothesis that increased QTd/Qtc-d is truly a predictive marker of sudden arrhythmic cardiac death in patients with diabetes mellitus needs further clinical investigation.[10]

A study done in 2016 concluded that QT interval calculation was a simple, low cost measurement , which is easily obtainable without the need of the patient's compliance and could help select patients who may need a detailed evaluation and strict observation.[11]

AIMS AND OBJECTIVES:

1 To determine the frequency of prolonged QT interval and increased QT dispersion in patients with type 2 Diabetes.

2 To study the correlation between prolonged QT and QTd and clinical and metabolic parameters, with particular emphasis on the parameters of glycemic control and type of diabetes treatment.

MATERIALS AND METHODS:

Study design: Cross sectional study.

Study sample: patients older than 39 years of age with the lack of need for insulin treatment within the first year after diagnosis of diabetes mellitus who presented to the outpatient medicine department of Father Muller Medical College Hospital , Mangaluru.

Exclusion criteria : patients with ECG signs of myocardial hypertrophy, ischemia , bundle branch block and patients on treatment with drugs known to affect the QT interval.

Methodology : QT interval was measured from the beginning of QRS complex to the end of the T wave in the intersection with the isoelectric line[12]. QT corrected for the length of the previous cycle (QTc) was obtained using Bazett's formulae: $QTc = QT / \sqrt{RR\ (sec)}$ [7].

QTc >440 ms was considered abnormally prolonged, whereas QTc> 500 ms was considered high-risk QT prolongation. RR and QT intervals were measured in three consecutive cycles in each of the six thoracic lead. QTc dispersion (QTd) was calculated as the difference between the maximum and minimum QTc at any thoracic lead. QTd >70 ms was considered to be abnormally increased.[13]

The clinical parameters mentioned in the aims included clinical evidence of peripheral neuropathy including absent ankle reflex and diminished vibration sense. The criteria for glycemic control used was fasting blood glucose and glycated hemoglobin levels.

Statistical analysis: Differences in clinical characteristics of patients between subgroups of QTc duration and QTc dispersion was assessed using the t-test for continuous variables and chi square tests.

RESULTS :

Age distribution :

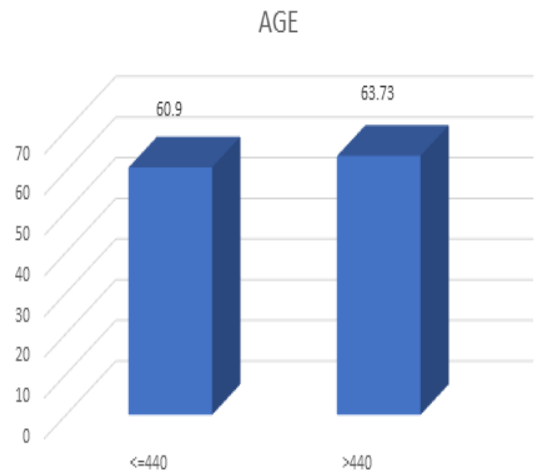

Figure 1: Age distribution

Comparison of the AGE between the two groups shows that AGE is higher in >440ms group with a t value of -0.829 and is statistically non significant with a p value of 0.409. (Fig 2)

Duration of Type 2 diabetes mellitus (in years)

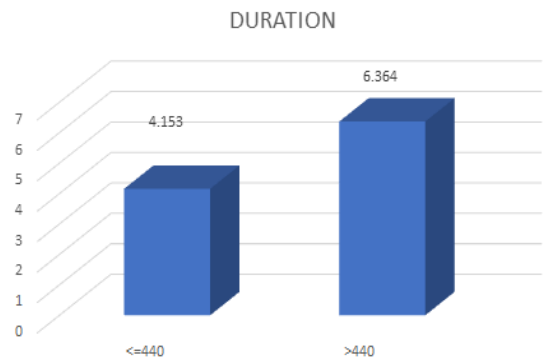

Figure 2: Duration of type 2 diabetes mellitus (in years)

Comparison of the DURATION of diabetes between the two groups shows that DURATION of the disease is higher in >440ms group with a t value of -3.147 and is statistically significant with a p value of 0.002. (Fig 2)

Systolic Blood Pressure (SBP)

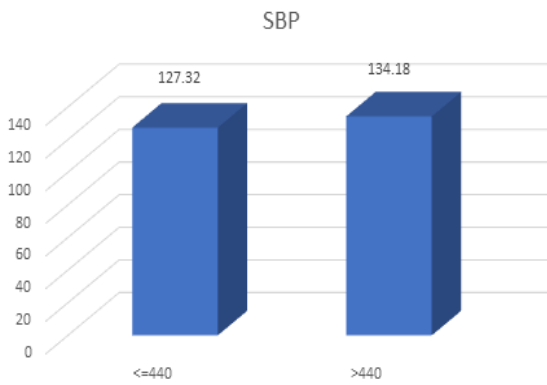

Figure 3: Systolic Blood Pressure

Comparison of the SBP between the two groups shows that SBP is higher in >440 group with a t value of -3.028 and is statistically significant with a p value of 0.003.(Fig 3)

Diastolic Blood Pressure

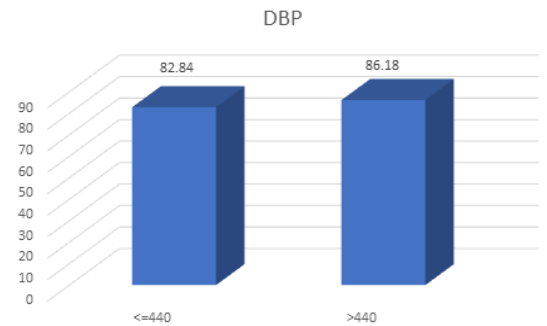

Figure 4: Diastolic Blood Pressure

Comparison of the DBP between the two groups shows that DBP is higher in >440 group with a t value of -1.042 and is statistically non significant with a p value of 0.32(Fig 4)

Glycosylated hemoglobin

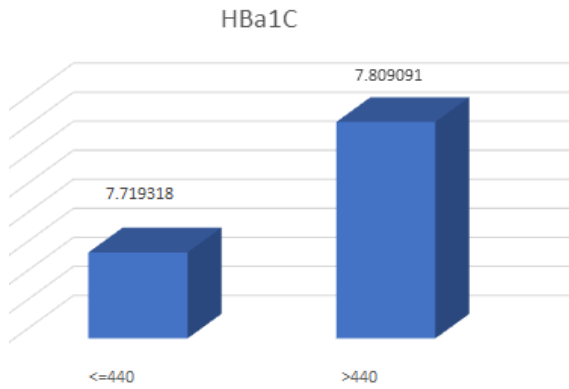

Fig 5: Glycosylate hemoglobin

Comparison of the HBa1C between the two groups shows that HBa1C is higher in >440 group with a t value of -0.33 and is statistically non significant with a p value of 0.748(fig 5)

Fasting Blood Glucose

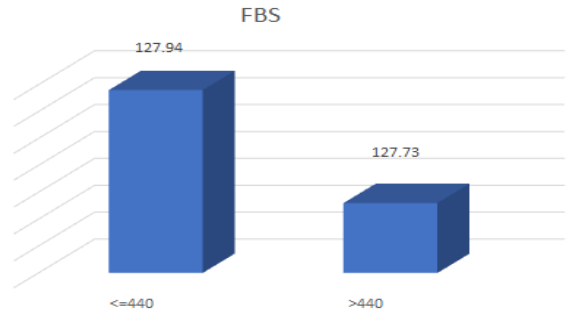

Figure 6: Fasting Blood Glucose

Comparison of the FBS between the two groups shows that FBS is higher in <=440 group with a t value of 0.08 and is statistically non significant with a p value of 0.936(fig 6)

QT dispersion (Qtd)

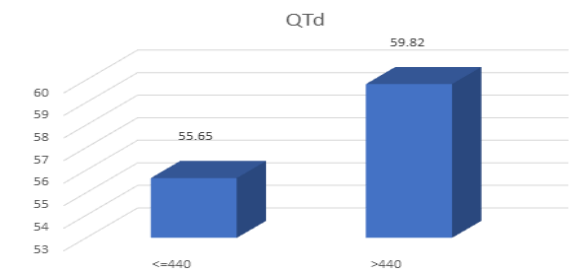

Figure 7 : QT dispersion (Qtd)

Comparison of the QTd between the two groups shows that QTd is higher in >440 group with a t value of -1.186 and is statistically non significant with a p value of 0.238 (fig 7)

	QTc	N	Mean	Std. Deviation	t	df	P VALUE
AGE	<=440	88	60.9	10.673	-0.829	97	0.409
	>440	11	63.73	10.734			
DURATION	<=440	88	4.153	2.1793	-3.147	97	**0.002**
	>440	11	6.364	2.3355			
SBP	<=440	88	127.32	6.545	-3.028	97	**0.003**
	>440	11	134.18	10.713			
DBP	<=440	88	82.84	6.093	-1.042	10.873	0.32
	>440	11	86.18	10.41			
HBa1C	<=440	88	7.719318	0.621244	-0.33	11.293	0.748
	>440	11	7.809091	0.875734			
FBS	<=440	88	127.94	8.434	0.08	97	0.936
	>440	11	127.73	8.223			

Table 1: QT c and continuous variables

		N	Qtc				Chi square	P value
			<=440		>440			
			Count	Column N %	Count	Column N %		
GENDER	F	45	40	45.50%	5	45.50%	0	1
	M	54	48	54.50%	6	54.50%		
Neuropathy	N	70	67	76.10%	3	27.30%	11.272	0.001
	Y	29	21	23.90%	8	72.70%		
Treatment	I	48	44	50.00%	4	36.40%	0.728	0.394
	O	51	44	50.00%	7	63.60%		
Microalbum	N	69	68	77.30%	1	9.10%	21.522	<0.001
	Y	30	20	22.70%	10	90.90%		
Retinopathy	N	70	69	78.40%	1	9.10%	22.683	<0.001
	Y	29	19	21.60%	10	90.90%		
Stroke	N	91	80	90.90%	11	100.00%	1.088	0.297
	Y	8	8	9.10%	0	0.00%		
Cad	N	97	87	98.90%	10	90.90%	3.126	0.077
	Y	2	1	1.10%	1	9.10%		

Table 2 : QTc and categorical variable

Among the 100 patients a total of 11 patients were found to have a prolonged QT . There was no statistically significant relationship noted between gender , treatment with insulin or oral hypoglycemic agents , past history of stroke or coronary artery disease . However there was a statistically significant relationship noted between presence of neuropathy , microalbuminuria, retinopathy and prolonged QTinterval. (Table 3)

Age and Qtd:

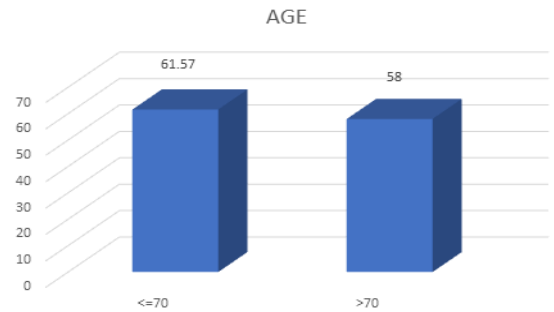

Figure 8: Age and Qtd

Comparison of the AGE between the two groups shows that AGE is higher in <=70 group with a t value of 1.005 and is statistically non significant with a p value of 0.317(fig 8)

Duration of type 2 diabetes mellitus and Qtd

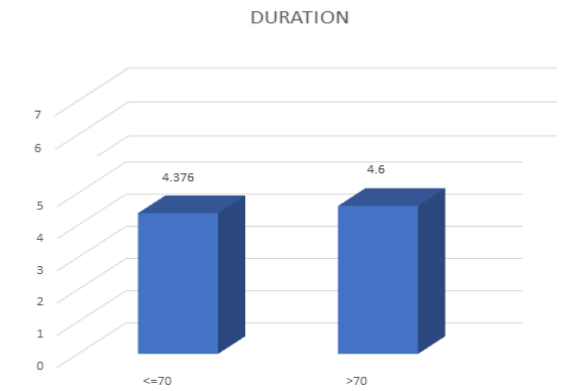

Figure 9: Duration of Type 2 DM and Qtd

Comparison of the DURATION between the two groups shows that DURATION is higher in >70 group with a t value of -0.291 and is statistically non significant with a p value of 0.772(fig 9)

Systolic Blood Pressure and Qtd

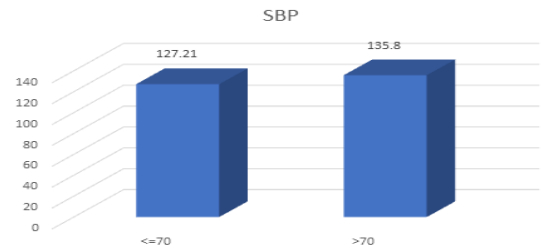

Figure 10 : Systolic Blood pressure and Qtd

Comparison of the SBP between the two groups shows that SBP is higher in >70 group with a t value of -2.253 and is statistically significant with a p value of 0.049(table 3)

Diastolic Blood Pressure and Qtd

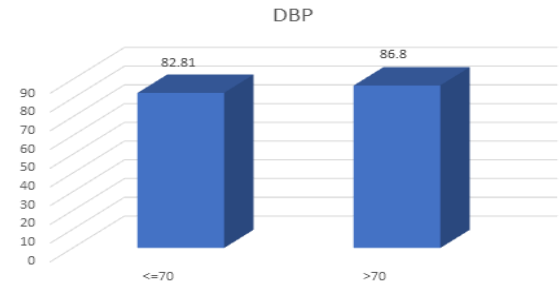

Figure 11: Diastolic Blood Pressure and Qtd

Comparison of the DBP between the two groups shows that DBP is higher in >70 group with a t value of -1.802 and is statistically non significant with a p value of 0.075.(Fig 11, table 3)

Glycosylated hemoglobin and Qtd

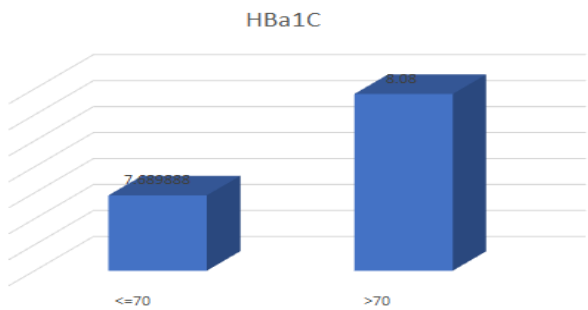

Figure 12 : Glycosylated hemoglobin

Comparison of the HBa1C between the two groups shows that HBa1C is higher in >70 group with a t value of -1.822 and is statistically non significant with a p value of 0.071(Fig 12)

Fasting Blood Glucose and Qtd

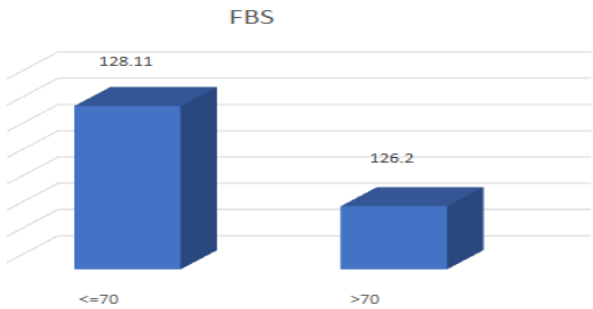

Figure 13 : Fasting Blood Glucose and Qtd

Comparison of the FBS between the two groups shows that FBS is higher in <=70 group with a t value of 0.683 and is statistically non significant with a p value of 0.496. (fig 13)

	QTd	N	Mean	Std. Deviation	t	df	P Value
AGE	<=70	89	61.57	11.009	1.005	97	0.317
	>70	10	58	6.325			
DURATION	<=70	89	4.376	2.2019	-0.291	97	0.772
	>70	10	4.6	3.134			
SBP	<=70	89	127.21	6.22	-2.253	9.563	**0.049**
	>70	10	135.8	11.868			
DBP	<=70	89	82.81	6.25	-1.802	97	0.075
	>70	10	86.8	9.67			
HBa1C	<=70	89	7.689888	0.646326	-1.822	97	0.071
	>70	10	8.08	0.595912			
FBS	<=70	89	128.11	8.661	0.683	97	0.496
	>70	10	126.2	5.073			
QTc	<=70	89	404.1	26.973	-1.382	97	0.17
	>70	10	416.5	26.12			

Table 3 : QTd and categorical variables

		N	QTd				Chi square	P value
			<=70		>70			
			Count	Column N %	Count	Column N %		
Gender	F	45	42	47.20%	3	30.00%	1.072	0.301
	M	54	47	52.80%	7	70.00%		
Neuropathy	N	70	63	70.80%	7	70.00%	0.003	0.959
	Y	29	26	29.20%	3	30.00%		
Treatment	I	48	45	50.60%	3	30.00%	1.522	0.217
	O	51	44	49.40%	7	70.00%		
Microalbuminuria	N	69	63	70.80%	6	60.00%	0.495	0.482
	Y	30	26	29.20%	4	40.00%		
Retinopathy	N	70	64	71.90%	6	60.00%	0.616	0.433
	Y	29	25	28.10%	4	40.00%		
Stroke	N	91	81	91.00%	10	100.00%	0.978	0.323
	Y	8	8	9.00%	0	0.00%		
Cad	N	97	87	97.80%	10	100.00%	0.229	0.632
	Y	2	2	2.20%	0	0.00%		

Table 4 : QTd and categorical variables

There was no statistically significant correlation between presence of QTd and gender , neuropathy , treatment modality , microalbuminuria , retinopathy , neuropathy or prior history of coronary artery disease or stroke(Table 4) .

DISCUSSION.

A total of 100 patients, who fit the inclusion criteria were included in the current study. They were evaluated in detail including clinical presence of micro and macrovascular complications, laboratory parameters were analyzed and QT duration calculated in each ECG. QTc and QTd values were them calculated and statistical analysis was done.

Among the 100 patients 54 (54%) were males and 46 (46%) were females). The sex and age distribution is comparable to a population based cohort study by Veglio et al . [5]

There was no significant association noted between gender or increasing age and QT prolongation comparable to a similar study done in Italy . [5,] This finding is in contrast to the results of a study by Vladan M et al , who found a statistically significant association between the female gender and QT prolongation[11] .

In this study QT was found to be prolonged in 11 patients accounting for 11% of the total study population. But there were no patients with high risk QT prolongation. This number is very small compared to a similar study done among type 2 diabetics which detected 44.1 % of its study subjects to have a prolonged QT [11]. However even in this study the prevalence of high risk QT prolongation was found to be only 2 % . There are, however , studies which show a very variable prevalence of QT prolongation , ranging from 15.4 to 67 % .[15-16] . The current study showed a much lower prevalence as compared to these.

There was no statistically significant association noted between prior history of stroke or coronary artery disease and prolonged QT interval consistent with the results of the study conducted by Nincovik et al ,[14] yet contrasting the results of Vladan et al[11] .

On clinical examination. a positive statistical association was detected between presence of retinopathy, microalbuminuria, neuropathy and prolonged QT intervals . These findings are in agreement with similar studies done in type 2 diabetics to assess prevalence of and risk factors for QT interval prolongation.. [5,8,11] In particular, they indicate the presence of a higher cardiovascular risk in patients with microvascular complications of diabetes , hence reinforcing the requirement to screen for them during routine follow up of all diabetic patients .

Among the 11 patients with prolonged QT interval there was no statistically significant association noted with the type of treatment. This finding also contrasts with the findings of Vladan et al which showed that sulfonylureas were a risk factor and prolonged QT levels were less common in patients who were on insulin. [11]

There was a statistically significant relationship noted between total duration of diabetes and presence of prolonged QT($p < 0.01$) association in agreement with the findings of the study by Vladan et al. [11]

In this study there was a positive association noted between elevated blood pressure readings and presence of a prolonged QT interval , however only presence of a elevated systolic blood pressure was found to be statistically significant . Most studies analyzing the QT interval among the diabetics [11] and even non-diabetics [19] have found a statistically significant association between a prolonged QT and both Systolic and Diastolic blood pressures .

In addition to prolonged QTc , this study also analyzed the presence elevated QTd values and various risk factors .A total of 10 patients were found to have increased QTd values and statistically significant association was only found with presence of elevated systolic blood pressure readings. Studies on QTd are less frequently encountered as compared to those on QTc , however the risk factors have been detected to be the same. [5,11] In the current study however the significance of prolonged QTd could not be established similar to a older stud by Chinaglia et al.[9]

CONCLUSIONS:

In this study the total prevalence of prolonged QTc was 11 % and a statistically significant association detected between presence of microvascular complications of diabetes, indicating increased cardiovascular risk in these patients . There was no statistically significant risk factors detected for prolonged QTd values.

LIMITATIONS:

- No follow up
- Small study sample

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