e-ISSN: 0975-1556, p-ISSN:2820-2643

Available online on www.ijpcr.com

International Journal of Pharmaceutical and Clinical Research 2024; 16(2); 617-626

Original Research Article

A Prospective Study of Heart Rate Variability and Serum Uric Acid with Blood Pressure in Normotensives and Stage 1 Hypertensives

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Received: 19-01-2024 / Revised: 02-02-2024 / Accepted: 15-02-2024

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Conflict of interest: Nil

Abstract:

Blood pressure is the pressure exerted by the moving blood column on the walls of the arteries. It is one of the vital parameters of a human being. Being a vital parameter, it is essential for the survival of human life. The blood pressure in a human undergoes multiple changes over different stages of life. At birth it is around 70/50 mmHg. Then it gradually increases to about 90/60 mmHg at the end of first year of life.

Materials & Methods: This study was conducted in the private clinic, Kalaburagi, A total of 120 subjects in the age group of 30 – 40 years attending Noncommunicable diseases OPD. Among them 60 subjects were normotensives with systolic blood pressure < 130 mm Hg and diastolic blood pressure < 80 mm Hg.

Result: The mean value of LF in hypertensives (348.77±325.90) is statistically more than the mean value of normotensives (216.15±249.78) with 't' value of 2.50 and a 'p' value of 0.014 (p<0.05). This signifies that the low frequency component is significantly

Conclusion: Hypertension is a noncommunicable disease, and its incidence is increasing drastically all around the world. Consequently, the need for complete understanding of the pathophysiology of the disease and proper diagnostic and therapeutic measures to counteract the disease burden has also increased.

Keywords: Hypertension, Uric Acid, HRV.

Introduction

Blood pressure is the pressure exerted by the moving blood column on the walls of the arteries. It is one of the vital parameters of a human being. Being a vital parameter, it is essential for the survival of human life. The blood pressure in a human undergoes multiple changes over different stages of life. At birth it is around 70/50 mmHg. Then it gradually increases to about 90/60 mmHg at the end of first year of life. [1] With an increase in age, the blood pressure gradually increases from neonatal life to adolescent life and reach adult value by 12 years of age. Thereafter there will be no significant changes as the age progresses. In the later decades the blood pressure may increase slightly in healthy adults but usually it will be within normal limits. Apart from age there are many factors which control, modulate and maintain the blood pressure inside the body. These factors act as a whole in maintaining the blood pressure and ultimately the homeostasis of the body. When any one of these factors get affected or modified during life it will result in fluctuations in blood pressure. The blood pressure thus can either drastically increase or fall based on the mechanism affected. These results are called hypertension and hypotension respectively. When either hypertension or hypotension occurs, the homeostasis gets affected. Usually, slight increase or decrease of blood pressure will not result in much significant changes in the body. But when these changes remain for a sustained period of time almost all of the internal organs which are constantly under the influence of blood pressure get affected resulting in end organ damage. Thus, hypertension becomes an important healthcare concern and has to be treated if not prevented at all costs. Hypertension, otherwise known as 'the silent killer' has become a worldwide pandemic. The incidence of hypertension is increasing every day. Thus, proper estimation, diagnosis, treatment and identifying the risk factors have become matters of paramount importance. Several cutoff values have been proposed by different studies for hypertension in the past years. But the recent one proposed was that by American Heart Association (AHA) in the year 2018, which classifies a systolic pressure of ≥ 130 mm Hg and/or a diastolic pressure of ≥ 80 mm Hg as hypertension. [2] Hypertension has ill effects on almost all organ systems of the body. Sustained uncontrolled hypertension can result in target organ damage in kidneys, eyes, liver, spleen, heart and brain. Hypertension itself is an independent risk factor for coronary artery disease, cerebrovascular accidents, thromboembolism, peripheral vascular occlusive disease etc. [3] The duration of hypertension rather than the actual age of the patient has more impact in the appearance of complications and target organ damage. Hypertension is a non-communicable disease with multiple risk factors like metabolic syndrome, obesity, positive family history etc. [4] Since regulation of blood pressure is under the control of multiple physical and chemical factors in the body, disruption of any one of them can result in the appearance of hypertension. Consequently, treatment of hypertension is also not a simple task. There are myriad of treatment regimens and drugs available for treatment of hypertension – lifestyle modifications, diet restrictions, regulating salt intake, drugs like beta blockers, calcium channel blockers, diuretics to name a few. [5,6] Most of the times a combination of above-mentioned treatment options is required to provide good control of blood pressure in hypertensives. This implies that there is a delicate and intricate balance between the parameters which are concerned with maintenance of blood pressure. Thus, hypertension has to be carefully evaluated and the treatment has to be titrated for that particular patient to achieve a sustained maintenance of blood pressure. In this study two of the most important risk factors for hypertension namely impaired autonomic function and hyperuricemia are studied. Autonomic nervous system has a significant role in the circulatory system and in blood pressure regulation. Impaired autonomic nervous system function has been implicated in the development of coronary heart diseases and hypertension. Autonomic modulation of Heart Rate is assessed by Heart Rate Variability [HRV]. [7] HRV is considered as a standard, non-invasive tool used to measure autonomic dysfunction. HRV denotes the variability between individual cardiac beats and is the most sensitive indicator of sympathovagal balance. The state of sympathovagal balance is used in the diagnosis of several cardiovascular disorders and many autonomic dysfunctional disorders. [8] HRV analysis is used to specifically assess the effectiveness of cardiac vagal control of the individual, as it denotes the variation that occurs mainly due to sinus arrhythmia. During inspiration vagal inhibition occurs, due to central irradiation of impulses from the medullary respiratory center to the cardiovascular center, responsible for the fluctuations in heart rate during respiration called Respiratory Sinus Arrhythmia (RSA). Heart rate is mainly regulated by the ANS. [9] Normally, parasympathetic stimulation has cardio inhibitory effect and sympathetic stimulation has cardio accelerating effect. HRV analysis is a tool of sympathovagal balance. It mirrors the fluctuations in the period in-between heartbeat (R waves) over time. R–R interval or inter beat interval (IBI) is the interval between two consecutive R waves which is measured in milliseconds. Autonomic Nervous System directs the inter beat interval via sympathetic and parasympathetic neural pathways. Under resting conditions in healthy individuals, parasympathetic system plays dominant part in controlling the HR. In stressful and emergency conditions sympathetic system plays a main part in regulating the HR. [10] High value of HRV denotes predominant parasympathetic activity, while lower HRV denotes predominant sympathetic activity. The aim of this study is to compare and correlate the HRV parameters with blood pressure in hypertensives and normotensives. Uric acid is the final breakdown product of purine degradation in humans. The normal values of serum uric acid in males is 3.1 - 7.0 mg/dl, and females is 2.5 - 5.6 mg/dl. [11] When the serum uric acid levels rise above the mentioned cut-off values it is termed as hyperuricemia. Uric acid at higher levels has a tendency to form crystals which are insoluble in water. Hence in hyperuricemia urate crystals are formed and get deposited in body tissues. [12] Uric acid tends to crystallise at lower temperatures and hence peripheral parts of the body are at risk. So the urate crystals get deposited commonly in peripheral joints resulting in gout. [13] The most well-known side effect of increased serum uric acid levels is gout. But deposition of the crystals has other side effects as well. Apart from depositing in joints, the crystals get deposited in renal interstitium and cause nephropathy, associated with increased risk of cardiovascular events, peripheral vascular events, metabolic syndrome etc. [14] The presence of higher level of serum uric acid also exaggerates the disease progression of the above-mentioned conditions. Uric acid is also hypothesised to be an individual risk factor for hypertension. Increased levels of serum uric acid have been found in the hypertensive groups by some studies, whereas some studies have shown increased incidence of hypertension in hyperuricemic subjects. [15] In the studies including blood pressure and serum uric acid levels, higher serum uric acid levels usually preceded the appearance of hypertension. This suggests that there is a probable relationship between serum uric acid and increased blood pressure. But studies involving treatment of hyperuricemia in hypertensives are very small and very few. Hence, whether treating hyperuricemia will result in a reduction in blood pressure is not yet known. One major drawback in determination of uric acid as a risk factor for hypertension is the fact that uric acid is not routinely investigated in hypertensives. But this trend is changing nowadays, and uric acid analysis is becoming a part of the routine investigations. But still, the awareness and understanding regarding the importance of uric acid levels in disease conditions, apart from gout, is minimal.

Materials & Methods

This study was conducted in the private clinic, Kalaburagi. A total of 120 subjects in the age group of 30 – 40 years attending Noncommunicable diseases OPD .Among them 60 subjects were normotensives with systolic blood pressure < 130 mm Hg and diastolic blood pressure < 80 mm Hg. 60 subjects were stage 1 hypertensives with systolic blood pressure between 130 and 139 mm Hg and/or diastolic blood pressure between 80 and 89 mm Hg. The hypertensives are newly diagnosed and have not been on any hypertensive medications.

Exclusion Criteria:

- Age < 30 years, > 40 years
- Diseases – gout, diabetes mellitus, known hypertensives on medication, previous cardiac events (MI, CAD, angina), renal dysfunction, psoriasis, dyslipidemia.
- Secondary hypertension, previous history of secondary hypertension
- History of malignancies
- History of connective tissue disorders
- History of alcoholism
- History of intake of drugs which affect serum uric acid levels (allopurinol, probenecid)
- History of intake of drugs which influence autonomic nervous system function – cholinergic, anticholinergic, sympathomimetic, sympatholytic.

Statistical Analysis

Required data collected from all the subjects were recorded in a master Chart. Data analysis was done by using Statistical Packaging of Social Science 25 (SPSS 25) Version. Statistical methods were used to calculate the mean and standard deviation. Independent student t test was applied to analyse the statistical significance in HRV parameters and serum uric acid levels with blood pressure. Pearson's correlation was done to establish a relation between HRV parameters and blood pressure values, and serum uric acid levels and blood pressure values. Microsoft word and excel has been used for making tables, charts and graphs.

Results

Table 1 Descriptive statistics of various clinical measurements in Normotensives (n=60)

Parameters	Pulse rate (/min)	Respiratory rate (/min)	Systolic blood pressure (mm Hg)	Diastolic blood pressure (mm Hg)	Mean arterial pressure (mm Hg)
Mean	79.97	14.15	114.13	68.70	83.94
Standard deviation	8.401	1.176	8.807	5.878	6.095
Minimum	66	12	100	60	73.33
Maximum	94	16	128	80	96.00

Table 2 Descriptive statistics of various clinical measurements in Hypertensives (n=60)

Parameters	Pulse rate (/min)	Respiratory rate (/min)	Systolic blood pressure (mm Hg)	Diastolic blood pressure (mm Hg)	Mean arterial pressure (mm Hg)
Mean	78.57	14.12	134.37	83.97	100.77
Standard deviation	6.700	1.027	2.864	2.840	2.071
Minimum	66	12	130	80	96.67
Maximum	96	16	138	88	104.67

Table 3: Descriptive statistics of low frequency (LF) values in Normotensives (n=60) and Hypertensives (n=60)

LF (ms^2)	Mean	SD	t value	p value
Normotensives	216.15	249.78	2.50	0.014
Hypertensives	348.77	325.90		

The mean value of LF in hypertensives (348.77±325.90) is statistically more than the mean value of normotensives (216.15±249.78) with 't' value of 2.50 and a 'p' value of 0.014 ($p<0.05$). This signifies that the low frequency component is significantly increased in hypertensives when compared with normotensives.

Table 4 Pearson's correlation values of LF with mean arterial pressure in study subjects (n=120)

HRV parameter	Pearson's r	p value
LF	0.22	0.014

The Pearson's correlation of LF component with the mean arterial pressure of the study group (both normotensives and hypertensives) has 'r' value of 0.22 with a statistically significant p value of 0.014 ($p<0.05$). This means that as the mean arterial pressure increased the low frequency component also increased.

Table 5 Descriptive statistics of high frequency (HF) values in Normotensives (n=60) and Hypertensives (n=60)

HF (ms^2)	Mean	SD	t value	p value
Normotensives	34.03	33.88	2.37	0.020
Hypertensives	57.47	68.83		

The mean value of HF in hypertensives (57.47±68.83) is statistically more than the mean value of normotensives (34.03±33.88) with 't' value of 2.37 and a 'p' value of 0.020 ($p<0.05$). This signifies that the high frequency component is significantly increased in hypertensives when compared with normotensives.

Table 6 Pearson's correlation values of HF with mean arterial pressure in study subjects (n=120)

HRV parameter	Pearson's r	p value
HF	0.23	0.011

The Pearson's correlation of HF component with the mean arterial pressure of the study group (both normotensives and hypertensives) has 'r' value of 0.23 with a statistically significant p value of 0.011 ($p<0.05$). This means that as the mean arterial pressure increased the high frequency component also increased.

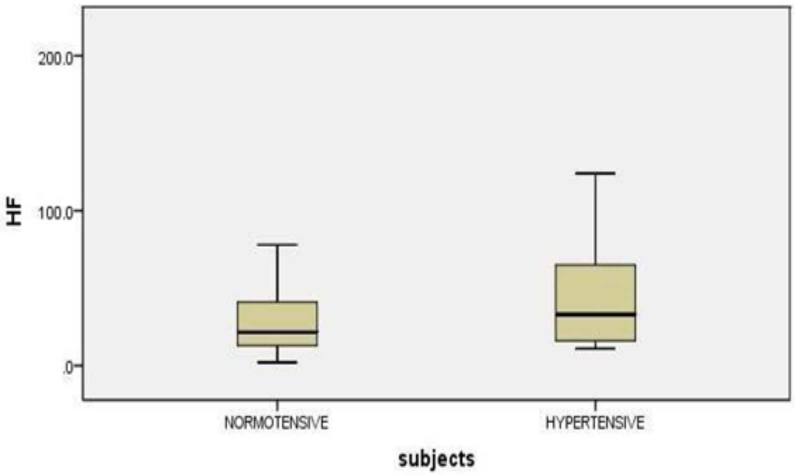

Figure 1 Box plot showing distribution of high frequency levels (HF) in Normotensives (n=60) and Hypertensives (n=60)

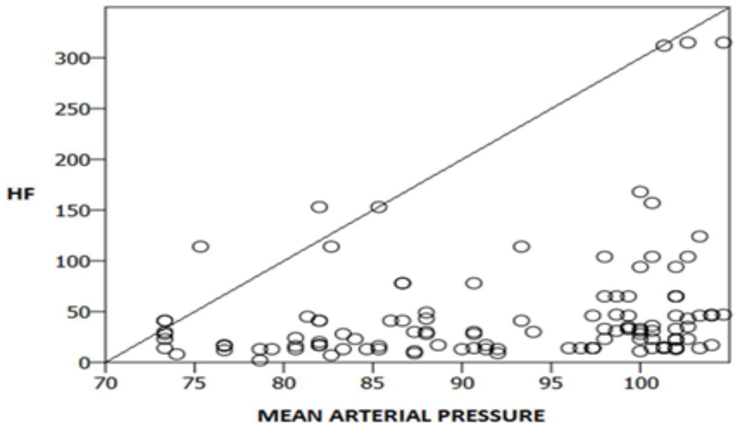

Figure 2 Scatterplot showing relationship between HF and mean arterial pressure in study subjects (n=120)

Table 7: Descriptive statistics of LF/HF ratio in Normotensives (n=60) and Hypertensives (n=60)

LF/HF ratio	Mean	SD	t value	p value
Normotensives	5.835	1.083	3.38	0.001
Hypertensives	6.587	1.338		

The mean value of LF/HF in hypertensives (6.587±1.338) is statistically more than the mean value of normotensives (5.835±1.083) with 't' value of 3.38 and a 'p' value of 0.001 ($p<0.01$). This signifies that the low frequency to high frequency ratio is significantly increased in hypertensives when compared with normotensives.

Table 8: Pearson's correlation values of LF/HF with mean arterial pressure in study subjects (n=120)

HRV parameter	Pearson's r	p value
LF/HF	0.24	0.009

The Pearson's correlation of LF/HF ratio with the mean arterial pressure of the study group (both normotensives and hypertensives) has ‘r’ value of 0.24 with a statistically significant p value of 0.009 ($p<0.01$). This means that as the mean arterial pressure increased the low frequency to high frequency ratio also increased.

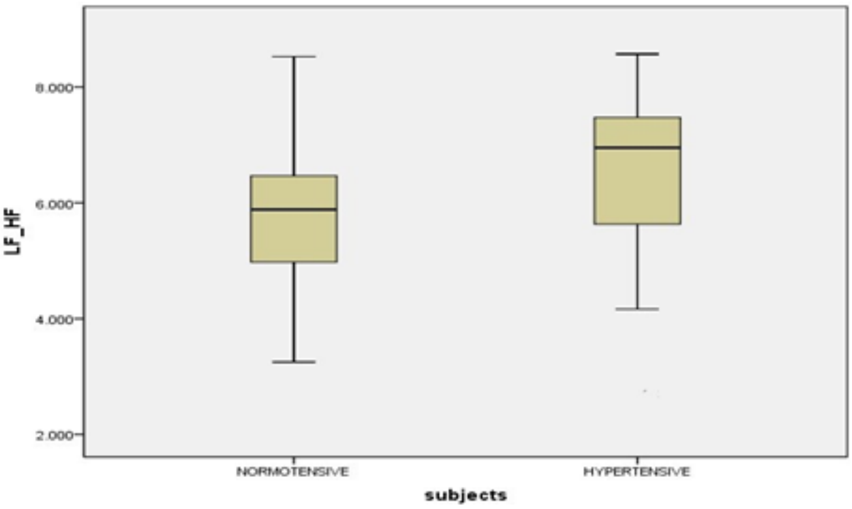

Figure 3 Box plot showing distribution of LF/HF ratio in Normotensives (n=60) and Hypertensives (n=60)

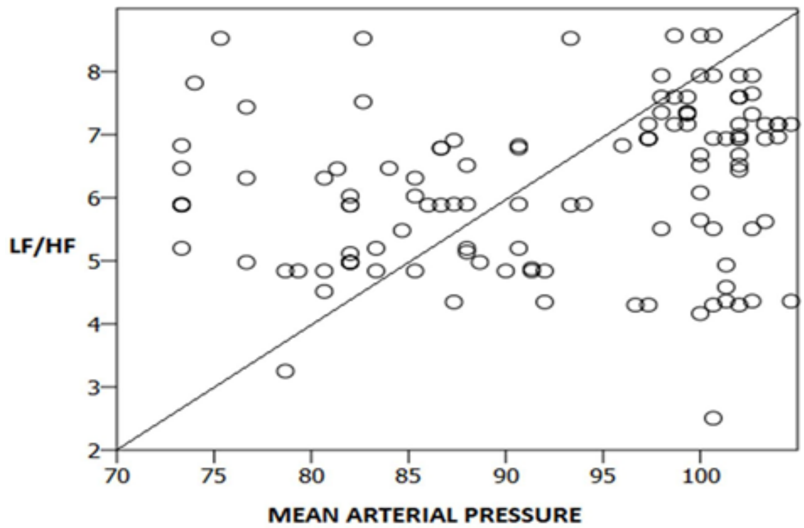

Figure 4 Scatterplot showing relationship between LF/HF and mean arterial pressure in study subjects (n=120)

Table 9: Descriptive statistics of LF normalised unit (LFnu) in Normotensives (n=60) and Hypertensives (n=60)

LFnu	Mean	Standard deviation	t value	p value
Normotensives	85.01	2.333	2.39	0.019
Hypertensives	86.23	3.220		

The mean value of LFnu in hypertensives (86.23±3.220) is statistically more than the mean value of normotensives (85.01±2.333) with ‘t’ value of 2.39 and a ‘p’ value of 0.019 ($p<0.05$). This signifies that the low frequency normalised unit is significantly increased in hypertensives when compared with normotensives.

Table 10: Pearson’s correlation values of LFnu with mean arterial pressure in study subjects (n=120)

HRV parameter	Pearson’s r	p value
LFnu	0.21	0.019

The Pearson’s correlation of LFnu with the mean arterial pressure of the study group (both normotensives and hypertensives) has ‘r’ value of 0.21 with a statistically significant p value of 0.019 ($p<0.05$). This means that as the mean arterial pressure increased the low frequency normalised unit also increased.

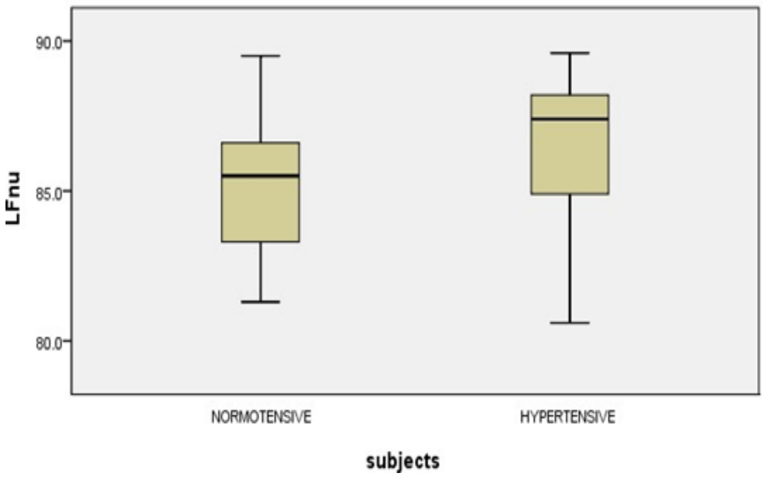

Figure 5 Box plot showing distribution of LF normalised unit (LFnu) in Normotensives (n=60) and Hypertensives (n=60)

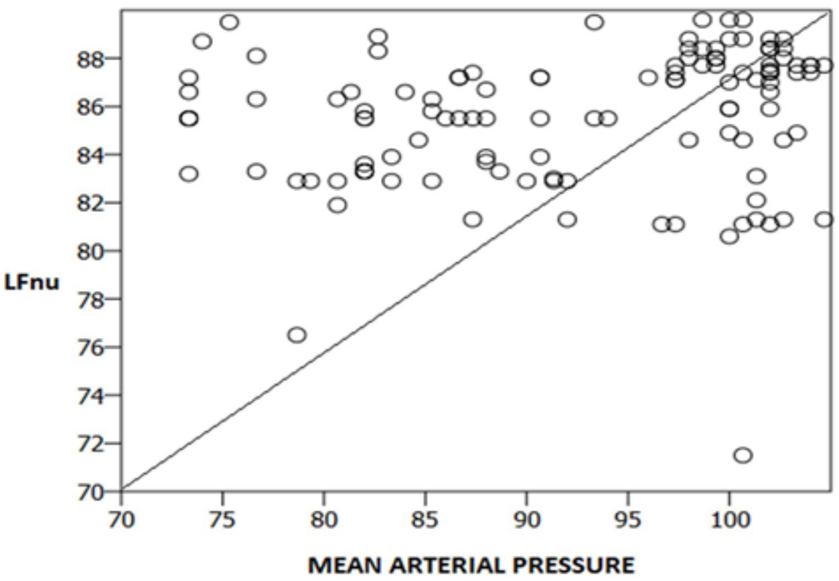

Figure 6: Scatterplot showing relationship between LFnu and mean arterial pressure in study subjects (n=120)

Table 11: Descriptive statistics of HF normalised unit (HFnu) in Normotensives (n=60) and Hypertensives (n=60)

HFnu	Mean	Standard deviation	t value	p value
Normotensives	14.97	2.344	2.42	0.017
Hypertensives	13.73	3.226		

The mean value of HFnu in normotensives (14.97±2.334) is statistically more than the mean value of hypertensives (13.73±3.226) with ‘t’ value of 2.42 and a ‘p’ value of 0.017 ($p<0.05$). This signifies that the high frequency normalised unit is significantly decreased in hypertensives when compared with normotensives.

Table 12: Pearson’s correlation values of HFnu with mean arterial pressure in study subjects (n=120)

HRV parameter	Pearson’s r	p value
HFnu	-0.22	0.017

The Pearson’s correlation of HFnu with the mean arterial pressure of the study group (both normotensives and hypertensives) has ‘r’ value of -0.22 with a statistically significant p value of 0.017 ($p<0.05$). This means that as the mean arterial pressure increased the high frequency normalised unit decreased.

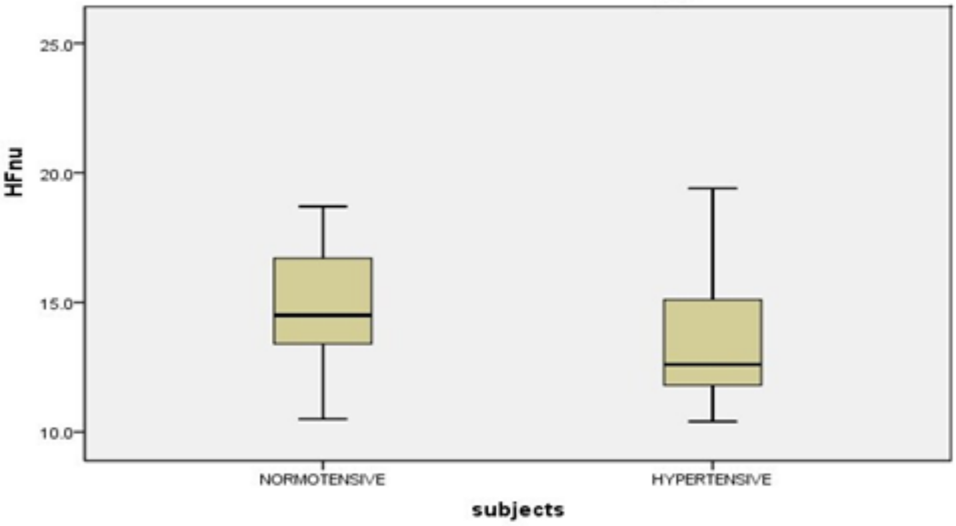

Figure 7 Box plot showing distribution of HF normalised unit (HFnu) in Normotensives (n=60) and Hypertensives (n=60)

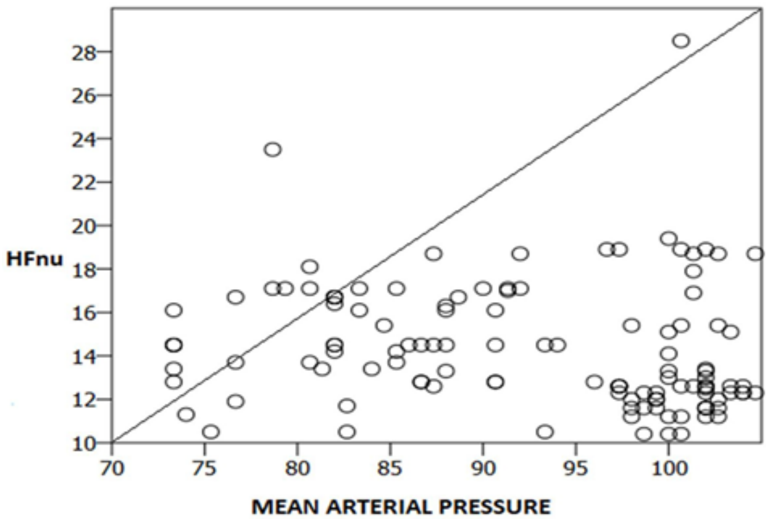

Figure 8 Scatterplot showing relationship between HFnu and mean arterial pressure in study subjects (n=120)

Table 13: Descriptive statistics of serum uric acid values in Normotensives (n=60) and Hypertensives (n=60)

Serum uric acid	Mean	Standard deviation	t value	p value
Normotensives	5.87	0.39	7.75	0.001
Hypertensives	6.87	0.92		

The mean value of serum uric acid in hypertensives (6.87±0.92) is statistically more than the mean value of normotensives (5.87±0.39) with 't' value of 7.75 and a 'p' value of 0.001 ($p<0.01$). This signifies that the serum uric acid is significantly increased in hypertensives when compared with normotensives.

Discussion

In this study 60 normotensive subjects and 60 stage 1 hypertensives were selected and subjected to HRV analysis and serum uric acid analysis. In HRV analysis low frequency (LF), high frequency (HF), LF/HF ratio, low frequency normalized unit (Lfnu) and high frequency normalized unit (HFnu) were analysed. In the low frequency analysis, the mean value of normotensives is 216.15±249.78 while the mean value of hypertensives is 348.77±325.90. The hypertensives have higher mean LF values than normotensives. It is statistically significant with 'p' value of 0.014 ($p<0.05$). Low frequency spectrum occurs mainly due to sympathetic component of autonomic nervous system. The study shows that the absolute value of the LF component was increased in hypertensives when compared with normotensives. The correlation between the low frequency component of HRV and the mean arterial pressure of the study subjects is calculated. The Pearson correlation coefficient 'r' has a value of 0.22 which has a statistically significant 'p' value of 0.014 ($p<0.05$). This shows that as the mean arterial pressure increased the LF component has also increased. In the high frequency analysis, the mean value of normotensives is 34.03±33.88 while the mean value of hypertensives is 57.47±68.83. The hypertensives have higher mean HF values than normotensives. It is statistically significant with 'p' value of 0.020 ($p<0.05$). This shows that there is an increase in the HF component of HRV in hypertensives. HF mainly reflects the parasympathetic system activity in the heart. The study shows that the absolute value of HF component was increased in hypertensive subjects. The correlation between the high frequency component of HRV and the mean arterial pressure of the study subjects is calculated. The Pearson correlation coefficient 'r' has a value of 0.23 which has a statistically significant 'p' value of 0.011 ($p<0.05$). This shows that as the mean arterial pressure increased the HF component also increased. In the LF/HF ratio analysis, the mean value of normotensives is 5.835±1.083 while the mean value of hypertensives is 6.587±1.338. The hypertensives have higher mean LF/HF ratio than normotensives. It is statistically significant with 'p' value of 0.001 ($p<0.01$). This shows that there is an increase in the LF/HF ratio of HRV in hypertensives. The ratio of LF with HF shows the balance between sympathetic and parasympathetic components of autonomic nervous system. Since the ratio of LF with HF is increased in hypertensives it signifies that the sympathetic activity is more when compared with parasympathetic activity resulting in sympathetic dominance over the heart. The correlation between the LF/HF ratio of HRV and the mean arterial pressure of the study subjects is calculated. The Pearson correlation coefficient 'r' has a value of 0.24 which has a statistically significant 'p' value of 0.009 ($p<0.01$). This shows that as the mean arterial pressure increased the LF/HF ratio also increased signifying that sympathetic predominance over the heart increased with increasing blood pressure. In the low frequency normalized unit analysis, the mean value of normotensives is 85.01±2.333 while the mean value of hypertensives is 86.23±3.22. The hypertensives have higher mean LFnu values than normotensives. It is statistically significant with 'p' value of 0.019 ($p<0.05$). This shows that there is an increase in the LFnu component of HRV in hypertensives. LFnu represents the ratio of LF with total power. Hence in hypertensives in the total activity in autonomic nervous system, the sympathetic component predominates.The correlation between the low frequency normalized unit of HRV and the mean arterial pressure of the study subjects is calculated. The Pearson correlation coefficient 'r' has a value of 0.21 which has a statistically significant 'p' value of 0.019 ($p<0.05$). This shows that as the mean arterial pressure increased the LFnu component also increased. This shows that total power of autonomic activity increased with increase in blood pressure. Even still significant increase was more in sympathetic component than parasympathetic component with increased blood pressure. In the high frequency normalized unit analysis, the mean value of normotensives is 14.97±2.344 while the mean value of hypertensives is 13.73±3.226. The hypertensives have lower mean HFnu values than normotensives. It is statistically significant with 'p' value of 0.017 ($p<0.05$). This shows that there is a decrease in the HFnu component of HRVin hypertensives. HFnu represents the ratio of HF with total power. Hence in hypertensives, though the activity of autonomic nervous system increased, the parasympathetic component receded. The correlation between the high frequency normalized unit of HRV and the mean arterial pressure of the study subjects is calculated. The Pearson correlation coefficient 'r' has a value of -0.22 which has a statistically significant 'p' value of 0.017 ($p<0.05$). This shows that as the mean arterial pressure increased the HFnu component decreased. Thus the study results show that when the arterial pressure increases the autonomic system activity over the heart also increases. This occurs due to increase in sympathetic component of HRV. This results in poor HRV which indicates poor autonomic balance over the heart. The increased HF values in hypertensives indicates an increase in absolute value of parasympathetic component, but the decreased HFnu indicates that the true influence of parasympathetic system over heart was actually decreased in hypertensives. The effect of new onset hypertension in heart rate variability was studied by Jagmeet P. Singh et al. The study was a cohort study which included 2722 subjects from the Framingham Heart study. All those subjects were age and gender matched and heart rate variability was assessed after taking careful blood pressure measurements. In this study only the LF values are statistically significant, while LF/HF values did not increase at all. The study concluded that LF values serve a predictive value for risk of hypertension. [15] A study conducted by Jin Shang Wu et al. found the effect of increased blood pressure and family history of hypertension on cardiac autonomic function. In this study 1436 subjects were included. Blood pressure and heart rate variability was measured in them along with recording of family history. In this study both LF and LF/HF ratio are positively correlated with increased blood pressure while HF is negatively correlated with increased blood pressure. The study also found similar results with normotensive subjects with family history of hypertension. [16] A study done by Asuman H. Kaftan and Osman Kaftan correlated QT interval and heart rate variability in hypertensives. In this study both time domain and frequency domain parameters were correlated with blood pressure in normotensives and hypertensives. A total of 76 hypertensives and 70 normotensives were used in this study. In both time domain and frequency domain parameter's parasympathetic function was found to be reduced in hypertensives, while sympathetic function was found to be increased in hypertensives. In frequency domain parameters LF and LF/HF ratio were increased, and HF was decreased. [17] A study done by Havlicekova et al. focused on HRV parameters in adolescents with untreated primary hypertension (22 hypertensives and 22 normotensives). The study was done for 24-hour period and HRV was analysed during wakefulness (9 a.m. to 1 p.m.) and sleep (12 a.m. to 4 a.m.). The results showed that there was increased sympathetic activity during day (increased LF). There was decreased parasympathetic activity during both day and night (decreased HF). There was decreased sympathovagal balance during both day and night (increased LF/HF ratio). This shows that there is sympathovagal imbalance in hypertensives in adolescent age group itself.[18] A study done by Xiaoyun Lin et al. studied the association of gender and age differences with hyperuricemia and hypertension. It was a cross sectional study which involved 78596 subjects (47781 men and 30851 women). The study subjects were in the age range of 20 – 70 years. They were then categorized based on their age decades into 5 categories. All the study subjects were examined for both hypertension and hyperuricemia. The prevalence of hypertension was more in females when compared with males. But the prevalence of hyperuricemia was more in males when compared with females. Both in male and female subgroups the prevalence of hyperuricemia in both normotensives and hypertensives were analysed. The study results showed that hyperuricemia was an independent risk factor for hypertension in males. The increase in serum uric acid levels which was associated with increased blood pressure was seen predominantly in younger age groups when compared with older age groups. Both systolic as well as diastolic blood pressure showed significant increase with increased serum uric acid levels in males. The picture in women on the other hand, was different. The rise in serum uric acid levels did not have significant association with hypertension in females. But there was a positive correlation between serum uric acid levels and diastolic blood pressure in females.[19]

Conclusion

Hypertension is a noncommunicable disease, and its incidence is increasing drastically all around the world. Consequently, the need for complete understanding of the pathophysiology of the disease and proper diagnostic and therapeutic measures to counteract the disease burden has also increased. Since the disease has multiple risk factors, the treatment modalities must also be diverse to account for all those risk factors. Autonomic system imbalance is one of the major pathophysiological feature of hypertension.

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