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IMPACT OF BODY MASS INDEX ON CORRECTED QT INTERVAL IN PREHYPERTENSIVES

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ABSTRACT

Obesity and hypertension are the major cardiovascular risk factors. Increased QT interval is shown to be associated with various cardiac diseases. The early impact of "prehypertension" on QTc and the contribution of BMI to sympathovagal imbalance are the areas that are least explored. So the objectives of the study were to assess the nature of autonomic dysfunction in prehypertensives by measuring the QTc interval and to evaluate the contribution of BMI to sympathovagal imbalance in the genesis of prehypertension. This was a cross sectional study involving 150 medical students, belonging to age group 18-25. ECG was recorded among all the students and their QTc was measured. Based on their blood pressure recordings and BMI, selected students (n=96) were divided into four groups: normotensives with normal BMI (group 1), normotensives with higher BMI (group 2), prehypertensives with normal BMI (group 3) and prehypertensives with higher BMI (group 4). The level of significance between the groups was tested by one-way ANOVA. The association between QTc and BMI with various blood pressure parameters was assessed by Pearson correlation. The independent contribution of various factors such as age, BMI, BHR, SBP and DBP to sympathovagal imbalance was assessed by multiple regression analysis. QTc was significantly increased among the prehypertensive group compared to the normotensives and the magnitude of these changes were more prominent in subjects with higher BMI compared to that of normal BMI. QTc, an indicator of sympathovagal balance had significant correlation with BMI (P = 0.000) and systolic blood pressure (DBP) (P = 0.002) in prehypertensives. BMI was found to be an independent contributing factor to QTc prolongation (P = 0.0003) in prehypertensives. The significant prolongation of QTc interval among the prehypertensives compared with normotensives indicate the altered autonomic homeostasis and a higher risk of arrhythmias in them, suggesting lifestyle modification at a younger age to reduce the cardiovascular risk.

KEYWORDS: **QTc interval, Body mass index, Prehypertension, Sympathovagal imbalance**

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INTRODUCTION

The epidemic of rapid socio-economic and nutritional transition in the past few decades poses a great threat to the health of Indian nation, documenting a significant hike in the prevalence of overweight and obesity among all age groups. Especially, the Asian Indians have been reported to be at significantly greater risk of developing diabetes, hypertension and heart diseases[1]. Obesity is being acknowledged as one of the most imperative risk factors for the development of hypertension[2]. Like hypertension, prehypertension-(systolic blood pressure [SBP] 120–139 mmHg and/or diastolic blood pressure [DBP] 80–89 mmHg), a novel blood pressure category of "The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC 7 report" [3], is also associated with increased cardiovascular risk [4]. Persons with pre-hypertension are at a greater risk of developing hypertension [5]. Several mechanisms are implicated to link obesity and hypertension [6] but the exact patho-physiological cause for cardiovascular dysfunction in prehypertension have not yet been fully elucidated. Recently sympathovagal imbalance, owing to sympathetic over activity and vagal withdrawal has been proposed as the fundamental cause for prehypertension [7] and obesity [8] associated cardiovascular diseases. There are various available measures for assessing the cardiac autonomic dysfunction like heart rate variability, QT interval and left ventricular hypertrophy [9]. The simplest and informative one is the QT interval, an electrocardiographic (ECG) measure that is calculated from the beginning of the QRS complex to the end of T-wave and averaged over 3 to 5 beats in a single lead representing ventricular depolarization and repolarization. The QT interval is influenced by heart rate and is usually inversely related but this correlation is lost at high and low heart rates [10]. So, QT interval must be corrected for rate for which the Bazett's square root formula is considered as the gold standard [11]. Studies reveal that QTc is affected by the autonomic nervous system, independent of heart rate [10] and been used to evaluate autonomic sympathovagal balance in healthy subjects [12]. Although the association between QT interval among the hypertensives and obese individuals has been vastly and independently elucidated, to our knowledge, there is no literature concerned with sympathovagal imbalance assessed using QTc interval in younger age group linking BMI with the causation of prehypertension. Owing to paucity of data regarding the QTc interval variations in young prehypertensives, the present study was aimed at investigating the nature and magnitude of autonomic imbalance and the role of BMI as an independent contributor to the genesis of autonomic dysfunction in prehypertensives.

METHODOLOGY

This was a cross-sectional study conducted in the department of Physiology, Sri Manakula Vinayagar Medical College and Hospital from June 2014 – February 2015. After obtaining approval from the Institutional Ethical Committee, all 150 medical students in the age group of 18-25 years entering the first year MBBS course, undergoing the general health check up programme organized by the institution were recruited for the study. Subjects with systolic blood pressure >140 mmHg, Diastolic blood pressure > 90 mmHg, subjects with ongoing medical illness or any drug treatment were excluded from the study. As the level of physical fitness is a major determinant of vagal tone [13], subjects performing regular athletic activities and body-building exercises were also excluded from the study. Informed written consent was obtained from all the study participants. A detailed review of medical history through structured questionnaire and physical examination were performed. All baseline characteristics and related anthropometrics including age, height, weight and BMI were acquired from the study participants. Blood pressure was measured in the right arm in the sitting position using a standard mercury sphygmomanometer after a 10-minute rest period. Three measurements were taken at 5 minutes interval and the mean of three measurements was considered for analysis. After considering the exclusion criteria, 96 subjects were selected for the study and were classified into following four groups based on their level of systolic and diastolic blood pressure as per JNC-7 classification [3] and the level of BMI as per the recommendation of world health organization (WHO) on BMI for Asian population [14].

Group1: Normotensives with normal BMI (n=26): Healthy subjects having systolic BP 100–119 mm Hg, diastolic BP 60–79 mmHg, and BMI 18.5-22.

Group2: Normotensives with higher BMI (n=21): Healthy subjects having systolic BP 100–119 mm Hg, diastolic BP 60–79 mmHg, and BMI 23 or above.

Group3: Prehypertensive subjects with normal BMI (n = 17): Healthy subjects having systolic BP 120–139 mm Hg, diastolic BP 80–89 mmHg, and BMI 18.5-22.9.

Group 4: Prehypertensive subjects with higher BMI (n = 32): Healthy subjects having systolic BP 120–139 mmHg, diastolic BP 80–89 mmHg, and BMI 23 or above. 12 lead automatic ECG recording (using RMS ECG machine, India) was obtained from all the study participants. ECG paper speed was kept at 25mm/sec. Heart rate corrected QT interval (QTc) was measured using Bazett formula $QTc = QT / \sqrt{RR}$.

Statistical Analysis

SPSS version 16 (SPSS Software Inc., Chicago, IL, USA) was used for statistical analysis. All the data were expressed as mean ± SD. Statistical significance within the groups was done by one-way ANOVA and post-hoc by Tukey-Krammer test. The association between QTc and BMI with basal heart rate, SBP, DBP and Rate pressure product (RPP) was assessed by Pearson correlation analysis. The independent contribution of various factors such as age, BMI, BHR, SBP and DBP to sympathovagal imbalance (QTc) in prehypertensives was assessed by multiple regression analysis. The p values less than 0.05 was considered statistically significant.

RESULTS

There was no significant difference in age among all the four groups (p=0.9) (Table 1). There was significant difference in the body weight and BMI when Group 1 (normotensives with normal BMI) were compared with

Group 2 (normotensive subjects with higher BMI) and group 4 (prehypertensives with higher BMI). Basal Heart rate and SBP reported a significant difference between the normotensives (Group 1 and Group 2) and the prehypertensives (Group 3 and 4). Likewise, DBP and RPP of group 3 and group 4 showed a significant difference compared to group 1 and group 2. The QTc values among the group 2 (normotensive subjects with higher BMI) showed a significant difference when compared to group 1(normotensives with normal BMI). The QTc value of the group 3 showed an increase compared to group 1 but the difference was not statistically significant. The group 4, QTc showed a significant difference when compared with group 1 and group 2. Pearson correlation analysis was done to assess the strength of association of various factors with QTc and all the cardiovascular parameters showed significant correlation (Table 2). In all the prehypertensive subjects taken together, QTc showed significant correlation with SBP and BMI. In the same way BMI showed significant correlation with SBP and QTc (Table 3).Multiple regression analysis was carried out to assess the independent contribution or link of various parameters to QTc. BMI, BHR, SBP and RPP were found to have significant impact on QTc (Table 4). BMI as an independent factor had maximum contribution (p =0.0003) to QTc followed by SBP (p=0.002).

Table 1

Age, anthropometric and basal cardiovascular parameters in different groups.

	Group1 (n=26)	Group2 (n=21)	Group3 (n=17)	Group4 (n=32)	P value
AGE (Yrs)	18.15±0.54	18.1±0.3	18.22±0.79	18.12±0.49	**0.91**
Body weight (Kg)	54.07±7.47	68.05±10.64*	51.83±8.4@	83.38±19.52 ***@$**	<0.00
BMI (Kg/m^2)	20.96±1.93	25.41±2.3*	20.19±1.45@	29.78±4.34 ***@$**	<0.00
BHR(/min)	75.31±6.58	77.095±6.54	87.59±4.89***@**	88.03±16.92*@	<0.00
SBP (mmHg)	108.77±5.79	110.43±6.27	124.06±3.38 ***@**	129.31±6.70 ***@$**	<0.00
DBP (mmHg)	67.35±5.97	66.29±7.5	76.059±5.27 ***@**	76.22±8.43 *@	<0.00
RPP (mmHg/min)	82.08±9.84	85.36±10.6	107.88±6.17 ***@**	114.38±24.85*@	<0.00
QTc (msec)	390.9±12.89	408.24±18.6**	403.47±20.5	420.25±22.24 *@	<0.00

Data presented are mean ± SD

Group 1: Normotensive subjects with normal BMI; Group 2: Normotensive subjects with higher BMI; Group 3: Prehypertensive subjects with normal BMI; Group 4: Prehypertensives with higher BMI. The * mark indicates comparison between group 1 and other groups, @ sign indicates significant difference between group 2 with group 3, 4 and $ sign indicates comparison between group 3 and group 4.

Table 2

Pearson correlation of QTc with age, BMI, basal heart rate, blood pressure and rate pressure product

	QTc	
	r	**p**
Age	0.09	0.36
BMI	0.48	0.000*
BHR	0.28	0.006*
SBP	0.48	0.000*
DBP	0.23	0.02*
RPP	0.38	0.000*

The p values less than 0.05 was considered significant.

Table 3

Pearson correlation of QTc and BMI with various parameters of all prehypertensive subjects (n=49)

	QTc		BMI	
	r	**p**	**r**	**p**
Age	0.14	0.36	0.25	0.08
BHR	0.11	0.44	0.11	0.45
SBP	0.29	0.04*	0.49	0.000*
DBP	-0.31	0.83	0.09	0.51
RPP	0.16	0.27	0.25	0.07
BMI	0.36	0.01*	-	-
QTc	-	-	0.36	0.01*

The p value less than 0.05 was considered significant

Table 4
Multiple regression analysis of QTc (as dependent variable)with various other associated factors (as independent variables)

Independent variables	Standard regression coefficient	95% CI		P value
		Lower bound	Upper bound	
BMI	3.086	1.45	4.73	0.0003
BHR	2.656	0.20	5.11	0.03
SBP	2.617	0.96	4.27	0.002
DBP	-0.404	-1.03	0.22	0.20
RPP	-2.178	-4.19	-0.17	0.04

The p value less than 0.05 was considered significant

DISCUSSION

In the present study QTc was significantly increased among the prehypertensives with higher BMI followed by normotensives with higher BMI and prehypertensives with normal BMI, indicating the crucial role of BMI in the prolongation of QTc. Prolonged QTc indicates sympathovagal imbalance. Studies report that sympathetic stimulation results in heart rate corrected QT interval (QT_C) prolongation, whereas parasympathetic activation protects against the lengthening of heart rate corrected QT interval (QT_C) [15]. Pal *et al* measured the heart rate variability and observed sympathovagal imbalance among the prehypertensives stating vagal withdrawal associated with sympathetic overactivity among the prehypertensives [7]. He also concluded that BMI could be a major predictor of sympathovagal imbalance in prehypertensives [8]. In the present study we reported a similar change in the form of prolonged QTc among individuals with prehypertension and higher BMI.There have been many outstanding reviews on the prognostic importance of increased QTc in clinical conditions [16, 17] and is viewed as an independent risk factor for sudden cardiac death [18] but till date no report is available on the nature of alteration in sympathovagal balance that tilts towards decremented vagal response in prehypertensives assessed using QTc. QTc was considered prolonged when it was more than 440 ms in agreement with the criteria commonly used in the literature [19]. It is observed that even small elevations in BP, as seen with prehypertension, can have detrimental effects on hemodynamics and cardiovascular structure and function in young adults [20]. Another study reports progressive left ventricular remodeling from normal, prehypertension to hypertension [21]. Increased QT interval duration is associated with the risk of sudden cardiac death in the hypertensive population, even among individuals without clinically recognized cardiac disease [22]. The mechanism underlying QT interval prolongation among the hypertensive subjects is multifactorial and includes cardiomyocyte hypertrophy, increased left ventricular mass, with consequent alterations in left ventricular transmural dispersion of the repolarization, as well as changes in autonomic nervous system tone in patients with hypertension, and less likely a mechanoelectrical feedback [23]. Thus, prolonged QTc in prehypertensives indicates left ventricular remodeling, and could also be used as a predictive tool for the future development of hypertension in these subjects. From the present study the precise cause for the sympathovagal imbalance in prehypertensive subjects cannot be perfectly ascertained. Prehypertensive with normal BMI reported to have increased QTc but was not statistically significant. The probable reason may be that the subjects belonged to younger age group and so the effects of prehypertension were less pronounced. On the other hand individuals with prehypertension and increased BMI reported a statistically significant QTc prolongation. Nevertheless, BMI could be a probable factor for the causation of SVI as it was significantly correlated with the QTc (Table 3). Moreover, BMI was highly correlated to SBP (Table 3). In addition, BMI was found to be an imperative contributor to SVI in as it was found to have independent correlation with QTc (Table 4) as determined by multiple regression analysis. Increased adiposity could be a crux factor behind the development of prehypertension in susceptible individuals as obesity has been reported to be associated with increased sympathetic and decreased parasympathetic activity [24]. Though several mechanisms are explained behind obesity induced sympathetic nervous system activation it is in part by increased leptin, stimulation of pro-opiomelanocortin (POMC) neurons, and subsequent activation of the melanocortin 4 receptors (MC4R) in the central nervous system [25]. Rate Pressure product is a valuable marker of the oxygen requirement in the heart and an important indicator of ventricular functional status and is described as an index to assess the sufficiency of coronary perfusion and the competence of myocardium in deriving the required O2 at rest and under stress [26]. RPP was reported to be significantly increased among the prehypertensive group indicating the increased myocardial energy expenditure in them and thus posing a greater risk of cardiovascular dysfunction.Though there are limitations in the present study, that we have not carried out the direct assessment of sympathetic activity, not evaluated the cardiac functions, gender differences not considered and the sample size was moderate, the present study emphasizes the apparently healthy prehypertensive individuals to improve their vagal tone.

CONCLUSION

In the present study QTc was significantly prolonged among the prehypertensives, which was highly pronounced among the subjects with higher BMI and less in subjects with normal BMI. BMI reported to have an independent role in causing QT prolongation. This reveals that prehypertension may lead to altered autonomic homeostasis. QTc prolongation is indicative of altered ventricular repolarisation and thus posing a higher threat of ventricular arrhythmias in future. Therefore, we suggest that, QTc assessment, a non invasive, economical and reproducible index of myocardial instability, can be used as an incentive tool by clinicians for screening alterations in sympathovagal balance. Further the present study also lays out the importance of regular blood pressure screening among

young individuals so that earlier lifestyle modifications can be carried out to prevent hypertension and cardiovascular dysfunction.

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CONFLICT OF INTEREST

Conflict of interest declared none.