ABSTRACT

Background: C-reactive protein (CRP) is a systemic inflammatory marker used extensively. QTc interval represents both ventricular depolarization and repolarization. Hypertension is one of the foremost leading causes of morbidity and mortality globally.

Objectives: To explore the relationship of systolic blood pressure with QTc interval and CRP levels. Likewise to investigate the association of diastolic blood pressure with QTc interval and CRP levels.

Materials and Methods: The study was carried out on 100 randomly selected subjects in the age group of 20-45 years. Both genders were included. Hypertensive subjects on treatment were also included. Three records of blood pressure in the supine position were obtained with 2 minute interval between each and average was considered. QT interval and RR interval were measured from standard 12 lead electrocardiogram (ECG). Tangent method was used for QT interval and later it was corrected for heart rate to arrive at QTc interval using Bazett’s formula. CRP levels were obtained using high sensitivity (hs-CRP) assay kits.

Results: There was a positive and significant association for systolic blood pressure with both QTc and CRP. Likewise we also found a positive and significant association for diastolic blood pressure with both QTc and CRP.

Discussion: The inflammatory modulatory processes are altered in hypertension, thereby increasing CRP levels. CRP increases endothelin-1 and reduces nitric oxide leading to vasoconstriction and hypertension. Further CRP causes autonomic imbalances by increasing sympathetic activity that lead to hypertension and indirectly prolonging QTc interval. QTc interval is also lengthened by left ventricular hypertrophy as a complication of hypertension.

Conclusion: Hypertension with left ventricular hypertrophy can cause cardiac arrhythmias and sudden cardiac death. This may be prevented by early detection of high risk hypertensive subjects or even those prone to develop hypertension using QTc and CRP indicators. Further these markers are cheap and widely used and they provide valuable diagnostic and prognostic features especially in developing countries like India.

KEYWORDS: systolic blood pressure, diastolic blood pressure, QTc interval, CRP levels, high sensitivity-CRP, hs-CRP, hypertension.

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mortality worldwide is hypertension [2]. Left ventricular hypertrophy which occurs as one of the complications of hypertension may cause fatal cardiac arrhythmias and sudden cardiac death. This can occur even in under control hypertensive subjects due to left ventricular hypertrophy.

In a standard 12 lead electrocardiogram (ECG), the duration between the start of Q wave and the end of T wave is termed the QT interval. It represents both the ventricular depolarization and repolarization. The autonomic discrepancy between cardiac sympathetic and parasympathetic supply lengthens the QT interval, the sympathetic causing and parasympathetic preventing the delay [3]. QT interval is corrected for heart rate (QTc interval) using Bazett’s formula. QTc interval when extended may be due to cardiac arrhythmias especially in hypertensive patients with left ventricular hypertrophy [4]. QTc interval is generally prolonged in women, and are more predisposed to cardiac arrhythmias as their QTc intervals are generally lengthier than men [5].

C-reactive protein (CRP) is an acute phase protein and an indicator of systemic inflammation. It is produced in the liver, Interleukin-6 being the stimulus. Some studies have shown elevated levels of CRP in hypertensive patients while others state that increased CRP levels lead to the development of hypertension [6]. Elevated CRP levels increases endothelin-1 and reduces nitric oxide, leading to vasoconstriction and hypertension [7]. Some consider hypertension to be an inflammatory disorder. Inflammation drives neuro-endocrine factors that cause non-structural cardiac dysfunction [8].

This contributes to prolonged ventricular repolarization. CRP levels at low plasma concentrations in the absence of acute infection or inflammation can be estimated by high sensitivity CRP (hs-CRP) assays. CRP may also help in detecting the first coronary heart event [9].

The present study tries to explore the relationship of blood pressure with CRP levels and QTc intervals. QTc interval is viewed to be helpful in screening hypertensive patients [10].

A clear consensus on this association has not been unambiguous [11]. There is scarcity of information investigating the association of CRP, blood pressure and QTc intervals particularly from the population of south India.

**AIM AND OBJECTIVES**: To study the association of blood pressure with CRP levels and QTc intervals.

1. To investigate the relationship of systolic blood pressure with QTc intervals and CRP levels.
2. To explore the relationship of diastolic blood pressure with QTc intervals and CRP levels.

**MATERIALS AND METHODS**

A cross-sectional study was carried out in our institute. 100 willing subjects were randomly selected. The sample included both men and women. Even hypertensive subjects were included in the study. The subjects belonged to the age group of 20-45 years to avoid coexisting factors and diseases other than hypertension. Alcoholics, smokers, tobacco chewers were excluded. Those suffering from any active/chronic infections, inflammations, neoplastic disorders, diabetes mellitus, thyroid disorders, liver disease were excluded from the study. Subjects taking drugs that may alter the QTc interval and/or CRP levels, and those taking antibiotics, anti-inflammatory, corticosteroids, postmenopausal hormone replacement therapy and subjects with CRP > 10 mg/dl were also excluded.

Blood pressure was recorded with the patient in the supine position. The subject was required to rest 10 minutes prior. Three records with two minute interval between each were carried out and the average was considered for data analysis. First the reappearance of the radial pulse by palpatory method indicated the approximate systolic blood pressure. Next systolic blood pressure (phase I of Korotkoff sounds) and diastolic blood pressure (phase IV/V of Korotkoff sounds) were recorded by auscultatory method.

Subjects were required to undergo a standard 12 lead electrocardiogram (ECG) recording. Lead II record in which the T wave is more unambiguous was used to measure the QT interval and RR interval [3]. QT interval (in seconds) is from
the start of Q wave (or R wave) till the end of T wave. QT is measured by the tangent method. A tangent along the steepest slope of the T wave limb is drawn which touches the baseline. This junction of the tangent with the baseline provides the end of QT interval. RR interval is from one R wave peak to the next successive R wave peak. QT interval is influenced by the heart rate. Hence QT interval is corrected for heart rate using Bazett’s formula [3]. Bazett’s formula is QT interval over the square root of RR interval (in seconds). If the heart rate was <60, QT was not corrected. QTc interval of >450 ms in males and >460ms in females were viewed to be abnormally extended. CRP levels were estimated using high sensitivity CRP (hs-CRP) assay kits. 

Institutional Ethical Committee approvals were obtained prior to the study. The purpose of the study was explained to the subjects and informed written consents were obtained from all the willing subjects. Pearson’s correlation test was performed to analyze the data.

RESULTS

Table 1: Mean±SD of measured variable.

| Variable                      | Mean±SD |
|-------------------------------|---------|
| Systolic blood pressure (SBP) (mm Hg) | 138.4±24.78 |
| Diastolic blood pressure (DBP) (mm Hg) | 84.9±13.39 |
| QTc interval (msec)           | 386.23±34.03 |
| C-reactive protein (CRP) (mg/L) | 1.13±0.86 |

Table 2: Correlation of systolic blood pressure (SBP) with QTc interval and CRP levels.

|                         | Correlation coefficient (R value) | P value |
|-------------------------|----------------------------------|---------|
| QTc interval            | 0.3125                           | <0.01*  |
| C-reactive protein (CRP)| 0.2574                           | <0.01*  |

*P<0.05=statistically significant

Table 3: Correlation of diastolic blood pressure (DBP) with QTc interval and CRP levels.

|                         | Correlation coefficient (R value) | P value |
|-------------------------|----------------------------------|---------|
| QTc interval            | 0.246                            | <0.05*  |
| C-reactive protein (CRP)| 0.3862                           | <0.001* |

*P<0.05=statistically significant

The descriptive data of the measured variables are represented as Mean±SD (Table 1). There was a positive and significant correlation for systolic blood pressure (SBP) with both QTc interval and CRP levels (Table 2). Similarly the present study also revealed a positive and significant correlation for diastolic blood pressure (DBP) with both QTc interval and CRP levels (Table 3).

DISCUSSION

The present study reports a positive and significant relationship for SBP with both CRP and QTc intervals. Likewise DBP was also found to be positively and significantly related to CRP and QTc intervals.

Since earlier studies have shown the link between QTc interval and hypertension, it becomes binding that we investigate other factors related to both QTc and blood pressure. Our study takes into account CRP level which is an extensively used inflammatory marker. Earlier studies have shown the correlation of CRP and QTc interval in healthy subjects [12,13]. But our study investigates CRP levels and QTc in normotensive as well as hypertensive subjects. The present study findings were in contrast to an earlier study that reported no association between CRP and DBP [14].

The present study was similar to an earlier study which showed CRP significantly and positively correlated with both SBP and DBP [15]. Among both hypertensive and normotensive subjects, a prolonged QTc interval implies increased morbidity and mortality [16]. Even under-control hypertensive subjects may have the enduring impact of left ventricular hypertrophy, making them prone to fatal cardiac arrhythmias and sudden cardiac deaths [17]. Both hypertension and left ventricular hypertrophy are considered to be related with prolonged QTc interval [18]. The autonomic dysfunction that occurs in hypertension, with increased sympathetic activity prolonging QTc interval and reduced parasympathetic activity protecting against QTc lengthening. Left ventricular hypertrophy attributable to hypertension causes delay in ventricular repolarization and subsequent QTc prolongation. Inflammation and CRP have been linked as a contributory factor in the development of
hypertension [7]. The inflammatory markers IL-6 and CRP cause imbalances in the vascular endothelium. They increase the production of endothelin-1 and reduce nitric oxide production, thus causing vasoconstriction and hypertension. These factors further have pro-thrombotic and pro-atherosclerotic properties and also have impact over the renin-angiotensin mechanism. All these have been associated with the pathogenesis of hypertension [19-23]. CRP increases Plasminogen activator inhibitor-1 (PAI-1) levels, with high PAI-1 levels being reported in hypertensive subjects [22,24]. Vasoconstrictor, thrombotic and atherosclerotic properties of CRP play a critical crucial role in hypertension development [25]. The inflammatory modulatory processes are affected by the autonomic dysfunctions that occur in hypertension, thereby increasing CRP levels [5]. CRP causes changes in the potassium and/or calcium conductance and increase in sympathetic activity, thus leading to autonomic imbalances [8,26]. Neurohumoral factors that causes non-structural cardiac modifications are viewed to be released by inflammation and CRP.

It has been suggested that drugs that lower CRP may be developed and used in treating hypertensive patients and those at risk of developing hypertension. But this has met with opposition since there are several co-founding factors that play role in hypertension development. Dietary fibers have been reported to reduce inflammatory cytokines and CRP in hypertensive as well as normotensive subjects [27].

Limitations: The causation and reverse causation of CRP and hypertension could not be assessed since the present study was a cross-sectional study. It is viewed that CRP changes over the course of the disease process but our study employed a single CRP measurement. The CRP levels are reported to be affected by diuretics and beta blockers [28]. Thus, the anti-hypertensive drugs and their number and combinations may alter CRP levels and/or QTc intervals.

CONCLUSION

QTc intervals from ECG and CRP levels are cheap, widely available markers. They should be employed in risk forecast of hypertensive patients as well as those at risk of developing hypertension. They have been traditionally ignored, thus we suggest that their importance should be valued especially in developing countries like India. This may help in early detection of high risk hypertensive patients and avoid fatal arrhythmias and sudden cardiac deaths.

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