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Original Research Article

The study of cardiovascular sympathetic reactivity in prehypertensives with normal and higher BMI

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ABSTRACT

Background: Hypertension is one of major causes responsible for cardiovascular disease. Prehypertension, as defined by joint national commission-2003 as condition with SBP 120-139 or DBP as 80-89mmH, was identified as a precursor for hypertension and also associated with 1.5 to 2 fold increase in cardiovascular disease. The aim of the study was to determine the sympathetic reactivity in pre-hypertensives with normal and higher body mass index (BMI).
Methods: A cross-sectional study was conducted at Seth G.S Medical College, Mumbai, India. A total of 129 study participants were recruited based on the inclusion and exclusion criterion of the study. Changes in diastolic blood pressure were measured in isometric hand grip and cold pressor tests.
Results: The prevalence of prehypertension was observed to be 66.66% in age group of 28-40 years. There was a statistically significant difference in change of diastolic blood pressure in isometric hand grip (IHG) and cold pressor test (CPT), in prehypertensives with higher BMI as compared to prehypertensives with normal BMI.
Conclusions: The finding of the study reveals that there is an increased sympathetic reactivity in prehypertensives with normal BMI as compared to normotensives. There is lesser sympathetic reactivity in prehypertensives with higher BMI compared to prehypertensives with prehypertensives with normal BMI.

Keywords: BMI, CPT, DBP, IHG, Prehypertension, SBP

INTRODUCTION

The prevalence of cardiovascular disease in India is 59.9 and 69.9 per 1000 in males and females respectively in urban population and 35.5 and 35.9 per 1000 in males and females respectively in rural population.[1,2] Hypertension is a major cause responsible for cardiovascular disease. The prevalence of hypertension in urban areas of India ranged from 2.6-5.2% between 1960-1980 and it has increased to 20-33 % in last decade. It is estimated that overall prevalence of hypertension in India will be 159.46/1000 population by 2020.[3] Prehypertension is an emerging and remarkably common risk factor for hypertension and thereby an increased risk of cardiovascular target organ complications. As per the Joint National Committee (JNC) on prevention, detection, evaluation and treatment of high blood pressure, Prehypertension is defined as a systolic blood pressure (SBP) of 120 to 139 mm Hg and diastolic blood pressure (DBP) of 80 to 89 mm Hg.[4] Prehypertension is not a disease category or a diagnosis. The main objective of creating this category was to create awareness among people and to identify individuals at risk of developing of hypertension. It has also been shown that prehypertension is associated with subclinical atherosclerosis, including increased coronary atherosclerosis and target organ damage [(4)]. The increasing incidence of prehypertension and hypertension is related to change in lifestyles and dietary patterns. According to 7th JNC, the causative factors for elevated BP were excess body weight, excess

sodium intake, reduced physical activity, inadequate intake of fruit, vegetables, and potassium, and excess alcohol intake.[5,6] Studies have reported that sustained sympathetic over reactivity increases the vasoconstrictor tone of the systemic vasculature and autonomic imbalance in hypertensive patients. Also increase in BMI is significantly associated with increase in sympathetic tone and increase in blood pressure in young healthy overweight subjects but there is fewer data available on autonomic reactivity in prehypertensives.[7-9] Individuals who are overweight or obese are at risk of pre hypertension condition progressing faster to hypertension stage 1 or stage 2.

The objectives of the study were to early determine the nature of sympathetic reactivity in pre-hypertensives, so that early health promoting lifestyle modification and intervention can be taken to prevent or delay the hypertension from developing. Autonomic function tests were used to assess the cardiovascular sympathetic reactivity. The sympathetic tests included changes in blood pressure during sustained hand grip, cold pressor test.

METHODS

The study design was observational and cross sectional. The study was conducted in the Department of Physiology, Seth G S Medical College and K.E.M. Hospital, Parel, Mumbai, India 400012. The study was approved by Institutional Review Board (IRB) of Seth G S Medical College and K.E.M. Hospital, Parel, Mumbai, India. The study participants were recruited from Medicine outpatient department. The data was collected from September 2014 to October 2015. The written informed consent was obtained from all the study participants. A total 129 study participants were recruited for the study. The participants were then sub categorised into following three groups on the basis of level of systolic BP and diastolic BP and the level of body mass index (BMI) as per JNC-7 and World Health Organization (WHO).[4,11]

Group I (Normotensive)

Participants between 25-40 years age of both sexes having systolic BP 100-119 Hg, diastolic BP 60-79 mm Hg & BMI within range of 18.5-22.9 were included.

Group II (Prehypertensives with normal BMI)

Participants between 25-40 years age of both sexes, systolic BP 120-139 Hg, diastolic BP 80-89 mm Hg & BMI within range of 18.5-22.9 were included.

Group III (Prehypertensives with higher BMI)

Participants between 25-40 years age of both sexes, systolic BP 120-139 Hg, diastolic BP 80-89 mm Hg & BMI within range of 23 or above were included.

The study participants having history of alcohol, smoking, hypertension known case of myocardial infarction, heart disease kidney disease or any history of medication were excluded from the study. History taking, general examination and systemic examination were carried out for all the participants before the experiments of the study. All female study participants' experiments were performed during the follicular phase of menstrual cycle.

Following equipments were used for performing the experiments

- Electrocardiograph (CARDIART 6108 T, BPL Limited, single channel 12 lead ECG machine) recorded the ECG for assessing heart rate variability. ECG was taken in lead II. To get the ECG in lead II all limb leads were attached.
- Mercury Symphgmomanometer
- Standard weighing scale
- Automated Blood Pressure Monitor (Omron health care Co. Ltd, SEM-1 model, 6607551LF) for recording blood pressure.
- Hand-grip dynamometer (Manufactured by ANAND agencies) for isometric hand grip test
- Wide mouthed insulated container

The participants were instructed not to take tea, coffee or any beverages 1 hour before and any food 2 hours before the recording. This was required to exclude the effects of food and water intake on the recording. All the recordings were performed in morning in the Physiology department laboratory at Seth G S Medical College and K.E.M. Hospital, Parel, Mumbai.

After informed consent, subject's height and weight were recorded. Weight was measured nearest to 0.1kg by weighing scale after removal of shoes with light clothing only. Height was measured to the nearest 0.5 cm against the wall without shoes using standard height scale. BMI was calculated by dividing the weight taken in kg by the square of height taken in meters.

Resting pulse rate

The subjects were asked to take rest for 10 minutes in supine position and radial pulse rate was recorded in supine position and expressed as beats / min. Three readings were taken and the average of the three was taken as the resting pulse rate.

Resting blood pressure

The subjects were asked to take rest for 10 minutes in supine position. The resting blood pressure (BP) was recorded in supine position using mercury sphygmomanometer and expressed in mmHg. Three readings were taken and the average of the three was taken as the resting blood pressure. The cardiovascular tests performed are detailed below. These tests were

demonstrated to the subjects. For assessing sympathetic reactivity the tests done were:

Isometric hand grip test

In this test, sustained muscle contraction is measured by a handgrip dynamometer, which causes a rise in systolic and diastolic blood pressure and heart rate. The dynamometer was first squeezed by dominant hand to isometric maximum, and then held at 30% maximum voluntary contractions for 5 min. The results were expressed as the difference between the highest diastolic blood pressure during handgrip exercise. A rise in DBP of less than 10 mm Hg was defined as abnormal, 11-15 mm Hg as borderline and 16 mm Hg or more as normal.

Cold pressor test

This test was performed after 5 minutes. Again blood pressure (arm not immersed) of the subject was recorded. The subject was asked to immerse the non-dominant hand up to wrist in cold water of 4º C for 1 minute in wide mouthed insulated container. Blood pressure was recorded at the pain threshold i.e. the interval between the immersions of hand to the subjective feeling of pain or at the end of 1 min and at the interval of 1.5 min and 4 min after removal of hand. If the subject was not able to tolerate the cold water, then water of 10ºC was used for the test. At the end of the procedure a dry hand towel was provided. Normal: - A rise in DBP >10 mm Hg.

Statistical methods

Data of various parameters measured were entered in Microsoft Excel (2010). The mean and standard deviation was calculated for all the parameters. Statistical analysis was done using n-Master 1.0 as per SPSS 16.0 and Graph Pad Instat 3.0 software. The statistical tests used were as per data requirement and our objectives of study. Data was presented as Mean ± Standard deviation. One way annova test with post hoc test (Tukey Kramer test) to compare autonomic function test in three group. Inter and Intra group comparisons were done using repeated measure one way annova with Tukey Kramer test with 5% level of significance. A p<0.05 was considered as statistically significant.

RESULTS

Total 129 subjects were divided into three groups on the basis of Blood pressure and BMI with 43 subjects in each group, and sympathetic test were performed. The three groups were as follows:

- Group I-Normotensives with BMI 18.9- 22.9
- Group II-Prehypertensives with BMI 18.9-22.9
- Group III-Prehypertensives with BMI 23 or above

In all the groups, age group ranges from 28-40 years with prevalence of prehypertensives is 66.66% (Table 1). Mean age in Group I (33.72±3.801), Group II (33.04±4.035), Group III (35.04±3.464). There was statistically no significant difference in age in all the groups. Group I consists of male 36 (83.72%) and female 9 (16.27%), Group II consists of male 35 (81.39%) & female 8 (18.60%) and Group III consists of male 35 (81.39%) and female 8 (18.60%).

Table 1: Comparison of different parameters between three groups.

	Age(years)			Sex	
	Mean	S.D	Range	Male	Female
I	33.72	3.801	28-40	36 (83.72%)	9 (16.27%)
II	33.04$^{\#*}$	4.035	27-40	35 (81.39%)	8 (18.60%)
III	35.04 $^{\sigma}$	3.464	26-40	35 (81.39%)	8 (18.60%)
Sample Size for all groups		**43**			

Comparison by one way Anova test with Tukey Krammer test:- # Group I and Group II, p > 0.05 not significant.* Group II and Group III, p >0.08 not significant$^{\sigma}$ Group I and Group III, p>0.8 not significant. There is no significant difference in mean age between three groups.

Table 2: Comparison of different parameters between three groups.

	BMI (mean±SD)	Resting SBP (mean±SD)	Resting DBP (mean±SD)
I	20.607±1.119	114.51± 4.453	73.209±4.389
II	20.730±0.845$^{\#*}$	125.95±4.24^{1,2}	83.441±2.839^{a,b}
III	26.541±1.592$^{\sigma}$	126.046±4.39^{3}	85.651±3.516^{c}

Comparison by one way Annova test with Tukey Krammer test, # Group I and Group II, p<0.001 highly significant. *Group II and Group III, p>0.05 not significant. $^{\sigma}$Group I and Group III, p<0.001 highly significant. ^{1}Group I and Group II, p<0.001 highly significant, ^{2} Group II and Group III p>0.05 not significant, ^{3}Group I and Group III, p<0.001 highly significant. ^{a}Group I and Group II, p<0.001 highly significant,^{b}Group II and Group III, p>0.05 not significant, ^{c}Group I and Group III, p<0.001 highly significant.

As mentioned in Table 2 there is significant difference in BMI in Group I (20.6077 ±1.119) and Group III(26.541 ± 1.592), Group II (20.730 ± 0.845) and Group III (p<0.001) and no significant difference in BMI between Group I and Group II, p>0.1. Resting SBP is significantly different in Group I (114.51±4.453) and Group II(125.95±4.24), Group I and Group III (126.046±4.397). There is no significant difference in Group II and Group III. Also table 2 gives details of Resting DBP, Group I (73.209±4.339), Group II (83.441±2.839), Group III (85.78 ± 3.516). There is significant difference in DBP in Group I and Group II, Group I and Group III and no significant difference in Group II and Group III.

As per Table 3 and Figure 1 mentioned ΔDBP in Isometric Hand Grip, Group I (19.55±2.737), Group II (26.046±4.440) and Group III (14.09±2.093). There is

significant difference in Group I and Group II, and Group II and Group III.

Table 3: Comparison of isometric hand grip test between three groups.

Groups	ΔDBP (Mean±SD
I	19.55±2.737
II	26.046±4.440#*
III	14.09±2.093σ

By One way Anova test with Tukey Krammer test # Group I and Group II, p<0.01 significant.* Group II and Group III, p<0.01 significant,σGroup I and Group III, p<0.01 significant.

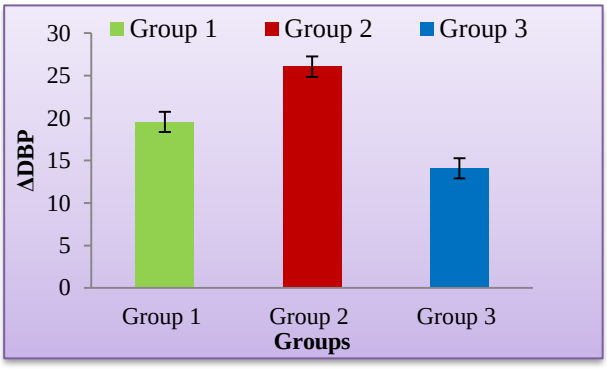

Figure 1: Comparison of isometric hand grip test between three groups.

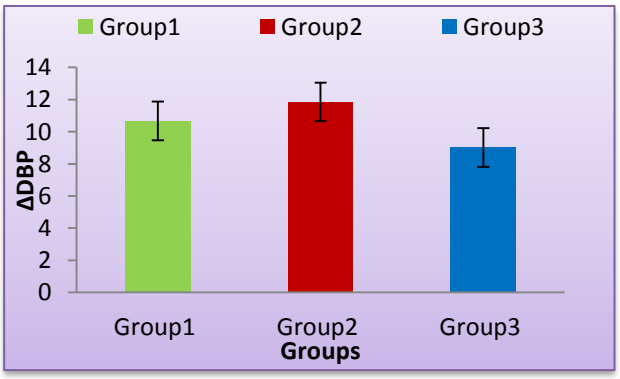

Figure 2: Comparison of cold pressor test between three groups.

Table 4: Comparison of cold pressor test between three groups.

Groups	ΔDBP (Mean ± SD)
I	10.674±1.796
II	11.860 ±1.684#*
III	9.02 ±1.336σ

Compariosn by One way Anova test with Tukey Krammer test:- # Group I and Group II, p<0.001 highly significant.* Group II and Group III, p<0.01 significant, σGroup I and Group III, p<0.001 highly significant.

Table 4 and Figure 2 gives the details of change in DBP (ΔDBP) during cold pressor test which are Group I (10.674±1.796), Group II (11.860±1.684), Group III (9.02±1.336). There is significant difference in Group I and Group II, Group II and Group III.

DISCUSSION

As per JNC-7 in 2003, Prehypertension is defined as SBP 120-139, or DBP 80-89. Prehypertension is a global major health risk that doubles the risk of cardiovascular disease in an individual independent of progression to overt hypertension.[12] It is associated with risk factors as obesity, diabetes mellitus and dyslipedemia. Various studies from all over world have shown increasing BMI, waist hip ratio and impaired glucose tolerance are independent risk factors for development of both Hypertension and prehypertension.[13] This study was designed to evaluate cardiac sympathetic reactivity in prehypertensives with normal and higher BMI. Sympathetic tests were performed on total 129 healthy subjects.

Tests for sympathetic reactivity

Isometric Hand Grip test and Cold pressor test are used to evaluate the sympathetic reactivity in prehypertensives.

Isometric hand grip

Rise in diastolic blood pressure with hand grip dynamometer is an indicator of increased sympathetic activity. Our study showed statistically significant rise in DBP in prehypertensives with normal BMI suggesting increase in sympathetic reactivity in them. The present study also showed a borderline response to IHG in prehypertensives with higher BMI which is suggestive of a reduced sympathetic reactivity in obese prehypertensives when subjected to stress. Kalpana et al and Khwaza Nawazzudin et al have found similar evidence of decrease in DBP response during IHG test in obese group.[14,15] The reason for reduced increase in DBP response is more likely due to reduced increase in peripheral vascular response to manoeuvres activating sympathetic system.

Cold pressor test

Cold pressor test provokes a remarkable increase in sympathetic reactivity in humans mediated by central command and local metabolites, particularly adenosine.[16] This test is used to sympathetic reactivity. Our study showed significant increase in diastolic blood pressure in prehypertensives with normal individuals as compared to normotensives and prehypertensives with higher BMI.This finding are consisted with findings of Grewal et all.[17]

These findings are suggestive of increase in sympathetic reactivity in prehypertensives with normal BMI and

decrease in sympathetic reactivity in prehypertensives with higher BMI, Several literatures has found increase in sympathetic activity influence vascular smooth muscle tone, heart rate the adrenal medulla to regulate epinephrine release, which may result in early development of hypertension in this individuals.[18]

Thus all the above studies reveal an increase in sympathetic reactivity in prehypertensives with normal BMI as compared to normotensives. These findings are similar to Wang et al in which they have seen increase in sympathetic reactivity in prehypertensives.[19] The increase in sympathetic reactivity to stress like isometric hand grip and cold pressor test make them prone for early development of hypertension.

Several mechanism are described for sympathetic nervous system activation in obesity induced hypertension; increased leptin concetration, decreased arterial baroreflex sensitivity, elevated plasma angiotensin, hyperinsulinemia.[20]

In our study the Group III subjects are prehypertensives with BMI in range of 25-27 that is they are in overweight category. This group of prehypertensives with higher BMI have shown lesser sympathetic reactivity compared to prehypertensives with normal BMI. This finding are consistent with studies of Rumantri MS et al and Grassi et al in which they have found there is heterogeneous increase in sympathetic activity in obese individuals by using novel techniques like ganglionic blockade, plasma and urinary norepinephrine levels, regional norepinephrine spill, microneurography in renal vasculature and skeletal muscle causing increase in blood pressure but suppression of cardiac sympathetic nerve reactivity in early stages of obesity.[21,22] Similar results of lesser sympathetic activation in prehypertensives with higher BMI are reported by Weyer et al, they observed influence of ethnicity, seen in pima Indians, in low sympathetic activation in mechanism of obesity-related hypertension.[23] Early identification of alteration in sympathetic reactivity in prehypertensives with higher BMI will help in taking preventive measures for reducing weight.

CONCLUSION

The purpose of defining prehypertension was to emphasize the risk associated with BP in the range SBP120-130mm Hg or DBP80-89 mmHg and to focus clinical and public attention on prevention. According to JNC-7 individuals with prehypertension are at a higher risk of developing hypertension than those with lower blood pressure levels. The studies reveals an increase in sympathetic reactivity in prehypertensives with normal BMI as compared to normotensives

- There is lesser sympathetic reactivity in prehypertensives with higher BMI compared to prehypertensives with normal BMI.
- Early detection of prehypertension will help practitioner to make individuals of prehypertension understand the cardiovascular complications and importance of taking preventive measures in delaying the development of hypertension.

Limitations

- The study has moderate sample size taken from one region. Future studies are recommended with larger sample to extrapolate the results of cardiac autonomic responses in prehypertensives
- As this study has few female subjects effects of gender on autonomic function test is not studied.
- Heart rate variability is a newer and better technique to evaluate the cardiac autonomic response than conventional autonomic function test.
- Further detailed assessment of BMI on autonomic function is needed.

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

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