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An Analytical Study of Heart Rate Variability in Newly Diagnosed Hypertensive Patients and Normotensive Subjects

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Abstract: Background: An adequate blood pressure is necessary for proper organ perfusion. Hypertension is a complex and non-communicable medical condition with increased blood pressure. The autonomic nervous system (ANS) regulates the cardiovascular system and sympathetic overactivity contributes not only to the initiation of essential hypertension but also to its progression and associated complications. Heart rate variability (HRV) is regarded as a non-invasive, sensitive measure of autonomic function, particularly useful for assessing sympathovagal balance. In this study, the changes in heart rate variability in patients of essential hypertension and age & sex matched healthy normotensive subjects were assessed. This study hypothesized that frequency domain parameters of heart rate variability may vary between patients with essential hypertension and in healthy normotensive subject. **Material and methods:** The present study was conducted on total 200 participants – 100 newly diagnosed essential hypertensive and 100 age & sex matched healthy normotensive subjects. Data collection was started after obtaining prior ethical approval from the institutional ethics committee. Anthropometric parameters were noted. HRV data was obtained using beat-to-beat human NIBP (non – invasive blood pressure) machine. Mean ± SD was used to expressed quantitative variables. Outcome variables were analyzed using parametric and non-parametric tests. Statistical significance was assigned at p-value<0.05. **Results:** The anthropometric parameters of essential hypertensive patients' group and normotensive subjects' group age, height weight and BMI were not statistically significant between the two groups. The mean ± SD difference of resting heart rate and resting blood pressure among hypertensive patients and normotensive subjects were statistically significant. The mean ± SD difference of HRV parameters among hypertensive patients and normotensive subjects were statistically significant. **Conclusion:** This study concluded that hypertensive patients have sympathovagal imbalance with increased sympathetic activity and decreased parasympathetic activity as compared to normotensive subjects.

Keywords: Essential Hypertension, Heart rate variability, Beat-to-Beat Human NIBP, Adrenergic dominance, Sympathovagal balance.

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INTRODUCTION

A sustained elevation of the systemic arterial pressure beyond the physiological range required for adequate tissue perfusion, known as hypertension [1]. Hypertension is a significant global health concern due to its widespread prevalence and association with serious health complications.

In India, hypertension has emerged as a major public health concern over the past three decades, driven by rapid urbanization, sedentary lifestyles, dietary transitions, and psychosocial stress. About 80% to 90% of all people who have hypertension are said to have essential hypertension. Essential hypertension is a multifactorial disorder arising from the interplay of genetic, environmental, and neurohumoral mechanisms [2].

ANS regulates the cardiovascular system and autonomic dysfunction may one of the most important mechanisms in essential hypertension. Sustained vasoconstriction raises peripheral resistance, while renal sympathetic activation promotes sodium retention and renin release in essential hypertension. Over time, sympathetic overdrive induces vascular remodelling, endothelial dysfunction, and left ventricular hypertrophy [3].

The assessment of sympathovagal balance, the balance between the sympathetic and parasympathetic activity at a given moment can be assessed by the HRV analysis. HRV is a non-invasive, sensitive measure of autonomic function, particularly useful for assessing sympathovagal balance. HRV evaluates autonomic modulation of the sinus node in normal subjects and in patients with different cardiac and non-cardiac diseases and to identify patients at risk for an increased cardiac mortality. Initially the report of *Wolf et al 1978* of the relationship of decreased RR variability on ECG and morality in post-MI patients released to understand the concept [4]. Different methodologies have been developed and are now available to measure HRV in the experimental laboratory and in the clinical setting.

HRV measures the variation in time intervals between consecutive heartbeats, reflecting the dynamic interplay between the sympathetic and parasympathetic branches of the ANS. Two spectral components are easily identified in HRV analysis: high frequency (HF) component (0.15–0.4Hz) and a lower frequency (LF) component (0.04–0.15Hz). A higher high-frequency (HF) component reflects parasympathetic activity dominance. A relatively higher low-frequency (LF) and higher LF to HF ratio, indicating a dominance of sympathetic activity over parasympathetic activity.

Essential hypertensive individuals, especially those with uncontrolled or newly diagnosed essential hypertension, may exhibit reduced HRV compared with age-matched normotensive subjects. Parasympathetic withdrawal diminishes vagal inhibition of the sinoatrial node, leading to higher resting heart rates and increased sympathetic activity leads to reduce HRV. These changes may reflect a shift in sympathovagal balance toward adrenergic dominance, which is proarrhythmic and predictive of adverse cardiovascular events [5].

In this study, we assessed the changes in heart rate variability parameters in patients of essential hypertension and compare them with healthy normotensive subjects. We hypothesized that frequency domain parameters of heart rate variability would vary between essential hypertension patients and healthy normotensive subject.

MATERIALS AND METHODS

The present study was conducted on essential hypertensive patients in the Department of Physiology in collaboration with Department of Medicine, S.M.S. Medical College and attached Hospitals, Jaipur. It was a hospital based cross sectional and comparative type of analytical study. Data collection was started after obtaining prior ethical approval from the institutional ethics committee (954/MC/EC/2024 Dated: 09/10/2024). The present study comprised of 200 subjects – 100 newly diagnosed essential hypertensive patients and age and sex matched 100 healthy normotensive subjects. A written informed consent was obtained from all participating subjects after explaining the purpose of the study and outcome prior to the commencement of study procedure. Detailed history and anthropometric parameters were obtained with resting heart rate (HR) and resting blood pressure (SBP & DBP). Blood sample of the recruited subjects were collected to measure fasting glucose (FG), lipid profile using Randox IMOLA RX or Backman counter AU 680 analyzer. Inclusion criteria for patients were newly diagnosed hypertensive patients of both sexes, diagnosis based on JNC-7 guidelines of hypertension, age group from 25 to 45 years. Exclusion criteria for participants were subjects with traumatic injuries and any acute illness, smokers and alcoholics, neuromuscular diseases, cognitive disturbances, pregnancy, history of limb injuries, subjects who were not cooperative.

The R-R intervals (iRR) from the electrocardiographic record were used to obtained HRV data. Subject was instructed to remain in the supine position for approximately 10 min to stabilize cardiovascular parameters. After this period, the ECG and blood pressure was recorded simultaneously for another 10 min in essential hypertensive patients and normotensive subjects were assessed using beat-to-beat human NIBP (non – invasive blood pressure) machine and Medicare system human NIBP NANO INL382 (AD Instruments, Australia) and ECG limb leads provided by the Department of Physiology, S.M.S. Medical College, Jaipur. RRi time series was integrated in bands of low frequency (LF) and high frequency (HF) and the results of HRV was expressed in normalized unit (nu) by using of software LabCart v8.1.10.

Mean ± SD were used to expressed quantitative variables. Analysis was done using PRIMER version 6. Outcome Variables were analyzed using parametric and non-parametric tests. Significance of difference in mean in both main groups were inferred by the student's unpaired t-test and the Mann-Whitney U test. Statistical significance was assigned at p-value<0.05.

RESULTS

Table 1: Comparison of anthropometric parameters between hypertensive patients and normotensive subjects

Parameters	Group (mean ± SD)		p-Value	Significance
	Hypertensive patients (n=100)	Normotensive subjects (n=100)		
Age (year)	36.78 ± 4.46	35.56 ± 4.56	0.057	NS
Height (cm)	163.48 ± 9.39	164.05 ± 9.05	0.663	NS

Weight (kg)	64.07 ± 8.61	62.98 ± 7.44	0.419	NS
BMI (kg/m^2)	23.80 ± 2.02	23.32 ± 1.39	0.052	NS

NS = Non-Significant, HS** = Highly Significant

The difference between the age of hypertensive patients' group and normotensive subjects' group is not found to be statistically significant (p>0.05). The results after applying student's unpaired 't'-test are shown in table-1. The difference between the height of hypertensive patients' group and normotensive subjects' group is not found to be statistically significant (p>0.05). The results after applying student's unpaired 't'-test are shown in table-1. The difference between the weight of hypertensive patients' group and normotensive subjects' group is not found to be statistically significant (p>0.05). The results after applying mann-whitney 'u'-test are shown in table-1. The difference between the BMI (body mass index) of hypertensive patients' group and normotensive subjects' group is not found to be statistically significant (p>0.05). The results after applying student's unpaired 't'-test are shown in table-1.

Table 2: Comparison of FG and lipid profile between hypertensive patients and normotensive subjects

Parameters	Group (mean ± SD)		p-Value	Significance
	Hypertensive patients (n=100)	Normotensive subjects (n=100)		
FG (mg/dl)	93.07 ± 7.38	91.66 ± 6.43	0.151	NS
Cholesterol (mg/dl)	153.11 ± 12.70	150.02 ± 13.76	0.100	NS
HDL (mg/dl)	46.40 ± 7.11	47.95 ± 6.34	0.105	NS
LDL (mg/dl)	108.24 ± 10.66	103.70 ± 10.19	0.002	S*
TG (mg/dl)	120.26 ± 23.08	89.40 ± 13.72	<0.001	HS**

NS = Non-Significant, S* = significant, HS** = Highly Significant

The difference between the FG (fasting glucose) of hypertensive patients' group and normotensive subjects' group is not found to be statistically significant (p>0.05). The results after applying student's unpaired 't'-test are shown in table-2. The difference between the cholesterol of hypertensive patients' group and normotensive subjects' group is not found to be statistically significant (p>0.05). The results after applying student's unpaired 't'-test are shown in table-2. The difference between the HDL (high-density lipoprotein) of hypertensive patients' group and normotensive subjects' group is not found to be statistically significant (p>0.05). The results after applying student's unpaired 't'-test are shown in table-2. The difference between the LDL (low-density lipoprotein) of hypertensive patients' group and normotensive subjects' group is found to be statistically significant (p<0.05). The results after applying student's unpaired 't'-test are shown in table-2. The difference between the TG (triglycerides) of hypertensive patients' group and normotensive subjects' group is found to be statistically highly significant (p<0.001). The results after applying student's unpaired 't'-test are shown in table-2.

Table 3: Comparison of resting heart rate and resting blood pressure between hypertensive patients and normotensive subjects

Parameters	Group (mean ± SD)		p-Value	Significance
	Hypertensive patients (n=100)	Normotensive subjects (n=100)		
HR (bpm)	80.42 ± 6.31	72.32 ± 5.02	<0.001	HS**
SBP (mmHg)	149.65 ± 5.30	118.77 ± 8.07	<0.001	HS**
DBP (mmHg)	95.08 ± 3.79	74.42 ± 3.84	<0.001	HS**

HS** = Highly Significant

The difference between the resting HR (heart rate) of hypertensive patients' group and normotensive subjects' group is found to be statistically highly significant (p<0.001). The results after applying student's unpaired 't'-test are shown in table-3. The difference between the SBP (systolic blood pressure) of hypertensive patients' group and normotensive subjects' group is found to be statistically highly significant (p<0.001). The results after applying student's unpaired 't'-test are shown in table-3. The difference between the DBP (diastolic blood pressure) of hypertensive patients' group and normotensive subjects' group is found to be statistically highly significant (p<0.001). The results after applying mann-whitney 'u'-test are shown in table-3.

Table 4: Comparison of heart rate variability parameters between hypertensive patients and normotensive subjects

Parameters	Group (mean ± SD)		p-Value	Significance
	Hypertensive patients (n=100)	Normotensive subjects (n=100)		
LF (nu)	64.96 ± 8.65	52.87 ± 5.40	<0.001	HS**
HF (nu)	33.64 ± 7.60	46.20 ± 5.53	<0.001	HS**
LF/HF ratio	2.14 ± 1.03	1.17 ± 0.24	<0.001	HS**

HS** = Highly Significant

The difference between the LF (low frequency) of hypertensive patients' group and normotensive subjects' group is found to be statistically highly significant (p<0.001). The results after applying student's unpaired 't'-test are shown in table-4. The difference between the HF (high frequency) of hypertensive patients' group and normotensive subjects' group is found to be statistically highly significant (p<0.001). The results after applying student's unpaired 't'-test are shown in table-4. The difference between the LF/HF ratio of hypertensive patients' group and normotensive subjects' group is found to be statistically highly significant (p<0.001). The results after applying mann-whitny 'u'-test are shown in table-4.

DISCUSSION

The mean LDL in hypertensive patients' group was found to be higher (108.24 ± 10.66 mg/dl) as compared with normotensive subjects' group (103.70 ± 10.19 mg/dl). (p-value<0.05, Table2). The mean TG in hypertensive patients' group was found to be higher (120.26 ± 23.08 mg/dl) as compared with normotensive subjects' group (89.40 ± 13.72 mg/dl). (p-value<0.001, Table 2). *Kumar R et al 2024* [6], *Chen S and Cheng W 2022* [7] found higher LDL and TG in hypertensive patients than normotensive subjects. Vascular endothelial function is probably the link between hypertension and higher levels of lipids. Vascular endothelial function plays a central role in regulating arterial contractility.

The mean resting HR in hypertensive patients' group was found to be higher (80.42 ± 6.31 bpm) as compared with normotensive subjects' group (72.32 ± 5.02 bpm). (p-value<0.001, Table 3). Many researchers such as *Pal G K et al 2021* [8], *Balakrishnan A 2018* [9] observed higher resting HR in hypertensive patients than normotensive subjects. Previous studies have also suggested that this might be due to an increase in centrally originating oscillations in sympathetic drive to the heart.

The mean resting SBP in hypertensive patients' group was found to be higher (149.65 ± 5.30 mmHg) as compared with normotensive subjects' group (118.77 ± 8.07 mmHg). (p-value <0.001, Table 3). The mean resting DBP in hypertensive patients' group was found to be higher (95.08 ± 3.79 mmHg) as compared with normotensive subjects' group (74.42 ± 3.84 mmHg). (p-value <0.001, Table 3). Essential hypertensive patients have higher SBP and DBP which is confirmed by many studies and hypertension guidelines and studies *Pal G K et al 2021* [8], *Yu et al 2018* [10], *JNC-7 guidelines* [11]. Less than or equal to 120 mmHg of SBP and less than or equal to 80 mmHg of DBP are considered as normal range for healthy normotensive subjects, equal to or more than 140 mmHg of SBP and equal to or more than 90 mmHg DBP are considered as blood pressure range for hypertensive patients [11].

The mean LF in hypertensive patients' group was found to be higher (64.96 ± 8.65 nu) as compared with normotensive subjects' group (52.87 ± 5.40 nu). (p-value <0.001, Table 4). The mean HF in hypertensive patients' group was found to be lower (33.64 ± 7.60 nu) as compared with normotensive subjects' group (46.20 ± 5.53 nu). (p-value <0.001, Table 4). The mean LF/HF ratio in hypertensive patients' group was found to be higher (2.14 ± 1.03) as compared with normotensive subjects' group (1.17 ± 0.24). (p-value <0.001, Table 4). In the present study, the LF and LF/HF ratio in hypertensive patients were higher and HF was lower as compared to normotensive subjects. Study by *Kapadia NA et al, 2023* [12] indicated that cardiac sympathetic drive is more common in hypertensive patients. Hence, autonomic dysfunction is seen in hypertensive patients. *Shah H et al, 2023* [5] found in their study that sympathetic over activities and reduced parasympathetic activities are common today due to sedentary lifestyles. Increased sympathetic tone is more prominent in hypertensive adults which makes vasculature more stressed. Increased vasoconstrictor tone of systemic vasculature increases blood pressure. Sympathovagal imbalance and impaired autonomic functions are responsible for change in blood pressure. Dysregulation of autonomic system is the key contributor for the essential hypertension and high blood pressure further changes the autonomic nervous system. *Prasad A et al 2023* [13], *Tank A 2019* [14] suggested increase in sympathetic activity and reduced parasympathetic activity in essential hypertensive subjects. They found LF was greater and HF was lower in hypertensives as compared to normotensives. *Goit RK et al 2016* [15] conducted a study and showed HF (ms^2) and HF (nu) which reflects parasympathetic activity, were significantly less in hypertensive subjects while LF (nu) and LF/HF ratio which reflects sympathetic activity, were comparable between the groups. There findings suggest early parasympathetic inhibition in the development of hypertension. Study conducted by *Julius S et al 1991* [16] quoted that increase sympathetic drive and parasympathetic inhibition are associated with patients with hypertension. This state is also characterized by high heart rate, high cardiac output and normal vascular resistance (hyperkinetic state). Cardiac output returns to normal values and the β-adrenergic receptors down regulate and stroke volume decreases. The high blood pressure increases vascular hypertrophy, that leads to increased vascular resistance. The mechanism of change of sympathetic drive from high to normal can be explained by "blood pressure seeking" properties of the brain. In hypertension, the blood pressure needs to be maintained at higher levels, as decrease progresses the vascular hypertrophy causes increased vascular resistance. The increase in sympathetic drive found in hypertension is still unsolved. The reason may include other factors as BMI, higher lipids, genetics, stress, sedentary lifestyle.

CONCLUSION

This study concluded that essential hypertensive patients have increased sympathetic activity and decreased parasympathetic activity, is known as sympathovagal imbalance as compared to normotensive subjects. Therapies to increase parasympathetic activity with proper pharmaceutical management can be introduce to the hypertensive patients and follow up with the patients; decreases the morbidity and mortality ratio of cardiovascular complications.

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