

## Original Research Article

# Effect of prehypertension on cardiovascular parasympathetic reactivity in adults with normal and higher BMI

Mangala Bhongade<sup>1</sup>, Amit Navare<sup>2</sup>

<sup>1</sup> Speciality Medical Officer, Department of Physiology, Seth G.S Medical College & KEM Hospital, Parel, Mumbai 400012 INDIA.

<sup>2</sup> Additional Professor, Department of Physiology, Seth G.S Medical College & KEM Hospital, Parel, Mumbai 400012 INDIA.

\*Corresponding author: Dr Mangala Bhongade

---

### Abstract:

**Background:** - Hypertension is one of major risk factor for cardiovascular disease. Prehypertension was defined by Joint National Committee (JNC-7) in 2003 as condition with systolic BP 120-139 or diastolic BP as 80-89mmHg. Prehypertension is associated with subclinical atherosclerosis. The aim of the study was to determine the parasympathetic reactivity in prehypertensives 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 heart rate were measured in deep breathing test (DBT) & orthostatic test.

**Results:** - The prevalence of prehypertension was observed to be 66.66% in age group of 25-40 years. There was a statistically significant difference in change in heart rate in deep breathing test and orthostatic test in prehypertensives with higher BMI as compared to prehypertensives with normal BMI.

**Conclusion:** The finding of the study revealed that there was a decreased parasympathetic reactivity in prehypertensives with normal BMI as compared to normotensives. There was lesser parasympathetic reactivity in prehypertensives with higher BMI compared to prehypertensives with normal BMI.

**Keywords:** - BMI, DBP, DBT, Orthostatic Test, Prehypertension, SBP.

---

### Introduction

Hypertension is the most common preventable non-communicable disease. The prevalence of hypertension is alarmingly increasing in India<sup>(1,2)</sup>. 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. According to Directorate General of Health Services, Ministry of Health and Family Welfare, Government of India, it is estimated that overall prevalence of hypertension in India will be 159.46/1000 population by 2020<sup>(3)</sup>. Prehypertension is identified as a precursor of hypertension and also as an independent factor for stroke, cardiovascular events<sup>(4)</sup>. The seventh report

of Joint National Committee (JNC-7) on prevention, detection, evaluation, treatment of high blood pressure in 2003 introduced the term prehypertension as systolic BP 120-139 mm Hg, and diastolic BP 80-89 mm Hg<sup>(5)</sup>. Meta-analysis of approximately 1 million individuals from 61 long-term epidemiological studies demonstrated that for each 20 mmHg increase in systolic blood pressure or 10 mmHg increase in diastolic blood pressure over 115/75 mmHg, there was a two-fold increase in mortality associated with coronary artery disease and stroke<sup>(6)</sup>. The other co-morbidities with hypertension are obesity, dyslipidaemia, type 2 diabetes mellitus, which increases the risk of cardiovascular events<sup>(7)</sup>. Obesity is a complex

disorder of energy imbalance with increasing incidence worldwide<sup>(8)</sup>. In developing countries like India and Asia, the incidence of overweight and obesity is increasing due to change in lifestyles like sedentary habits and increased intake of fatty foods<sup>(9)</sup>. Studies have reported that sustained increase in sympathetic reactivity causing vasoconstriction of the systemic vasculature 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<sup>(10, 11, 12)</sup>. In another study by Messina et al, observed an increase in the resting energy expenditure (REE) in sportswomen in spite of increased parasympathetic reactivity which is usually related to lower REE<sup>(13)</sup>. Therefore, these studies suggest that not only the sympathetic activation but also the parasympathetic inhibition plays a vital role in the genesis and pathophysiology of obesity and hypertension by regulating food intake and energy homeostasis.

The objectives of the study were to determine the nature of parasympathetic reactivity in prehypertensives, 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 parasympathetic reactivity. The parasympathetic tests included changes in heart rate during deep breathing test (DBT) and orthostatic test.

#### **Materials & 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).<sup>(4,11)</sup>

*1. Group 1 (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.

*2. Group 2 (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.

*3. Group 3 (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:**

1. 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.
2. Mercury Sphygmomanometer
3. Standard weighing scale

The participants were instructed not to take tea, coffee or any beverages 1 hour before and any food 2 hours before the experiments. 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 meter

Resting Heart rate: - The subjects were asked to rest for 10 minutes in supine position. ECG recording is taken in Lead II and heart rate is calculated from  $1500 / \text{no. of small boxes between R-R intervals}$

**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 autonomic tests performed are detailed below. These tests were demonstrated to the subjects.

**For assessing parasympathetic reactivity the tests done were:**

**1. Deep Breathing Test:** With patient supine and lead II ECG recording, patient breathes deeply and evenly at 6 breaths per minute (5 sec. in, 5 sec. out) for 3 cycles. Heart rate difference ( $\Delta HR$ ) during each cycle is measured and average of the 3 differences is taken. Normal  $HR > 15$  beats/min. E: I ratio is ratio of longest R-R interval and shortest R-R interval. E: I ratio averaged over 3 cycles is taken. Normal E: I ratio  $> 1.21$ .

**2. Orthostatic Test:** After making the subject lie supine for about 5 minutes, the subject was asked to stand up unaided and erect as quickly as possible. During this period lead II ECG was recorded and the point at the start of standing was marked on the ECG record. The 30:15 ratio was calculated by taking the ratio of maximum R-R interval around the 30th beat to the minimum R-R interval around 15th beat after standing. Normal 30:15 is  $> 1.04$ .

*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  $\pm$  Standard deviation. One Way Anova test with post hoc test (Tukey Kramer test) was used to compare autonomic function tests in three groups. Inter and Intra group comparisons were done using repeated measure one way anova with Tukey Kramer test with 5% level of significance. A p value  $< 0.05$  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 Autonomic function tests were performed.

The three groups were as follows:-

Group 1-Normotensive subjects with normal BMI.

Group 2-Prehypertensive subject with normal BMI.

Group 3-Prehypertensive subject with higher BMI.

In all the groups age group ranges from 25-40 years with prevalence of prehypertension is 66.66 %.

As mentioned below in Table 1 , Mean age in Group 1(33.72 ± 3.801),Group 2 (33.04 ± 4.035),Group 3 (35.04 ± 3.464). There was statistically no significant difference in age in all the groups. Group 1 consists of males (83.72%) and females(16.27%), Group 2 consists of males (81.39%) &females (18.60%) and Group 3 consists of males (81.39%) &females(18.60%).

**Table 1 :- Comparison of different parameters between three groups**

		Group 1(n=43)	Group 2 (n=43)	Group 3 (n=43)
Age	Mean ± SD	33.72 ± 3.89	33.04 ± 4.035 <sup>#,*</sup>	35.04 ± 3.464 <sup>σ</sup>
	Range	28-40	27-40	26-40
Male		36(83.72%)	35(81.39%)	35(81.39%)
Female		9(16.27%)	8(18.60%)	8(18.60%)

Comparison by Anova test with Tukey Kramer test:-# Group 1 & Group 2 , p > 0.05 not significant.\* Group 2 & Group 3 , p > 0.08 not significant,<sup>σ</sup> Group 1 & Group3 , p>0.80 not significant. There is no significant difference in mean age between three groups.

As mentioned below in Table 2,there is significant difference in BMI in Group1 (20.6077 ±1.119) & group 3(26.541 ± 1.592), Group 2 (20.730 ± 0.845) & Group 3 (p< 0.001) and no significant difference in BMI between group 1 and group 2 (p value> 0.110).As per Table no 2 Resting heart rate in Group1 (76.837 ± 4.231) ,Group2 (84.139

±6.006),and Group 3 (87.627 ± 3.910). There is significant difference in Group1 &Group 3, Group 1 & Group 2 (p<0.001).As per Table no.2 Resting SBP is significantly different in Group 1(114.51 ± 4.453) & Group 2(125.95 ± 4.24), group 1 & Group3 (126.046 ±4.397). There is no significant difference in Group2 & Group3. Table no. 2 gives details of Resting DBP, Group 1(73.209 ± 4.339), Group 2 (83.441 ±2.839), Group 3 (82.697 ± 3.516). There is significant difference in DBP in Group 1 & Group 2, Group 1 & Group 3 and no significant difference in Group2 and Group3.

**Table no. 2:- Comparison of BMI, Resting Heart rate, Resting SBP, Resting DBP**

Parameter	Group 1 (n=43)	Group 2 (n=43)	Group 3 (n=43)
BMI	20.6077 ± 1.119	20.730 ± 0.845 <sup>#,Δ</sup>	26.541 ± 1.592 <sup>*</sup>
Resting Heart rate	76.837 ± 4.231	84.139 ± 6.006 <sup>α,β</sup>	87.627 ± 3.910 <sup>μ</sup>
Resting SBP	114.51 ± 4.453	125.95 ± 4.24 <sup>α,b</sup>	126.046 ± 4.397 <sup>c</sup>
Resting DBP	73.209 ± 4.389	83.441 ± 2.839 <sup>x,y</sup>	82.697 ± 3.516 <sup>z</sup>

Comparison by One Way Anova test with Tukey Kramer test:- <sup>#</sup>Group 1 & Group 2 ,p > 0.05 not significant, <sup>Δ</sup>Group 2 & Group 3 p < 0.001 significant, <sup>\*</sup>Group 1 & Group3, p < 0.001 significant. <sup>α</sup>Group 1 & Group 2 ,p < 0.001 significant, <sup>β</sup>Group 2 & Group 3 p < 0.01 significant, <sup>μ</sup>Group 1 & Group3, p < 0.001 significant. <sup>a</sup>Group 1 & Group 2 ,p < 0.001 significant, <sup>b</sup> Group 2 & Group 3 p > 0.05 not significant, <sup>c</sup>Group 1 & Group3, p < 0.001 highly significant. <sup>x</sup>Group 1 & Group 2 , p < 0.001 significant, <sup>y</sup> Group 2 & Group 3 , p > 0.05 not significant, <sup>z</sup> Group 1 & Group3, p < 0.001 highly significant

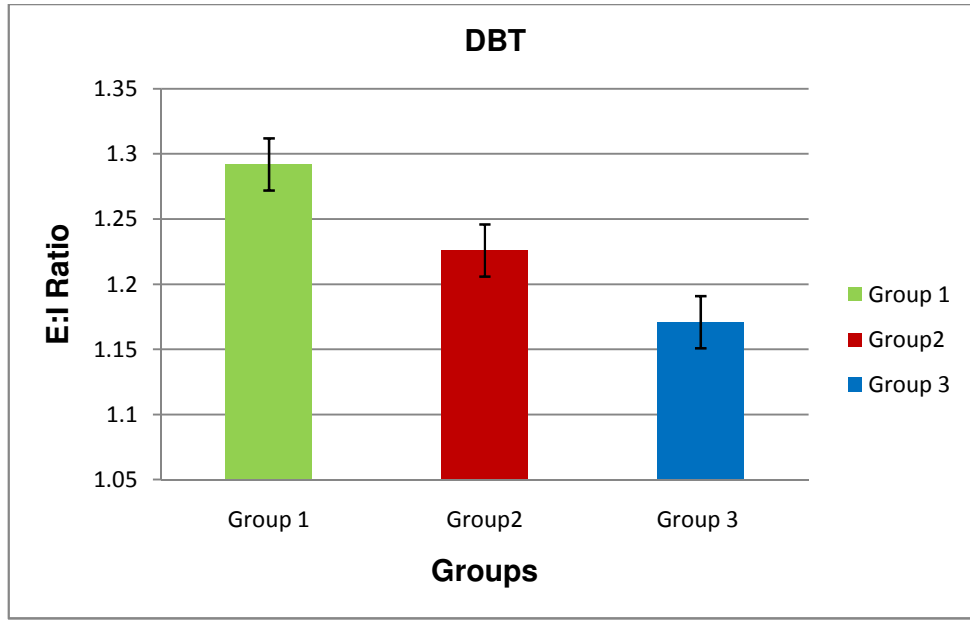
As mentioned below in Table 3 for Deep Breathing Test , ΔHR ranges in Group 1 (26.733 ± 4.684),Group2 (21.345 ± 3.649),Group3 (17.341 ± 2.446).There is significant difference in ΔHR in Group 1 & Group 2 ,Group 2 & Group3 .also significant difference in , Group 1 & Group3.As mentioned in Table no.3, for Deep Breathing Test , E: I ratio in Group 1(1.292 ± 0.110) is significantly different with Group 3 (1.71 ± 0.041).

**Table 3:-Comparison of Deep breathing Test (ΔHR and E: I ratio)**

Deep Breathing Test	Group 1	Group 2	Group 3
Δ HR	26.733 ± 4.684	21.345 ± 3.649 <sup>#,*</sup>	17.31 ± 2.446 <sup>σ</sup>
E: I Ratio (Mean ± SD)	1.292 ± 0.110	1.226 ± 0.053 <sup>α,β</sup>	1.171 ± 0.041 <sup>μ</sup>

Comparison by One Way Anova test with Tukey Kramer test :- # Group 1 & Group 2 , p < 0.001 significant.\* Group 2 & Group 3 , p < 0.001 significant,<sup>σ</sup> Group 1 & Group3, p < 0.001 significant. <sup>α</sup>Group 1 & Group 2 ,p < 0.001 highly significant, <sup>β</sup> Group 2 & Group 3 p < 0.01 significant, <sup>μ</sup> Group 1 & Group3, p < 0.001 highly significant

FIG 1:- Comparison of Deep Breathing Test (E: I ratio)



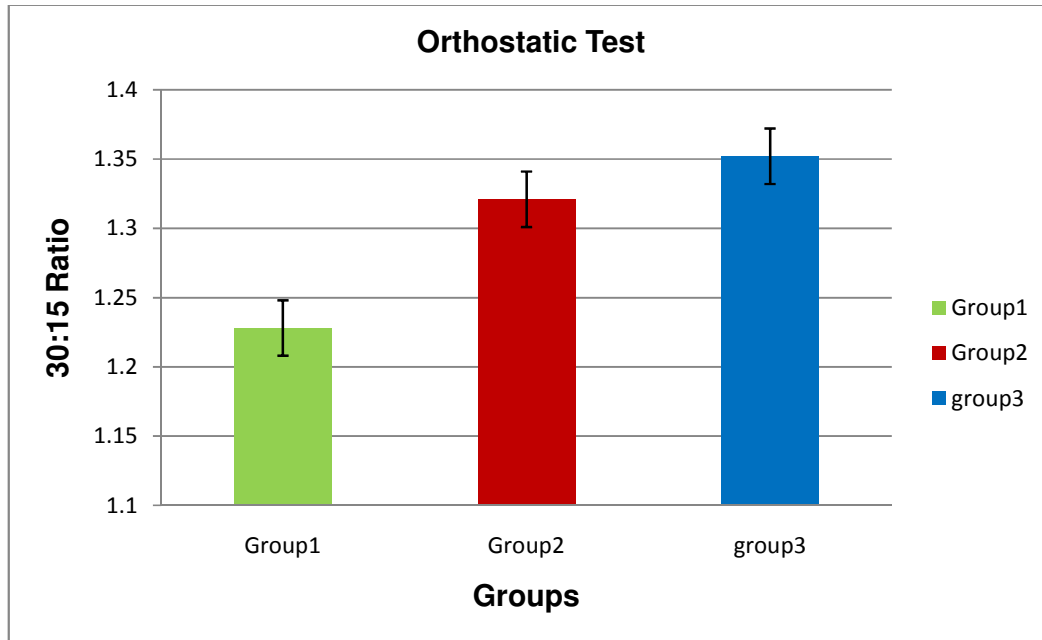
As mentioned below in Table 4, for Orthostatic Test,the 30:15 ratio in Group 1 (1.228 ± 0.076), Group2 (1.321 ±0.086), Group 3 (1.352 ±0.512). There is statistically significant difference in 30:15 ratios in Group 1 & Group 2, Group 2 & Group 3 and Group 1 & Group 3.

**Table 4:- Comparison of Orthostatic Test between three groups:-**

Orthostatic Test	Group 1	Group 2	Group 3
30:15 Ratio (Mean ± SD)	1.228 ± 0.076	1.321 ± 0.086 <sup>#σ</sup>	1.352 ± 0.512*

Comparison by One way Anova test with Tukey Kramer test :- # Group 1 & Group 2 , p < 0.001 significant,<sup>σ</sup> Group 1 & Group3, p < 0.001 highly significant, \*, Group 2 & Group 3 , p <0.001 significant

FIG 2:- Comparison of Orthostatic test between three groups:-



### Discussion

Cardiovascular disease is associated with risk factors such as obesity, diabetes mellitus and dyslipidemia. Various studies from all over world have shown that increasing BMI, waist hip ratio and impaired glucose tolerance are independent risk factors for development of both hypertension and prehypertension.<sup>(14,15)</sup> This study was designed to evaluate cardiac parasympathetic reactivity in prehypertensives with normal and higher BMI and normotensives. Autonomic function tests were performed on total 129 healthy subjects.

Obesity and cardiac autonomic nervous system are intrinsically related. A 10% increase in body weight is associated with a decline in parasympathetic tone, accompanied by a rise in resting heart rate.<sup>(16)</sup> Maheshwari et al in their study has found out BMI as a significant contributor for increase in resting heart rate. Our finding is also consistent with it; there was significant increase in resting heart rate in Group 3 as compared to group 1 & 2. As resting heart

rate is mainly regulated by parasympathetic nerves, increase in resting heart rate in group 3 suggests decrease in parasympathetic tone in them.<sup>(17, 18)</sup>

### Tests for parasympathetic function:-

Deep Breathing Test and Orthostatic Test are used to evaluate the parasympathetic function in Prehypertensives.

**Deep Breathing Test:** - This test is based on the phenomenon of deep breathing which is most pronounced at the respiratory rate of 6 breaths per minute. Sinus arrhythmia is physiological increase in heart rate during inspiration and a decrease in heart rate during expiration. The magnitude of changes of heart rate during the procedure is given by expiration and inspiration RR interval ratio in ECG( E:I ratio ) and it reflects the cardiac parasympathetic activity<sup>(19)</sup>. In our study there was decrease in E:I ratio in group 2 compared to group 1 and more decrease in E:I ratio in group 3 compared to group2 and decrease in  $\Delta$ HR suggesting decrease in parasympathetic reactivity .

**Orthostatic Test:**-Changing posture from lying to standing position produces an integrated response of cardiovascular system which includes alteration in heart rate and blood pressure changes. The difference in heart rate on standing is due to withdrawal of vagal tone. Thus significantly higher 30:15 ratio following standing in Group 3 compared to Group 1 and Group 2 represents decreased parasympathetic activity in prehypertensives with higher BMI & prehypertensives with normal BMI compared to that of normotensive subjects. Similar findings are reported by G.K. Pal et al in their study.<sup>(20)</sup>

#### **Conclusion**

The purpose of defining prehypertension was to emphasize the risk associated with BP in the range SBP 120-130 mm Hg or DBP 80-89 mmHg and to focus public attention on prevention.

#### **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 reactivity 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 reactivity than conventional Autonomic function tests.
- Further detailed assessment of BMI on autonomic function is needed.

#### **Acknowledgement**

Dr Shaina Begum, Scientist D, NIRRH (ICMR) Parel, Mumbai for the valuable help in statistics. All the study participants are thanked

#### **References**

1. Gupta R: Trends in hypertension epidemiology in India. *J Hum Hypertension* 2004, 18:73-78. doi:10.1038/sj.jhh.1001633.
2. Park K. Park's textbook of preventive and social medicine. 21<sup>st</sup> edn. Jabalpur: Bhandarsidas Bhanot; 2011:344-348.
3. The World Health Report 1999: The double burden: emerging epidemics and persistent problems. Geneva: WHO; 1999. Available from: <http://www.who.org/>, accessed on June 2, 2007.
4. Ghaffar A, Reddy KS, Singhi M. Burden of noncommunicable diseases in South Asia. *BMJ* 2004; 328: 807-10.



5. Classification of blood pressure. In The seventh report of the Joint National Committee on prevention, detection, evaluation, and treatment of high blood Pressure. USA: National Heart, Lung and Blood Institute; National High Blood Pressure Education Program; NIH Publication; 2004:12
6. XiuanGua et al "Prehypertension –A Metaanalysis of Epidemiology,risk factors & predictors of progression Review" Texas Heart Institute Journal.,vol38 no6.Nov ,2011;PP 643-648
7. AMuruganatham , "Prehypertension – review" Medicine Update Vol 22 nov 2012 pp105-110
8. World Health Organization. Obesity and overweight factsheet number 311. 2011. Available from: <http://www.who.int/mediacentre/factsheets/fs311/en/index.html>. [Last accessed on 2014 Apr,16]
9. Madrigal L, Brady J, Raxter M, Ruiz E, Otarola F, BlellM. Obesity, hypertension, and migration: A meta-analysis of populations of the South Asian diaspora. *Hum Biol* 2011;83:
10. F. Dangardt, R. Volkmann, Y. Chen, W. Osika, S. Mårild, and P. Friberg, "Reduced cardiac vagal activity in obese children and adolescents," *ClinicalPhysiologyandFunctionalImaging*, vol. 31, no. 2, pp. 108–113, 2011. .
11. Gopal Krishna pal et al "Body mass Index contributes to sympathovagal imbalance in prehypertensives" *BMCcardiovascular disorders* 1471-2261/12/54
12. Bruno RM, et al "Interactions between sympathetic nervous system and endogenous endothelin in patients with essential hypertension." *Hypertension*
13. Messina G, Vicidomini C, Viggiano A, Tafuri D, CozzaV, Cibelli G, et al. Enhanced parasympathetic activity of sportive women is paradoxically associated to enhanced resting energy expenditure. *AutonNeurosci* 2012;169:102-6.
14. Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies (WHO Expert Committee Report). *Lancet* 2004, 363:157–163
15. Kinra S Bowen LJ, et al Sociodemographic patterning of non-communicable disease risk factors in rural India: a cross sectional study *BMJ* 2010,341:c4974.doi:10.1136/bmj.c4974
16. Sulayma Albarwaniet al. Prehypertension: underlying pathology and therapeutic options *World journal of cardiology* Aug. 2014, vol6 issue 8 pp728-743
17. Talay Yar. Resting heart rate and its relationship with general and abdominal obesity in young male Saudi University students. *Pak J Physiol*, VI : (1), 2010.
18. Maheshwari et al "Correlation of resting heart rate with general and visceral obesity indices in young male adult of western Rajasthan" *IJBAP*, vol3(1) 2014 pp-297-300
19. Piepoli Metall., "Origin of Respiratory Sinus Arrhythmia in conscious Humans. An important role for Arterial Carotid Baroreceptors." *Circulation*, 1997;37(1):56-58
20. Gopal Krishna pal et al "Body mass Index contributes to sympathovagal imbalance in prehypertensives" *BMC cardiovascular disorders* 1471-2261/12/54