ORIGINAL ARTICLE

Corrected QT Interval in Hypertension Seen in a Tertiary Health Institution in North Central Nigeria

C. M. Chundusu, S. S. Danbauchi, B. N. Okeahialam

Department of Medicine, Jos University Teaching Hospital, PMB 2076 Jos, Nigeria

ABSTRACT

Introduction: QT abnormality and hypertension are both causes of sudden cardiac death. Quite a number of therapeutic agents being introduced have effect on QT interval. **Methodology:** A retrospective study of QT corrected (QTc) was undertaken in the Jos University Teaching Hospital considering gender and presence of hypertension. **Results:** A total of 1004 results were analyzed, the age ranged from 18 to 70 years, 637 females (259 hypertensive, 378 non-hypertensive) and 367 males (142 hypertensive and 225 non-hypertensive). Male mean age was 49.78 ± 16.64 years and female mean age was 45.68 ± 12.20 years ($P = 0.001$). QTc did not correlate with age (r^2 0.03). Male mean QTc was 431.57 ± 46.29 ms (hypertensive) and 427.95 ± 31.30 ms (non-hypertensive), $P = 0.207$. Female QTc values were 438.15 ± 35.51 ms (hypertensive) and 436.14 ± 48.13 ms (non-hypertensive), $P = 0.046$. **Conclusions:** Although QT generally gets prolonged with age poorly, female gender has a relatively higher QTc even more so when hypertensive.

Key words: Gender, hypertension, QT corrected

INTRODUCTION

The QT interval is a measure of time between the start of Q wave and the end of T wave on an electrocardiogram (ECG). It represents both electrical depolarization and repolarization of the ventricles. The corrected QT interval adjusts the QT interval correctly for heart rate extremes. There are a variety of formulae used for this correction, the Bazett's correction formula is the most commonly used formula; however, the Fridericia and Framingham correction formulae are said to be better for QT correction (QTc), significantly improving prediction of mortality.[1] Other formulae are Hodges and Rautaharju.

Recent molecular evidence in large cohorts implicates inherited cardiac channelopathies (mostly the long QT syndrome [LQTS]) in 35% of sudden unexplained deaths in the young and in 9% of cases of sudden infant death syndrome.[2] The severity of the clinical manifestations of LQTS is highly variable.[3]

An LQTS may also be acquired by drugs[4] (Class IA or III antiarrhythmic drugs, psychotropic drugs, antimicrobials,[5] and anti-malaria - Artesunate), electrolyte abnormalities,[6] hypothermia, toxic substances,[7] and central nervous system injury (subarachnoid hemorrhage).[4] It has also been reported in intensive weight reduction programs that involve the use of liquid protein diets and in anorexia nervosa. Lithium carbonate can prolong the QT interval and has been reported to be associated with an increased incidence of sickle cell disease (SCD) in cancer patients with preexisting heart disease. Drug interactions have been recognized as a mechanism of prolongation of the QT interval and torsade de pointes.[8,9] In acquired LQTS, as in the congenital form, "torsade de pointes" is the specific arrhythmia that triggers or degenerates into VF.[4]

Less commonly, inherited short QT is seen but could be difficult to identify in infants and very young children.[9] Secondary causes of a short QT (SQT) interval are hypercalcemia, hyperkalemia, hyperthermia, acidosis, and digoxin therapy.

Address for correspondence:
C. M. Chundusu, Department of Medicine, Jos University Teaching Hospital, PMB 2076 Jos, Nigeria.
E-mail calebchundusu@yahoo.com

Uncertainties still exist about the clinical management of SQT syndrome, largely due to the small number of case findings.

Disparity among QT intervals in various ECG leads referred to as QT dispersion is generating interest in ECG study, the greater the difference between maximum and minimum QT intervals (increased QT dispersion) the greater the variability in myocardial repolarization.[10,11] An increased dispersion has been proposed as a marker of increased arrhythmia risk after myocardial infarction and is a marker of acute ischemia with atrial pacing.[10] The practical usefulness of QT dispersion measurements in patients with coronary syndromes and certain other cardiac pathologies is a focus of ongoing investigation and debate.

Hypertension is a common disease that has recently been seen to associated with LQTs.[11-13] Elevated blood pressure,[13] hypertensive heart disease,[11,12] and bundle branch block are associated with LQT. In a society like ours where most individuals do not actually know they have hypertension and when they do, only a few access health care. Furthermore, much fewer hypertensive has optimal blood pressure control.[13] These individuals are exposed to various pharmacological agents that have effects on the QT interval. In this study, QTc value was observed considering gender and diagnosis of hypertension irrespective of care given.

METHODOLOGY

The study was a retrospective analysis of ECG taken in patients <18 years of age at the Jos University Teaching Hospital during a 3-month period between January 2018 and April 2018. All ECGs were standard 12-lead resting ECGs (25 mm/s paper speed, 10 mm/mV amplitude), recorded by GE medical system information technology (MAC 1200ST v 1.2 ECG machine).

Data extracted were age, sex, indications, heart rate, PR interval, QRS, and QTc. QT was corrected using the inbuilt Bazett's formula. ECGs were visibly inspected for quality. Approval was obtained from the Ethical Committee of the Jos University Teaching Hospital.

Analysis

Data were analyzed with Epi Info version 7.2.1.6. All continuous variables were given as mean ± standard deviation (SD). Means are compared using Student's *t*-test, $P = 0.05$ was considered statistical significance.

RESULTS

A total of 1004 were included in the analysis 624 (62.3%) females and 380 (37.7%) males. The age range varies from 18 to 70 years (male 49.78 ± 16.64 years and female 45.68 ± 12.20 years, $P = 0.001$). There were 389 (38.7%) (246 females and 143 males) diagnosed hypertensive and 616 (62.3%) (379 females and 237 males) non-hypertensive subjects. Table 1 summarizes the mean ± SD of gender considering hypertension or otherwise. The mean and SD of corrected QT was 435.58 ms and 21.43 in the whole subjects. QTc (male 438.99 ± 43.50 ms and female 429.35 ± 37.80 ms, $P = 0.004$) the interquartile QTc ranges considering gender and hypertension is shown in Figure 1. The gender QTc differences are shown in Table 2. There was a positive correlation between age and QTc with r^2 0.03.

DISCUSSION

Reports from Kano (north-east) Karaye[12] and Lagos (south-west) Ale *et al*.[11] Nigeria have initially documented the relative increase in QTc in hypertensive individuals. Similarly, reports from Asia (India)[13] and other continents have also reported this correlation. This is a non-racial finding. Hypertension is a common disease with a local prevalence of 35–45% in our environment[12,13] diagnosed only when blood pressure is taken and noted to be persistently high. Hypertensive subjects made up about 38% of the study population. The proportion of which might have been underestimated. The presence of undiagnosed cases in non-hypertensive group may be

Table 1: Mean±SD of ages of subjects considering gender and hypertension

Gender	Hypertensive	Non-hypertensive	*P*-value
Male	52.02±16.40	49.78±16.64	0.207
Female	48.01±14.58	45.68±12.20	0.001*w

*Significant difference statistically. SD: Standard deviation

Table 2: Mean±SD QTc of subjects considering gender and hypertension

Gender	Hypertensive	Non-hypertensive	*P*-value
Male	431.57±46.29	427.95±31.30	0.372
Female	443.14±35.51	436.15±48.13	0.046*

*Significant difference statistically. SD: Standard deviation, QTc: QT corrected

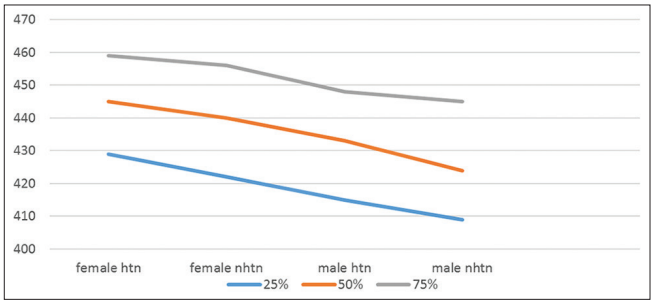

Figure 1: Interquartile ranges of QT corrected of subjects considering gender and hypertension. htn: Hypertensive, nhtn: Non-hypertensive

significant, and for the fact that some cases indicated another diagnosis as reasons for ECG test. We expected a higher proportion because we expect some bias toward recruiting patients with cardiovascular diseases.

As we grow old, it is natural that our blood pressure signifying increases cardiovascular risk, but this study has shown that age had little or no effect on QTc statistically. To further buttress on this fact, QTc was lower among the male who had a higher mean age than the female gender. The difference in QTc was more significant among the female gender, suggesting more of famine factor. Perhaps, estrogen may play a role in expressing this difference. Elderly, women are likely to be hypertensive without the cardiovascular protective effect of estrogen, and younger women are likely to be normotensive, so QTc will likely be higher because of hypertension rather than age. Studies have shown that there appear to be differences in ventricular repolarization and beta-adrenoceptor blockade modulation, due to a gender-related factor[14] not well defined. Parameter assessing distribution in statistics, mean and interquartile range of QTc showed relatively higher QTc in female gender, a finding that is consistent with accepted documented and reports. Universal acceptance of the differences in QTc with gender has resulted into accepting different cutoff mark for diagnosing abnormally prolonged QTc in human. QTc is universally and is considered higher in human female gender.[11-13]

We further observed that individuals with hypertension had a relatively higher QTc than those without hypertension in the same gender. There is no clear-cut reason why hypertension causes LQT, but a number of factors have been postulated and are being studied. Hypokalemia,[6] anemia,[15] and QT dispersion have been reported as possible factors. High blood pressure in animal study was notice to cause LQT more than the presence of structural heart changes (LVH) in hypertensive heart disease.[16] Human study is on-going.

There are a lot of pharmaceutical agents introduced into the market for the treatment of various ailments that prolong QT interval, some of which are likely to augment each other to further prolong QT. Antimalarial (Artesunate) is commonly prescribed, antibiotic (erythromycin), antipsychotic (fluoxetine), anti-arrhythmic (amiodarone), etc., are all administered not considering if an individual is hypertensive or not. Halfan (halofantrin) has been withdrawn in some communities because of the SCD it can cause due to prolongation of the QT interval. Coadministrations of these substances could prolong QT and cause "torsade des pointes"[17,18] and VF.

Limitations

A limitation of the study was the fact that hypertension was likely underestimated because only one indication per patient was used for the analysis and secondary or background diagnosis of hypertension was not captured. The paper speed on ECG used was at 25 mm/s, a speed of 50 mm/s gives a more appropriate time measure, and a test of interobserver variability was not done. The Bazett's correction formula was used for analysis, and some researchers considered it a less favorable formula for QTc.

CONCLUSIONS

We observed that QT duration was poorly associated with increasing age and generally longer in female gender due to an unknown mechanism. Hypertension appears to prolong QT interval in an undefined manner, particularly in female.

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