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Original Research Article

Prevalence of QTc prolongation among hypertensive patients and its association with other co-morbidities

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ABSTRACT

Background: Hypertension, an iceberg disease contributes significantly to the global health burden. This pan-endemic disease is a harbinger for cardiovascular events, especially life-threatening arrhythmias. A simple and cost-effective electrocardiogram serves as an effective tool to identify and evaluate hypertensives with high cardiovascular risk. QTc interval which indicates repolarization abnormality is one such effective tool. The study aimed at describing the prevalence of QTc prolongation among hypertensive individuals and also to assess the association of QTc prolongation with various co-morbidities.
Methods: One hundred and fifty-nine hypertensive patients were evaluated in this cross-sectional study for six months. Demographic variables, biochemical parameters, blood pressure and electrocardiogram were recorded for all the patients. Data obtained were statistically evaluated.
Results: The mean age of participants was 55.6 years (SD±6.76). There were 103 males (64.4%) and 43 females (35.6%). QTc prolongation was noted in 52.5% of the population studied. Statistically significant QTc prolongation among poorly controlled hypertensive was 59% when compared to that of controlled hypertensive at 37.5% was noted. About 26% of the participants were smokers, 27% were alcoholics and 60% had co-existing diabetes mellitus. Diabetes and gender were found to have a statistically significant association with QTc prolongation.
Conclusions: The study found a positive correlation between prolonged QTc and hypertensives and hypertensives with coexisting diabetes. To mitigate the consequences of hypertension, the study recommends early diagnosis, stringent blood pressure control, efficient and effective use of QTc measurement, and preventive pharmacotherapy.

Keywords: QTc interval, Electrocardiogram, Hypertension

INTRODUCTION

Hypertension, a global health issue, is a major cause of morbidity and mortality worldwide, particularly in developing countries such as India. Epidemiological studies have estimated that one in every three Indians is at risk of developing hypertension. The disease is expected to double by 2025 as compared to 2000. Hypertension per se and its severity has been frequently associated with a plethora of other cardiovascular risk factors, all of which have synergistic effects on their cardiovascular risk. Left ventricular hypertrophy, microalbuminuria, heart failure, retinopathy, peripheral artery disease, coronary artery disease and stroke are all associated with hypertension. Hypertensive patients, particularly those with left ventricular hypertrophy (LVH) are more likely to succumb

to sudden cardiac death. LVH can result in ventricular repolarization defects. When these defects exist, they can be easily detected using electrocardiogram (ECG) parameters such as the QT interval.[1,2]

Prolonged QT intervals have been linked to an increased risk of cardiovascular death in people with diabetes, hypertrophic cardiomyopathy and heart failure. It has also been linked to several components of insulin resistance syndrome, age, body mass index, left ventricular hypertrophy, persistently elevated blood pressure and, in some studies, female gender.[3]

The QT interval represents the time between ventricular depolarization and the ensuing repolarization. The QT-interval is a phase in an ECG, measured in milliseconds (ms) from the start of the QRS-complex to the end of the T-wave. Since the QT-interval varies depending on the heart rate (HR), the corrected QT-interval (QTc-interval) should be employed. There are numerous correction formulas available for this correction (Bazett, Fridericia, Framingham, Rautaharju, Hodges). Various studies have stated different definitions for prolonged QTc interval. The European medicines agency advises labelling the QTc-interval as prolonged when it is higher than 450 ms in adults and higher than 470 ms in adult females. Studies by Pasquier et al and Soliman et al recorded it had prolonged when it was ≥450 ms in males and ≥460 ms in females.[4,5]

Long QT intervals have been shown in clinical studies to potentially lead to sudden death and malignant ventricular arrhythmias. An increase in the QT interval may be an imbalance of sympathetic and parasympathetic nervous systems activity. An inequity in cardiac sympathetic function (increased or decreased) either shortens or lengthens the QT interval of the ECG.[4]

In a limited resources setting, the importance of accessible and accurate evaluative clinical and laboratory parameters which can aid to identify hypertensive patients with increased cardiovascular risk cannot be overstated. One tool for such screening is the QT interval, which measures the duration of ventricular depolarization and repolarization. Assessment and quantification of risk factors may assist in identifying patients at the highest risk for developing QTc interval prolongation and thus enable interventions to reduce mortality and morbidity. Hence, this study was initiated to estimate the prevalence of QTc prolongation among hypertensive individuals and also to assess the association of QTc prolongation with various co-morbidities.

METHODS

This cross-sectional study was conducted from May 2020 to October 2020 in Sri Manakula Vinayagar medical college, a teaching hospital in Pondicherry, India. The study was cleared by the institutional review board. Also, informed consent was obtained from all the study subjects.

The sample size was calculated using Open Epi software version 0.3. A sample size of 159 was arrived at by computing the percentage QTc prolongation in hypertensive patients to be 36.4% basis previous studies, with an absolute precision of 7.5% at a 95% confidence interval. A convenient sampling research methodology was adopted. All hypertensive patients coming to the department of general medicine were included in the study. Those patients who were critically ill, with known coronary artery disease, with renal failure, cardiac arrhythmias and with cardiac pacemakers were excluded from the study. Following a detailed history and clinical examination, socio-demographic and clinical findings were recorded. Age, gender, body weight, height, random blood sugar, lipid profile, serum urea, serum creatinine, heart rate, systolic and diastolic blood pressure and ECG were documented. According to joint national committee on prevention, detection, evaluation, and treatment of high blood pressure (JNC 7) blood pressure was recorded and classified. Blood pressure was recorded compliant with American heart association guidelines. Systolic blood pressure more than or equal to 140 and diastolic pressure more than or equal to 90 was recorded as uncontrolled hypertension. A resting ECG was obtained from the subjects using a 12-lead electrocardiograph, in accordance with American heart association. Patients and ECG lead-2 was used to measure the QT interval. QT interval was estimated by the tangent method. QTc in seconds was obtained by correcting the QT interval for heart rate using Bazett's formula. QTc ≥450 ms (males) and ≥460 ms (females) was considered as prolonged as per 2009 AHA/ACCF/HRS recommendations for the standardization and interpretation of the ECG.

Bazett's formula

$$QTc = QT \Big/ \sqrt{RR}.$$

The data was collected in a standardised manner and was analysed using SPSS (statistical package for the social sciences) version 21. Qualitative variables were expressed in percentage, while quantitative variables were expressed in means. Chi square test was performed as a test of significance.

RESULTS

The study consisted of 159 adult hypertensive patients who met the research criteria. The mean age of participants was 55.6 years (SD±6.76). Twenty-seven per cent of the subjects were in the 51-60 years age group (Figure 1). There were 103 males (64.4%) and 43 females (35.6 %) (Figure 2).

The majority (50%) of the study population had been hypertensives for less than 5 years, while 43% for 6-10 years and 4% for more than 16 years. QTc prolongation was noted in 52.5% of the population studied. QTc prolongation among poorly controlled hypertensive was

59% when compared to that of controlled hypertensive at 37.5% (Table 2). There was a statistically significant difference (p=0.01) between the groups. A comparison of risk factors with QTc is represented in Table 5. About 26% of the participants were smokers, 27% were alcoholics and 60% had co-existing diabetes mellitus. Of all the demographic and biochemical parameters evaluated diabetes and gender were found to have a statistically significant association with QTc prolongation (Table 3).

Table 1: Comparison of patient characteristics between HT control status.

Variables	HT control status				P value
	Good control		Poor control		
	Mean	SD	Mean	SD	
PR	84.88	11.89	83.49	14.04	0.55
SBP	120.21	8.69	156.2	7.84	<0.0001
DBP	80.63	4.7	97.25	8	<0.0001
S. urea	28.46	11.02	29.3	10.84	0.656
S. creatinine	1.15	0.42	1.16	0.11	0.815
TC	170.81	43.17	177.49	47.13	0.401
LDL	109.31	8.76	96.61	6.89	<0.0001
VLDL	31.85	6.12	30.99	11.04	0.613
HDL	35.19	3.46	34.16	0.18	0.002
TG	156.38	67.27	153,64	64.78	0.809
RBS	146.44	40.27	139.96	39.86	0.349

Table 2: Cross-tabulation HT control status with QTc prolongation.

HT control status	QTc prolonged	QTC not prolonged	Total	Chi square	P value
Good control	18 (37.5%)	30 (62.5%)	48	6.48	0.01
Poor control	66 (59%)	45 (41%)	111		
Total	84	75	159		

Table 3: Cross-tabulation risk factors with QTc prolongation.

Risk factors		QTC prolonged	QTC not prolonged	Chi square value	P value
Age	≤30	2	3	2.17	0.703
	31-40	5	7		
	41-50	16	12		
	51-60	26	18		
	≥61	35	35		
Sex	Male	64	39	13.06	0.004
	Female	20	36		
Smoking	Yes	21	21	0.7	0.72
	No	63	54		
Alcoholism	Yes	21	22	0.57	0.59
	No	63	53		
DM	Yes	58	31	3.84	0.05
	No	26	44		
HTN duration in years	<5	42	38	1.33	0.85
	6-10	36	33		
	11-15	2	3		
	≥16	4	1		
Hyperlipidemia	Yes	42	30	1.59	0.206
	No	42	45		

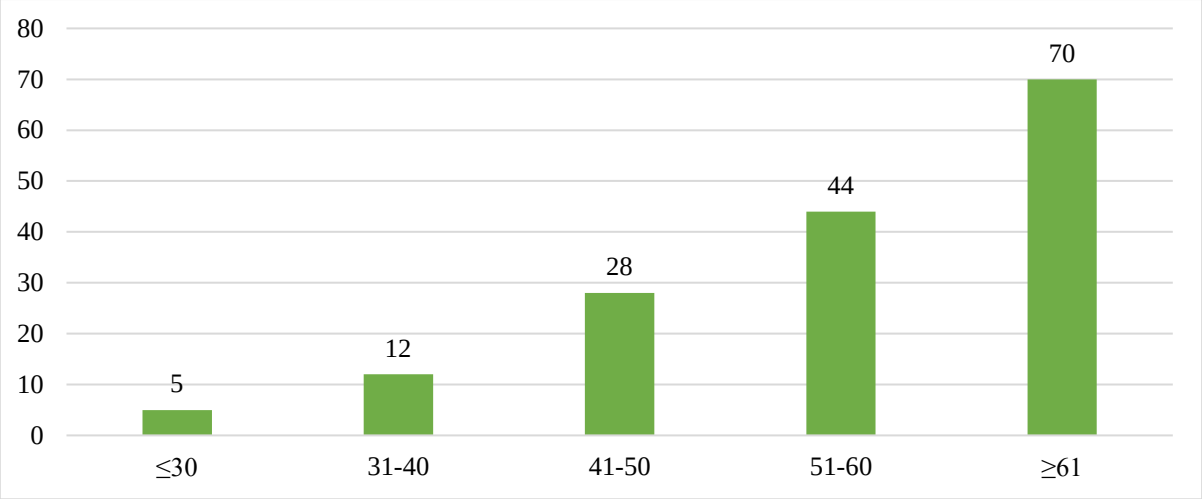

Figure 1: Age group distribution.

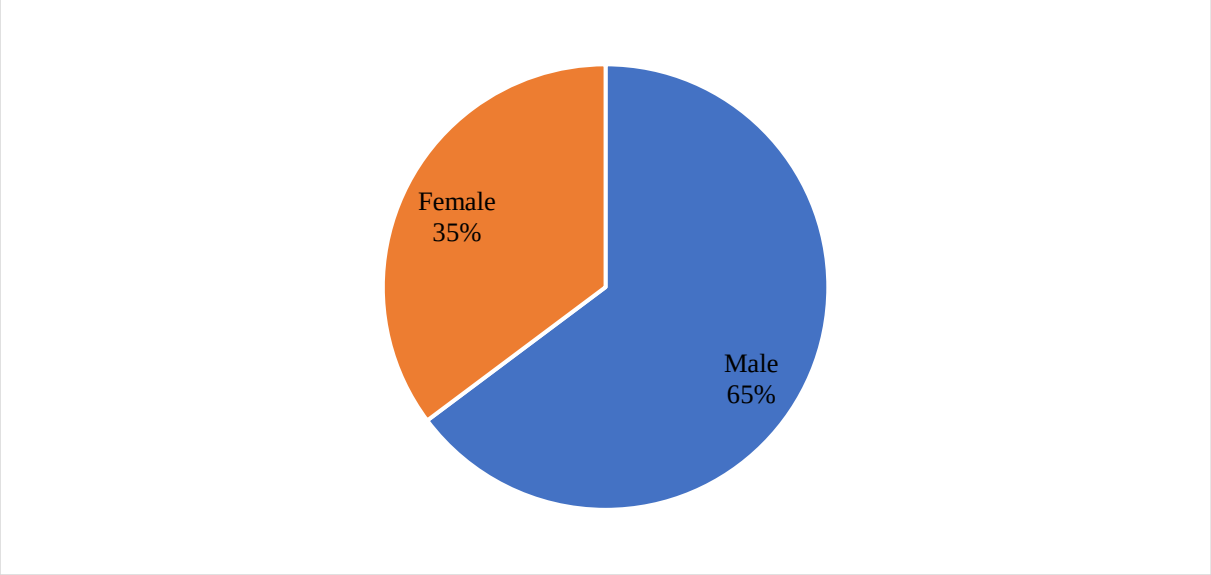

Figure 2: Gender distribution.

DISCUSSION

The AHA/ACC defines stage 1 hypertension as systolic BP ≥130 mm Hg or diastolic BP ≥80 mm Hg and stage 2 hypertension as systolic BP ≥140 mm Hg or diastolic BP ≥90 mm Hg. The major predisposing and predictive factor for cardiovascular events such as cardiac death, coronary heart disease, heart failure and ischemic or haemorrhagic stroke is hypertension. Being mostly asymptomatic, patients with hypertension were more likely to develop a variety of structural and functional cardiac changes including prolonged ventricular repolarization. It went overlooked until it was screened by a tool like the QTc interval which was a known predictive factor of cardiovascular events. Endless research was nevertheless required to fortify this analysis.[2,6-8]

Hence, this study aimed to estimate the prevalence of QTc prolongation among hypertensive individuals and also further evaluate the interrelationship of prolonged QTc with other co-morbidities.

The present study found that diabetes and gender were found to have a statistically significant association with QTc prolongation. Also, a statistically significant difference was noted in QTc prolongation among poorly controlled hypertensive and controlled hypertensive patients.

Various studies have researched along similar lines. A cross-sectional comparative study evaluated 140 adult Nigerian subjects with systemic hypertension along with 70 controls, to assess the epidemiology of QT interval abnormalities amongst recently diagnosed hypertensives

and the concomitant clinical correlates. Clinical and demographic characters and electrocardiographic parameters were matched between the two groups. The mean age of hypertensive subjects was 55.9±12.6. The prevalence of prolonged QTc in this study was 52.14%, which correlated with our study. The Nigerian study also noted that hypertensive patients with QT abnormalities had a significantly higher proportion of smoking than controls. In contrast to the present study, the Nigerian study found to be no significant gender association with QT abnormalities.

The Bremen diabetes study recruited 475 types 2 diabetic patients (age 55-75 years; 304 women, 171 men) and studied them from 1990-1991. Amongst others, the study assessed metabolic parameters, cardiovascular risk factors through routine tests. The purpose of this study was to compare the prediction of QTc interval prolongation and/or heart rate for cardiovascular mortality to traditional cardiovascular risk factors. QT intervals were measured with ECG and Fridericia's equation was used to obtain corrected heart rate. The multivariate analysis concluded that QTc interval prolongation (p=0.0008), elevated heart rate, serum creatinine, smoking and peripheral arterial disease at baseline were independent predictors for cardiovascular death. The study established that prolonged QTc time and elevated heart rate were strong predictors of cardiovascular death in type 2 diabetic patients and maybe superior to traditional cardiovascular risk factors. A similar relation between diabetes and QTc prolongation was noted in the present study.[10]

A study by Solanki et al conducted a case-control study in Gujarat, India and analysed the effect of disease duration, treatment and risk factors on QTc interval amongst young hypertensives having monotherapy with either calcium channel blocker or angiotensin-converting enzyme inhibitor. The study consisted of 142 hypertensives (60 males, 82 females) and blood pressure measurement and ECG was recorded. Using Bazett's formula, QTc was calculated. The study recorded that the average duration of hypertension was 5 years, the average age was 40 years and has poor blood pressure control. The study discovered that newly diagnosed hypertensives had significantly higher QTc values when compared to that of matched known hypertensive patients. Hypertensives who smoked, those with co-existing diabetes and those with a positive family history had significantly higher QTc values. The results were in tandem with the present study with respect to diabetics, but not with of smokers.[2]

A systematic review aimed to review and evaluate the evidence for different risk factors like demographics, comorbidities, electrolytes, medication associated with QTc-prolongation and their association with prolonged QTc. The researchers included ten observational studies comprising 89,532 patients and data was extracted compliant with the review strategy. In contrast to the present study, this review found low evidence of significance with diabetes. But, similarity in results was noted with hyperlipidaemia and alcohol abuse.[5]

Another cross-sectional case study compared 142 hypertensives on monotherapy and 72 matched normotensives. The group aimed to study the association of QTc in HTN with age, gender and pressure control and also assess the prevalence of QTc prolongation in the Gujarati population studied. Twenty-nine hypertensives had coexisting diabetes mellitus. The prevalence of abnormally prolonged QTc among hypertensive was deduced to be 41%, which was lesser than that of the present study (52.5%). The study concluded that a high prevalence of prolonged QTc was noted in monotherapy hypertensive patients with poor pressure control and a positive correlation with female gender and age was noted.[11]

The results of another 10-year longitudinal follow up study were in line with the present study. It found that prolonged QTc interval was frequent in type 1 diabetic patients and was also a strong predictor for mortality in patients.[12]

Shouten et al evaluated 3091 patients, in the age group of 40-65 years with no evident cardiovascular disease. They were followed for 28 years. They found that QTc interval greater than 420 ms was associated with all over mortality in both genders and there was a significant association with diastolic blood pressure in both the genders.[13]

Takebayashi et al evaluated the co-relationship between the QTc and blood pressure, serum lipid concentrations, haemoglobin A1C concentration and duration of diabetes in addition to its association with the combined intimal-medial thickness of the carotid artery. They concluded that QTc had a significant correlation with systolic and diastolic blood pressure.[14]

Another Chinese study assessed 1480 hypertensive patients to evaluate the connection between the length of QTc and blood pressure. It established a positive association between QTc and blood pressure in both men and women mean. However, in contrast to the present study, the Chinese study found that QTc was longer in females than in males.[4]

Limitations

The study was limited by small sample size, manual measurement of QTc interval and presence of confounding factors which cannot be negated.

CONCLUSION

A high percentage of hypertensives in this study exhibited a prolonged QTc. Notwithstanding the limitations of the study, a positive correlation between diabetes, gender and prolonged QTc was established. Considering the high prevalence of hypertension in India, routine blood pressure monitoring in adults is a mandatory part of patient

assessment. Similarly, QTc screening also should be incorporated into routine practice as it carries the advantage of being real-time, cost-effective and requires no expertise. The screening and diagno-prognostic role of this marker cannot be trivialised, as it can serve as a valuable asset to identifying at-risk subjects and initiating appropriate preventive therapy for cardiovascular events.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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