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Frequency domain analysis of heart rate variability in response to cold pressor test in young offspring of hypertensive parents

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Abstract

Background: Cardiovascular reactivity to stress was revealed to be a predictor of future cardiovascular risk. A positive family history of hypertension is an important risk factor for the development of hypertension in the children of hypertensive parents. We applied cold pressor test (CPT) to measure heart rate variability (HRV) with the objective to assess the cardiovascular autonomic response to stress.

Methods: A case-control study was conducted between from December 2022 to November 2023 at the department of Physiology, Government Medical College, Kota in India. A total of 70 Cases and 70 Controls underwent to CPT technique to evaluate the autonomic function to stress. Descriptive and bivariate analysis including Mann-Whitney U- and ANOVA tests were performed.

Results: In this study, the mean ± SD values of HRV in control group before CPT was 79 ± 13, during CPT was 81 ± 11 and after CPT was 77 ± 9. The HR in control group was increased during CPT and the level decreased after CPT. The HRV level in control group was statistically significantly different before CPT, during CPT and after CPT, and p= 0.04.

Conclusion: The autonomic measurements were found higher in offspring of hypertensive parents (OHTPs) compared to offspring of normotensive parents (ONHTPs). The offspring of hypertensive parents have higher chances of future development of hypertension than the offspring of normotensive parents.

Keywords: Heart Rate Variability, Cold Pressor Test, Hypertension, Offspring of Hypertensive Parents, India

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Background

Hypertension is a risk factor for the development of cardiovascular disease and leads to 7.1 million deaths every year [1]. Globally, about 24% of cardiovascular diseases deaths can be attributed to hypertension alone [2]. The risk of cardiovascular death increases nearly two-fold in a linear fashion for each 20/10 mm Hg increment in blood pressure (BP) levels above 115/75 mm/Hg [3]. Better emotional and behavioural regulation, as well as improved health and well-being, are linked to higher resting heart rate variability (HRV), which is a reflection of increased parasympathetic nervous system activity [4,5]. Clinical research has linked depression and other mental health issues to low levels of vagally mediated HRV (vmHRV) [6]. The cardiovascular system and other systems have already undergone negative modifications by the time the person is diagnosed with hypertension. Therefore, it is critical to identify or anticipate normotensive hypertensive concepts as soon as possible [7]. In addition to several other mechanisms, stress is linked to the development of cardiovascular disease through the formation of atherosclerosis. The Framingham Heart Study shows that people with pre-hypertension are more susceptible to myocardial infarction, stroke, and sudden coronary mortality. High blood pressure largely caused by hereditary and environmental causes [8]. Family history may connections between blood pressure in siblings and between parents and children, is a crucial non-modifiable risk factor for hypertension [9]. Excessive activation of the sympathetic nervous system has been linked to hypertension. Children of parents with high blood pressure have been found to exhibit autonomic imbalance in the form of elevated sympathetic tone [10]. Very few studies have been done exploring the hereditary manifestations in the off-springs when their blood pressure is still optimal i.e<120/80 mmHg i.e at a young age when effect of environmental factors is still less. Handgrip strength (HGS) measurement is an indicator of an individual's overall strength and can serve as a predictor of

morbidity and mortality. Some research has examined sympatho-vagal balance solely using the isometric handgrip test [11]. The cold pressor test measures how the heart responds to discomfort. Unpredictable CPT response indicates of hypertension. Heart rate and blood pressure are also affected by the temperature. A person's physiological response to outside stimuli is evaluated using the Cold Pressor Test. A measure of the autonomic cardiovascular function linked to stress is the rise in blood pressure (BP) by the cold pressor test. Numerous systems, including the neurological, endocrine, cardiovascular, and immune systems, are impacted by stress. Stress immediately causes the sympathetic nervous system to become active [12]. Dutta and Bora [13] studied in healthy participants submerging both feet up to the ankle in a pail of cold water that was kept between 8 and 100 degrees Celsius, and localized cold stimuli were created in an externally controlled setting. After two minutes, parameters were recorded. In response to the cold stimuli, they found that the tidal volume and inspiratory capacity significantly increased while the expiratory reserve volume, forced vital capacity, and inspiratory reserve volume significantly decreased. Efferent vagal fibers are stimulated by cold both directly or reflexively, increasing airway resistance and decreasing anatomic dead space as a result of airway constriction. In response, the first-second forced expiratory volume, forced vital capacity, and inspiratory reserve volume all decrease [13].

Heart Rate Variability (HRV)

Spectral analysis of Heart rate variability has been recently used as sensitive tool for assessment of autonomic dysfunctions in various clinical disorders [14]. Frequency domain analysis methods use Fast Fourier transforms to yield three main spectral components from short-term recordings of ECG of 2 to 5 min viz. very low frequency (VLF), low frequency (LF), and high frequency (HF) components. Further analysis of these frequency components through Power spectral density (PSD) analysis provides the basic information of how power (i.e. variance) distributes as a function of frequency. At present spectral analysis beat to beat cardiovascular variability was novel method in the assessment of risk in primary hypertension [15, 16]. This study aimed to assess the cardiovascular autonomic reactivity by using frequency domain analysis of Heart rate variability (HRV) in response to CPT.

Methods

Study design

In this study, a case-control design was employed from December 2022 to November 2023 at the Department of Physiology, Government Medical College, Kota, Rajasthan. The data were collected after a verbal and written consent was obtained from all participants. All the selected subject recruited in the Department at 8:00 a.m. in overnight fasting state. CPT technique is used to assess the autonomic function to stress (stage -1, stage -2, stage -3). At the end of 2 minutes and 5 minutes of hand emersion, blood pressure (BP) and heart rate (HR) measurement were done by using digital BP instrument (Beurer BM35) in supine position. Frequency domain analysis, and electrocardiography (ECG) was recorded for 5 minutes to determine the HRV at supine with normal quite respiratory movements (12-16/minutes) included in this study. A total of 70 normotensive subjects of age 18–30 years with a family history of hypertension. Age- and sex-matched 70 normotensive subjects with no family history of hypertension. The subjects were advised to sit in the lab for 10 minutes to get accustom to the new environment. The subjects have been clearly instructed not to have Coffee, Tea or cool drinks 2 hours before test.

Inclusion and exclusion criteria

Healthy young adults between the age group of 18-30 years, of both sexes with family history of hypertension included in present study. Below 18 years age and above the age of 30 years, endocrine disorders, recent infections, cardiorespiratory disorders, and medications affecting central and autonomic nervous system, alcoholics, pregnant women, emotional stress, anxiety, and depression were excluded in this study.

Participants

Case group (GA) including those having family history of hypertension (34 females and 36 males). Control group including those having no family history of hypertension (32 females and 38 males).

Procedure

Phase I- instructions for the subjects prior to data collection.

Instructions for the Subjects prior to Data collection	
Do's	**Don't**
Took proper sleep (6-8 hours)	Alcohol consumption
Took proper and healthy diet on time	Smoking
Avoid stress	Excessive mobile use
Routine daily activity like Yoga and meditation	Coffee and tea consumption
Avoid Excessive Mobile use	Excessive workout

Phase II – Day of study

Stages of Data collection	
Stage	Description
Stage-1	Before Cold Pressor Test
Stage-2	During Cold Pressor Test
Stage-3	After Cold Pressor Test

The Evaluation of Heart Rate Variability (HRV)

The technique of heart rate variability analysis was adapted as mentioned in the Task force report of the European Society of Cardiology, 1996 [17]. Electrodes were fixed in the following position after cleaning the site to record the ECG.

1. The electrodes were connected to RMS ECG equipment.
2. ECG was recorded for 5 minutes to determine the HRV at supine with normal quite respiratory movements (12-16/minutes) Table A.

Table A- Positions of ECG Electrodes	
Electrode	**Position**
Exploring electrode	Left shoulder
Exploring electrode	Right shoulder
Reference electrode	Right leg

The temperature of the ice water must be between 0-7 ℃, because data of the research of Kregel et. al suggested that the

sympatho excitation only occurs when the skin temperature falls to less than 15 ℃ [18].

a. Pre-CPT HRV: After a supine rest of 10 minutes, the pre –CPT and ECG were recorded for 5 minutes to determine the pre –CPT and HRV from a period of ECG.

b. Post-CPT HRV: After 5 minutes of the onset of immersion of the hand in cold water, the post –CPT and ECG were recorded for 5 minutes to determine the post –CPT from a period of ECG. Blood Pressure (BP) and Heart Rate (HR) measurement done by using digital BP instrument (Beurer BM35), at the end of 2 minutes and 5 minutes after hand submersion.

Statistical analysis

The Mean ± SD values, and maximum (max) - minimum (min) and median (Inter-quartile rage) of heart rate variability (LF Power, HF Power & LF: HF Ratio) in case and control groups before CPT and to find out if there is any clinical significance between case and control group, Mann-Whitney U-test was performed. The Mean and SD values of SBP and DBP in case and control group before CPT, during CPT & after CPT and to find out if there is any significant difference between this ANOVA test was performed. HRV analysis in frequency domain method was done by using Kubios HRV, version 2.1.

Results

A total 140 participants (Case group: 34 females and 36 males; Control group: 32 female and 38 male). The participants gender distribution in case and control group were 'non-significant', p< 0.8. The blood pressures measurement (SBP, DBP) and Heart Rate in case and control groups during CPT were Significant. We found the SBP, DBP levels and Heart Rate in case and control groups after 5 minutes of CPT were highly significant.

Table 1: Shows the Mean ± SD values of blood pressure measurement (SBP, DBP) and heart rate in case and control groups before CPT and significance.

Mean ± SD values of blood pressures	Case Group	Control Group	p-value and statistical significance (independent t-test)
Systolic blood pressure (SBP)	132 ± 9	126 ± 9	t-value = 3.9181 p-value= 0.00013 (Significant)
Diastolic blood pressure (DBP)	89 ± 10	82 ± 8	t-value = 4.6449 p-value= 0.000008 (Significant)
Heart Rate (HR)	88 ± 13	79 ± 13	t-value = 3.877 p-value= 0.0001 (Significant)

Table 2: Shows the Mean ± SD values, and maximum (max) - minimum (min) and median (Inter-quartile range) of heart rate variability (LF Power, HF Power & LF: HF Ratio) in case and control groups before CPT and statistical significance.

Variables	Measurements	Case Group	Control Group	p-value and statistical significance
LF	Mean ± SD	1262 ± 761	1108 ± 1155	p-value =0.03163 Significant
	Max-Min	5306-433	9781-153	
	Median (IQR)	994(990)	869(455)	
HF	Mean ± SD	1073 ± 1487	1545 ± 1252	p-value=0.000001 Significant
	Max-Min	9877-234	7902-358	
	Median (IQR)	718(435)	1143(976)	
LF:HF ratio	Mean ± SD	1.6 ± 0.9	0.8 ± 0.4	P value =0.000000001 Significant
	Max-Min	5.2-0.3	2.4-0.1	
	Median (IQR)	1.3(0.8)	0.8(0.4)	

Table 3: Shows the Mean ± SD, and maximum (max) - minimum (min) and median (Inter-quartile range) (IQR) of heart rate variability (LF Power, HF Power & LF: HF Ratio) in case and control groups after CPT and significance.

Variables	Measurement	Case Group	Control Group	p-value and statistical significance
LF	Mean ± SD	1565 ± 1030	1211 ± 372	p-value=0.009386 Significant
	Max-Min	8028-826	2159-115	
	Median (IQR)	1402(754)	1204(434)	
HF	Mean ± SD	1148 ± 849	1545 ± 2442	p-value= 0.0441 Significant
	Max-Min	5442-227	19755-633	
	Median (IQR)	950(478)	1205(654)	
LF:HF ratio	Mean ± SD	2 ± 4.1	1.2 ± 0.5	p-value= 0.03892 Significant
	Max-Min	35.4-0.2	2.8-0.04	
	Median (IQR)	1.4(0.8)	1.2(0.8)	

Table 4: Shows the Mean and SD values of SBP in case and control groups before CPT, during CPT & after CPT.

Group	Mean ± SD of SBP			p-value and statistical significance
	Before CPT	During CPT	After CPT	
Case Group	132 ± 9	137 ± 12	125 ± 11	F-value = 54.29 p-value= 0.00000000001 (Significant)
Control Group	126 ± 9	132 ± 8	121 ± 7	F-value = 70.73 p-value= 0.00000000001 (Significant)

In our study the Mean ± SD values, and maximum (max) - minimum (min) and median (Inter-quartile range) of heart rate variability (LF Power, HF Power & LF: HF Ratio) in both groups case and control before CPT, after CPT were statistically Significant. Correlation of SBP levels before CPT, during CPT & after CPT in case and control groups were highly significant, p-value< 0.05. The values of HR before CPT, during CPT & after CPT in case and control groups were statistically Significant and the p value < 0.05. The median values of LF in case group after CPT was increased as compare to control group. The LF level in case group was found significant before CPT and after CPT used by Wilcoxon signed rank test and the p-value < 0.05. The Mean and SD values, minimum-maximum and median (Inter-quartile rage) of LF: HF ratio in case and control group before CPT & after CPT was found statistically significant. We observed the HR levels in case group was increased during CPT and decreased after CPT may indicate for future hypertension.

Discussion

In the present study, we assess the cardiovascular autonomic effect to stress through the measurement of Heart rate variability (HRV) using Cold pressor test (CPT) as a stressor in 70 case group participants and 70 controls group participants. We observed the median of LF in case group was higher before CPT but in control group LF values was lower before CPT. The LF values of both subjects was statistically significant. HF value in Case group was lower as compared to control group. The LF: HF values in case group was higher before CPT and after CPT as compare to control subjects. The LF: HF in both subjects statistically significant in present study. In a recent study, Wang et al., also observed higher LF, LF: HF Ratio and HF values in depression group compared to control group [20]. Singh S et al, [19] shows that the metrics VLF, LF, and LF/HF ratio have increased, low HF level indicates LOW variability in heart rate. A shift in the autonomic control of the heart, such as a decrease in parasympathetic tone or dominance of the sympathetic nervous system, is indicated by decreased HRV. As a result, the patient is more susceptible to developing CVD. A study shows the no significant difference between LF before CPT and after CPT in control group, but previous studies also have shown that over activity of the sympathetic nervous system during drug treatment of depression increases the LF/HF ratio [21]. The present study observed the SBP level in the case group was found significantly difference before CPT, during CPT, and after CPT and the DBP levels in the case and control groups were significant before CPT, during CPT, and after CPT. We also observed the HR in case group was increased during CPT and decreased after CPT. CPT test was proven to be useful for assessment of autonomic reactivity. Similarly, Kapoor A et al, [22] demonstrated in young subjects increased and prolonged responsiveness for blood pressure (diastolic) may stress-induced sympathetic nervous system stimulation (cold test) who had not return the diastolic blood pressure to baseline value after five minutes were found to be at risk for developing hypertension in the future. Tamilselvan et al 2018 et al, [23] carried out an observational cross-sectional study. They found the statistically significant increase in sympathetic response and a decrease in parasympathetic response when the posture changed. Despite being normotensives at rest, they conclude the normotensive children of hypertension parents exhibited a greater sympathetic reaction to physical stimuli, indicating sympathetic over activity, sympatho-vagal imbalance. A similar study by Keller-Ross et al, [24] showed an age-and sex-dependent females increase the muscle sympathetic nerve activity incidence and frequency with the CPT session, which correlate of BP during the CPT session in the older women. The case group participant had increased the values of LF, and LF/HF which relates the higher autonomic modulation, it indicates the sympathetic dominance in case group. The case group had decreased the HF values, showed the reduction of parasympathetic activity, it may due to feel lot of burden, hard work, stress, fatigue in young age and lifestyle. Our study suggests the life style modification for offspring of hypertensive parents.

Conclusion

The present study concluded that the heart rate variability measurements were significantly increased after cold pressor test in case group. The case subjects had increased level of LF and LF: HF ratio may indicate the high sympathetic activity in young age. Our findings indicate the offspring of hypertensive parents have higher sympathetic activity even in quite a young age, they are having higher risk of future development of hypertension and cardiovascular diseases as compared to offspring of normotensive parents.

Abbreviation

HRV: Heart Rate Variability; CPT: Cold Pressor Test; SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; LF: Low-Frequency; HF: High-Frequency; LF/HF: Ratio of LF-to-HF power. ONHTPs: Offspring of Normotensive Parents; OHTPs: Offspring of Hypertensive Parents. CVD: Cardiovascular Disease

Declaration

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Availability of data and materials
Data will be available by emailing tyagishikha@4gmail.com

Authors' contributions
All authors were equally participated in designing, supervising, the study and conceiving the idea. They worked together in data analysis, interpreted the results and curated and drafted the manuscript. All authors read and approved the final manuscript.

Ethics approval and consent to participate
We conducted the research following the declaration of Helsinki. The study protocol was approved by the ethical committee of Government Medical College, Kota, Rajasthan, reference no. No. F.3 /Acad/Ethical Clearance/Batch 2021/2022/62. Date of issue on 15th December 2022, and the consent form was guaranteed from each participant before performing this study.

Consent for publication
Not applicable

Competing interest
The authors declare that they have no competing interests.

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