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Obesity Contributes to Cardiac Autonomic Dysfunction in Prehypertensives

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ABSTRACT

Background & Objectives: A simple non-invasive method for evaluating the extent of heart rate variation caused by the cardiac autonomic nervous system (ANS) is heart rate variability (HRV). The study's objective was to evaluate the effects of isometric handgrip exercise (IHG) on HRV in pre-hypertensive obese and non-obese subjects.

Materials & Methods: 180 healthy young adults between the ages of 18 and 30 took part in this observational study. Subjects in group I had a "Body Mass Index" (BMI) <25 and were normotensive; those in group II had a BMI <25 and were pre-hypertensive; and those in group III had a BMI >25 and were pre-hypertensive. Groups I, II, and III each included sixty members. "Low-Frequency Power" (LF), "High-Frequency Power" (HF), and the LF/HF ratio had been computed as part of the HRV study (Chart HRV module, AD Instruments Pty Ltd).

Results: It was found that pre-hypertensive individuals had a considerably higher LF/HF ratio than controls. In comparison to pre-hypertensive participants with a BMI < 25, those with a BMI >25 exhibited significantly higher values of the LF/HF ratio. The current research demonstrated a correlation between the LF/HF ratio and both hypertension (HTN) and BMI.

Conclusion: The dysfunction of the cardiac ANS, particularly with regard to sympathetic activity, was examined by HRV measures in obese pre-hypertensive patients. Our results provide evidence that autonomic dysfunction occurs in the early stages of HTN.

Keyword: *Heart Rate Variability; Isometric Handgrip Exercise; Pre-hypertension;Obesity*

1. INTRODUCTION

Hypertension is a common disease and a significant global health challenge. Hypertension and pre-hypertension, whether separately or in conjunction with other metabolic disorders that include obesity and diabetes, elevate cardiovascular disorder (CVD) risk, including ischemic heart disease and stroke. Pre-hypertension, the transitional stage between normal blood pressure (BP) and HTN, is related to subclinical atherosclerosis and organ damage.[1] A study found that pre-hypertension increases by three the risk of heart attack and 1.7 times the risk of heart disease.[2] An essential risk factor for pre-hypertension is excess weight. Additional risk factors involve a familial predisposition to hypertension, sedentary lifestyle, a diet challenging in sodium, tobacco use, and excessive consumption of alcohol or caffeine. Pre-hypertension constitutes a significant public health issue, impacting 25% of individuals globally.[3] In India, pre-hypertension was identified in 38.1% of women.[4] Autonomic dysfunction has been suggested to contribute causally to the onset of HTN.[5,6,7] CVD is a primary cause of mortality and disability. Insufficient data exist to support the correlation between pre-hypertension and autonomic dysfunction.[8-14]

In India, the number of children and adolescents who are overweight or obese is increasing.[15,16] The role of obese in the development of HTN has been conclusively exhibited.[17] We propose that pre-hypertensive people demonstrate an increased response to isometric handgrip training compared to normotensive individuals, particularly among those who are obese. Consequently, this research assessed the impact of IHG on HRV in pre-hypertensive obese and non-obese individuals

2. MATERIAL AND METHODS

This research had been carried out in Department of Physiology at a tertiary care facility in North India from 2014 to 2015. The current study had 180 participants, aged 18 to 30years. The institutional ethics committee approved this investigation, and informed approval had been acquired from each participant before the experiment started.

Inclusion and exclusion Criteria:

Participants with "Systolic Blood Pressure" (SBP) and "Diastolic Blood Pressure" (DBP) <140/90mm/Hg, who had been physically and mentally fit, non-smokers, non-alcoholic, and absence of any respiratory or cardiac ailments, had been involved in this study. The exclusion criteria involved: (i) individuals with SBP ≥140mm/Hg and/or DBP ≥90mm/Hg, (ii) those engaged in regular physical training, (iii) participants on antihypertensive medications or any other pharmacological treatment, (iv) individuals with a history of acute or chronic illnesses that include renal disease, diabetes, or any neuropsychiatric disorders that may influence autonomic function, and (v) smokers.

The individuals had been classified into 3 groups of 60 based on their BMI, following the World Health Organization (WHO) guidelines, as well as their SBP and DBP levels. Group I: Normotensive subjects with a BMI < 25; Group II: Pre-hypertensive subjects with a BMI < 25; Group III: Individuals with pre-hypertension and a BMI above 25.

Anthropometric Parameters

Height: The measurement was conducted with a standard stadiometer in cm, with each individual standing upright, looking ahead, and with heels touching. **Weight:** The measurement was taken in kilos by employing a calibrated weighing scale, with subjects wearing light clothing and standing upright without shoes. **Body mass index:** Body mass in kilograms divided by height in meters squared.

3. METHODOLOGY

All subjects were informed about the technique and assessed in a comfortable setting under consistent laboratory circumstances. Participants were directed to refrain from consuming caffeine and different stimulants for 24hours before the trial. The laboratory temperature was maintained at 22 to 24°C. Continuous ECG was recorded in a seated posture throughout the entire process using Power Lab, "AD Instruments Pty Ltd, Bella Vista, NSW, Australia".

Heart Rate Variability (HRV) Analysis:

HRV analysis had been obtained from a 'Lab Chart Recording' of heart beat signal from a pulse transducer at 1000 Samples/Sec with LAB CHART PRO-7.HRV was recorded for 5 minutes, three times during the whole procedure, in resting condition i.e. before isometric handgrip exercise. Subjects then performed handgrip dynamometer isometrics. The subjects had been instructed to grasp the hand dynamometer with their right hand completely. The subject was advised to exert maximum effort on the dynamometer, and the resultant tension was computed. This represented maximal isometric tension (Tmax). Three readings were obtained, each at maximal effort, and the mean of these three was calculated. The subject was again asked to perform the isometric exercise up to thirty percent of his/her maximum strength till he/she got exhausted. ECG was re-recorded immediately after the stoppage of exercise and again 5 minutes after exercise to observe the immediate effect of exercise. LF, HF, and LF/HF ratios had been noted in various groups.

Ethical consideration

The research had been performed according to ethical principles established in the Declaration of Helsinki. Inclusion of study subject were on voluntary basis after their verbal and analytical approval, informed written consent was taken from every subject. The study protocol and the subject information and consent form were reviewed and approved by a Local Ethics

Committee according to the document number IEC/ SGRRMC/2014-101 dated March 15, 2014.

Statistical Analysis:

Qualitative data were represented as proportions, whilst quantitative variables had been denoted as means ± standard deviation. Descriptive along with univariate analytical approaches were employed for data analysis. The Chi-square test/Fisher's exact test had been employed to compare categorical variables, whilst Student's t-test for independent samples was applied to continuous variables. The Pearson correlation coefficient had been employed to determine the correlation. *p*-values <0.05 had been considered statistically significant. Every analysis had been carried out by employing SPSS Version 21 ("IBM SPSS Statistics for Windows, version 21, Armonk, NY, USA: IBM Corp.").

4. RESULTS

Table 1 outlines anthropometric characteristics of the patients involved in investigation, while Table 2 illustrates the impact of handgrip training across several groups. Table 3 presents a comparative analysis of the impact of handgrip exercise on HRV between Group I and Group II. The mean values of LF, HF, and the LF/HF ratio of HRV at rest, immediately following IHG, and five minutes post-IHG did not exhibit significant differences among group II and group I.

Table 4 contrasts the impact of handgrip exercise on HRV between group I and group III. At rest, the values of HF (p=0.003) and the LF/HF ratio (p=0.042) were considerably elevated in group III in contrast to group I. The LF/HF ratio had been markedly elevated in group III compared to group I immediately following handgrip exercise and five minutes after isometric handgrip exercise.

Table 5 contrasts the impact of handgrip exercise on HRV between group III and group II. At rest, the mean value of HF was considerably elevated, but the LF/HF ratio' mean value was insignificantly elevated not group III in contrast to group II. The LF/HF ratio had been markedly elevated in group III in contrast to group II immediately following handgrip exercise and five minutes after isometric handgrip exercise.

Table 1: Anthropometric Parameters of Different groups

Parameters	**Group I**	**Group II**	**Group III**
	Mean±SD	**Mean±SD**	**Mean±SD**
Age (years)	22.3±2.1	20.3±1.6	22.1±3.8
Height (cms)	158.9±6.3	168.3±8.2	162.5±9.1
Weight (kg)	55.9±4.5	63.7±6.1	90.1±30.2
BMI (kg/m^2)	22.2±1.5	23.0±1.1	31.9±2.5

BMI: “Body Mass Index”

Table 2: Comparison of effect of Handgrip Exercise on HRV in Different Groups

Variables		**GROUP I**			**GROUP II**			**GROUP III**		
		At rest	**Immediately after IHG**	**At 5 minutes post IHG**	**At rest**	**Immediately after IHG**	**At 5 minutes post-IHG**	**At rest**	**Immediately after IHG**	**At 5 minutes post IHG**
LF (ms^2)	Mean	7075.6	5071.6	6200.9	6427.8	10350.8	5871.1	4441.2	3658.1	4031.4
	SD	8151.9	4611.4	13740.6	5720.9	17541.9	5265.6	7317.9	5768.2	6374.3
HF (ms^2)	Mean	11343.5	6340.9	4477.7	11451.5	10858.9	8950.4	94291.2	6929.7	7621.4
	SD	13312.9	7579.2	10751.6	26149.2	16237.1	9722.7	135043.2	16307.3	13973.1
LF/HF	Mean	0.8	1.2	2.1	1.1	1.2	2.3	1.3	1.7	3.8
	SD	0.5	0.7	1.2	0.8	0.6	2.5	1.1	1.0	2.2

*p-value <0.05 is considered statistically significant

HRV: “Heart Rate Variability”, IHG: “Isometric Handgrip Exercise”, HF: “High-Frequency Power”, LF: “Low-Frequency Power”

Table 3: Comparison of the Effect of Handgrip Exercise on HRV between Group I and Group II

Variables		**Group I**	**Group II**	***p*-value**
At Rest	**LF (ms^2)**	7075.6 ± 8151.9	6427.8 ± 5720.9	0.75
	HF (ms^2)	11343.5 ± 13312.9	11451.5 ± 26149.2	0.98

	LF/HF	0.8 ± 0.5	1.1 ± 0.8	0.22
Immediately After IHG	**LF (ms²)**	5071.6 ± 4611.4	10350.8 ± 17541.9	0.15
	HF (ms²)	6340.9 ± 7579.2	10858.9 ± 16237.1	0.21
	LF/HF	1.2 ± 0.7	1.2 ± 0.6	0.87
At 5 minutes post IHG	**LF (ms²)**	6200.9 ± 13740.6	5871.1 ± 5265.6	0.91
	HF (ms²)	4477.7 ± 10751.6	8950.4 ± 9722.7	0.13
	LF/HF	2.1 ± 1.2	2.3 ± 2.5	0.76

**p*-value <0.05 is considered statistically significant

HRV: "Heart Rate Variability", IHG: "Isometric Handgrip Exercise", HF: "High-Frequency Power", LF: "Low-Frequency Power"

Table 4: Comparison of Effect of Handgrip Exercise on HRV between Group I and Group III

Variables		**Group I**	**Group III**	***p*-value**
At Rest	**LF (ms²)**	7075.6 ± 8151.9	4441.2 ± 7317.9	0.23
	HF (ms²)	11343.5 ± 13312.9	94291.2 ± 135043.2	**0.003**
	LF/HF	0.8 ± 0.5	1.3 ± 1.1	**0.04**
Immediately After IHG	**LF (ms²)**	5071.6 ± 4611.4	3658.1 ± 5768.2	0.34
	HF (ms²)	6340.9 ± 7579.2	6929.7 ± 16307.3	0.87
	LF/HF	1.2 ± 0.7	1.7 ± 1.0	**0.04**
At 5 minutes post IHG	**LF (ms²)**	6200.9 ± 13740.6	4031.4 ± 6374.3	0.48
	HF (ms²)	4477.7 ± 10751.6	7621.4 ± 13973.1	0.38
	LF/HF	2.1 ± 1.2	3.8 ± 2.2	**0.002**

**p*-value <0.05 is considered statistically significant

HRV: "Heart Rate Variability", IHG: "Isometric Handgrip Exercise", HF: "High-Frequency Power", LF: "Low-Frequency Power"

Table 5: Comparison of Effect of Handgrip Exercise on HRV between Group II and Group III

Variables		**Group II**	**Group III**	***p*-value**
At Rest	**LF (ms²)**	6427.8 ± 5720.9	4441.2 ± 7317.9	0.29
	HF (ms²)	11451.5 ± 26149.2	94291.2 ± 135043.2	**0.004**
	LF/HF	1.1 ± 0.8	1.3 ± 1.1	0.32
Immediately After IHG	**LF (ms²)**	10350.8 ± 17541.9	3658.1 ± 5768.2	0.07
	HF (ms²)	10858.9 ± 16237.1	6929.7 ± 16307.3	0.39
	LF/HF	1.2 ± 0.6	1.7 ± 1.0	**0.02**
At 5 minutes post IHG	**LF (ms²)**	5871.1 ± 5265.6	4031.4 ± 6374.3	0.27
	HF (ms²)	8950.4 ± 9722.7	7621.4 ± 13973.1	0.69
	LF/HF	2.3 ± 2.5	3.8 ± 2.2	**0.03**

*A *p*-value less than 0.05 can be considered statistically significant.

HRV: “Heart Rate Variability”, IHG: “Isometric Handgrip Exercise”, HF: “High-Frequency Power”, LF: “Low-Frequency Power”

5. DISCUSSION

Research indicates that the risk of CVD related to BP is continuous, consistent, and independent of other risk variables, risk of cardiovascular disease doubles with every increase of 20/10mmHg in BP, starting at 115/75mmHg.[18] Males had higher pre-hypertension, and vagal withdrawal is more important than sympathetic overactivity.[19] Research conducted by our lab on young adults revealed increased sympathetic reactivity in pre-hypertensive individuals during conventional autonomic assessments, with males exhibiting greater sympathetic activity than females.[21]

HRV decreases in individuals with HTN, and the extent of this reduction correlates with the severity of the condition.[22] HRV widely acknowledged as a measure of cardiovascular risk.[23] Our investigation reveals that the values of HRV parameters at rest are consistent among groups I, II, and III. The LF/HF ratio is a precise and dependable indicator of sympathovagal equilibrium. An elevation in this ratio signifies heightened sympathetic activity.[24,25] The LF/HF ratio was markedly elevated in pre-hypertensive individuals (groups II and III) relative to normotensive individuals (group I), indicating an enhanced sympathetic discharge in pre-hypertensives. Nevertheless the slight difference in sample size, and LF/HF ratio exhibited significant differences among the normotensive and pre-hypertensive groups, a finding not corroborated by other investigations.[26,27]The difference could be explained by variances in the changed cardiovascular autonomic tone in response to high BP and racial differences in the basal LF/HF ratio.[28]

Our study indicates increased sympathetic activity during IHG. Normotensive individuals with an inherited susceptibility to hypertension exhibit increased sympathetic activity during IHG, resulting in an elevated LF/HF ratio, similar to our findings.[29,30]Research has shown increased sympathetic activity coupled with reduced parasympathetic tone in the development of pre-hypertension.[10-12,31] Research indicates that normotensive males with reduced HRV face an elevated risk of developing HTN in the future.[32] Consequently, the diminished HRV seen in pre-hypertensive individuals in our investigation corroborates previous findings regarding cardiac autonomic regulation.

Our investigation demonstrated that decreased vagal tone significantly influences the shift in sympathovagal balance from a normotensive to a pre-HTN state, as indicated by the reduction in LF/HF in pre-hypertensives. The severity of sympathovagal imbalance was more pronounced in pre-hypertensive individuals with elevated BMI compared to those with normal BMI. The study indicated that the alteration in vagal drive exceeded that of sympathetic drive in pre-hypertensive individuals with elevated BMI. Elevated adiposity is a important attributes in the onset of pre-HTN in predisposed individuals, as obesity correlates with decreased parasympathetic and increased sympathetic activity.[33,34] Research indicates that changes in plasma concentrations of neuropeptide-Y, leptin, and α-MSH (“Melanocyte-Stimulating Hormone”) may elevate sympathetic activity, resulting in hypertension among obese individuals.[35] Consequently, we propose that the sympathovagal imbalance induced by elevated BMI is a primary predictor of heightened blood pressure in pre-hypertensives. Schmid et al. showed that in young, overweight patients, a greater BMI is substantially related to improved sympathetic tone and BP.[36] After six months of calorie restriction and exercise, research shows that sympathetic activity returns to normal in overweight people.[37] According to a study, pre-hypertension, which is related to decreased sympathetic reactivity, is strongly predicted by high IL-17 levels.[38]

Several constraints of our investigation must be acknowledged. Because this research was cross-sectional, it is unable to conclusively prove a causal relationship between autonomic dysfunction and prehypertension. Another issue was the small sample size.

6. CONCLUSION

Our study revealed that the HRV parameters at rest were comparable across groups I, II, and III; Pre-hypertensive others had considerably higher LF/HF ratios (groups II and III) relative to normotensive individuals (group I), indicating increased sympathetic activity in pre-hypertensive subjects, particularly those with a higher BMI. Additional extensive longitudinal studies are essential to determine the impact of modifications to lifestyle on altered autonomic function.

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