

## Comparison of Nonlinear Dynamical Parameters in Newly Diagnosed Hypertensives and Normotensives Adults

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### Abstract

**Background:** The cardiac autonomic modulations might be responsible for the pathogenesis of essential hypertension. Various measures of heart rate variability (HRV) are used to reveal autonomic tone. The present study used the Poincare plot to compare newly diagnosed hypertensives with normotensives.

**Methods:** In this cross-sectional study, hypertensives (N=70) and normotensives (N=70) were compared using geometrical parameters of the Poincare plot. The study was conducted in the Department of Physiology, SMS Medical College and attached Hospital, Jaipur (Rajasthan, India), after approval from the Institutional Ethics Committee. The HRV was acquired using the standard protocol, and the SD1, SD2, and SD1/SD2 ratio were calculated using Kubois software. The groups were compared using the Mann-Whitney U test with statistical significance considered at 5%.

**Results:** The age and gender showed no significant differences [ $p > 0.05$ ]. The two groups were significantly differed in cardiovascular parameters including heart rate [ $W=4209$ ;  $p < 0.001$ ], systolic blood pressure [ $W=4899.5$ ;  $p < 0.001$ ] and diastolic blood pressure [ $W=4696.5$ ;  $p < 0.001$ ]. The Poincare parameters including SD1 [ $W=711.5$ ;  $p < 0.001$ ], SD2 [ $W=1764$ ;  $p = 0.004$ ] and SD1/SD2 ratio [ $W = 540$ ;  $p < 0.001$ ] was significantly decreased in hypertensives as compared to normotensives.

**Conclusion:** The present study endorsed Poincare analysis as an independent prognostic tool to predict autonomic dysfunction in newly diagnosed hypertensives

**Keywords:** heart rate variability, hypertensives, nonlinear methods, Poincare plot

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### Introduction

The Seventh Report of the Joint National Committee (JNC) on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure defines optimal systolic and diastolic blood as less than 120 mmHg and 80 mmHg, respectively. JNC defined prehypertension"

as SBP/DBP 120-139/80-89, "Stage1 Hypertension" as SBP/DBP 140-159/90-99, and "Stage 2 Hypertension" as SBP/DBP  $\geq 160/100$ . [1] Hypertension doubles the risk of cardiovascular diseases, including coronary heart disease, congestive heart failure, ischemic and

hemorrhagic stroke, renal failure, and peripheral arterial disease.[2] Recommended criteria for the diagnosis of hypertension is average (of two or more seated blood pressure readings during each of two or more outpatient visits) clinic blood pressures of  $>140/90$  mmHg. [3]

Heart rate variability (HRV) has emerged as a practical, non-invasive tool to investigate cardiac autonomic dysregulation in hypertension quantitatively. Assessment of HRV may provide quantitative information on the modulation of cardiac vagal and sympathetic nerve input. HRV analysis is a recognized tool for the estimation of cardiac autonomic modulations. The Joint Task Force Of The European Society Of Cardiology And The North American Society Of Pacing And Electrophysiology (1996), established minimum technical requirements, definitions, and range of Power bands in the frequency domain. and provide recommendations on conducting clinical research and patient examinations with the help of heart rate variability.[4]

Multiple factors interact nonlinearly, leading to the pathogenesis of essential hypertension. The heart rate variability analysis can be done using various linear and nonlinear methods.[5][6] The present study analyzes heart rate variability data of newly diagnosed hypertensives with controls using the Poincare method.

**Material and Methods:** This cross-sectional study compared the Poincare parameters in newly diagnosed hypertensives with normotensives aged 30 to 50 years. The study was conducted in the Department of Physiology, SMS Medical College and attached Hospitals, Jaipur (Rajasthan, India), after approval from the Institutional Ethics Committee. Seventy patients with confirmed hypertension (systolic blood pressure  $\geq 140$  mmHg or diastolic pressure  $\geq 90$  mmHg) who had never been treated with any hypertensive medication were enrolled

in the study group, and healthy age and sex-matched seventy normotensive subjects were enrolled in the control group. The exclusion criteria were diabetes, secondary hypertension, obesity, known history of acute and chronic illness, patients taking any drug known to affect the autonomic nervous system, smokers and alcoholics, and uncooperative subjects.

#### Experimental protocol

The data of the participants were recorded between 09:00 AM and 12:00 PM. Subjects were instructed to avoid tea, coffee, and food at least 2 hours before the start of the recording. The participants underwent general examination, including body mass index, waist-hip ratio, blood pressure, and heart rate. Blood pressure was recorded with an automated digital device to avoid manual error.

The ECG signals were recorded with RMS Polyrite D (version 1.0) after a supine rest of 15 minutes. The resting ECG was recorded for five minutes at a sampling frequency of 256 Hz. The discrete ECG time series consists of P-QRS-T waves. By calculating the RR interval from this signal, another signal is constructed that consists of RR interval data. This RR-interval data series for each beat is called a tachogram. Poincare parameters were calculated from the tachogram, as mentioned in the next section.

Calculation of geometrical parameters of the Poincare plot

The Poincare plot is an HRV analysis technique that quantifies the correlation between consecutive points in the tachogram.[7] It can express the nonlinearity of RR interval series. On the Poincare plot, the y-axis and x-axis depict  $RR_n$  and  $RR_{n+1}$  points, respectively. An ellipse was fitted to the points over the plot, and the geometrical properties of the ellipse were measured. The minor and major axes of the ellipse were SD1 and SD2, respectively, and the SD1/SD2 ratio

was calculated.[8] The above fitting and calculations were performed by the Kubois software.

#### Statistical Analysis

As data follows non-normal distribution, quantitative data were expressed in the median and interquartile range (IQR) and compared using the Mann-Whitney U test. Qualitative data were expressed as proportions and compared using the chi-squared test. The level of significance was considered at 5%. The statistical analysis was performed using JASP version 0.16.2.0.[9]

#### Results:

The demographic profile of the two groups showed no significant differences across age [W=2508; p =0.81], gender [ $\chi^2$  0.144; p =0.704], BMI [W=3206; p =0.002] and WHR [W=2793.5; p=0.149]. The two groups were significantly differed for cardiovascular parameters including heart rate [W=4209; p <0.001], SBP [W=4899.5; p <0.001] and DBP [W =4696.5; p <0.001]. (Table 1)

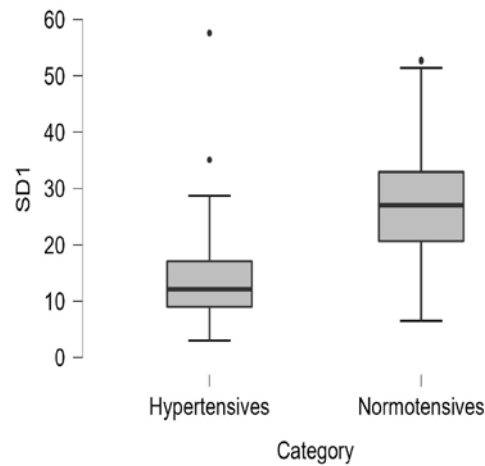
**Table 1. Comparison of demographic, cardiovascular parameters in hypertensives and normotensives**

Variable	Category	Median	IQR	W	p
Age(Years)	Hypertensives	43.5	5.75	2508	0.81
	Normotensives	43	2		
BMI	Hypertensives	26.4	3.963	3206	0.002
	Normotensives	24.77	3.24		
WHR(m)	Hypertensives	0.95	0.227	2793.5	0.149
	Normotensives	0.91	0.01		
Heart Rate(beats/min)	Hypertensives	85.5	4	4209	< .001
	Normotensives	76	10.75		
SBP (mmHg)	Hypertensives	152	5	4899.5	< .001
	Normotensives	130	4		
DBP (mmHg)	Hypertensives	88.5	5	4696.5	< .001
	Normotensives	79	3		

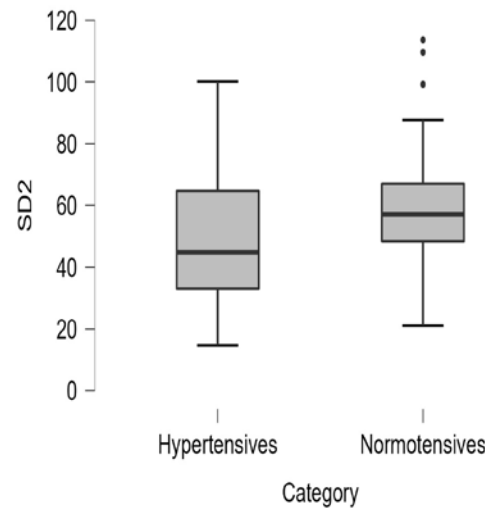
The Poincare parameters including SD1 [W=711.5; p <0.001], SD2 [W=1764; p = 0.004] and SD1/SD2 ratio [W =540; p<0.001] was significantly decreased in hypertensives as compared to normotensives. (Table 2 and Figure 1,2 and 3).

**Table 2. comparison of Poincare parameters across hypertensives and normotensives**

Variable	Category	Median	IQR	W	p
SD1	Hypertensives	12.15	8.1	711.5	< .001
	Normotensives	27.055	12.305		
SD2	Hypertensives	44.8	31.65	1764	0.004
	Normotensives	57.12	18.602		
SD1/SD2	Hypertensives	0.275	0.088	540	< .001
	Normotensives	0.47	0.118		

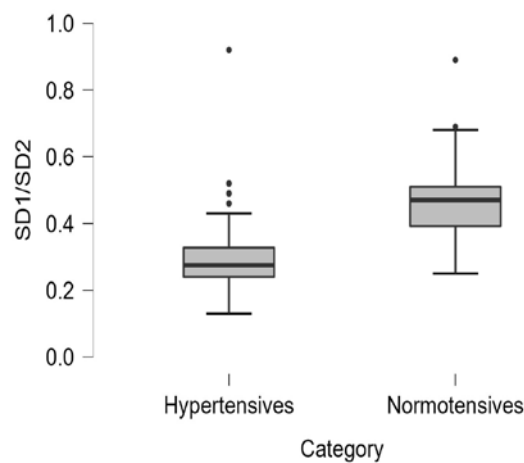


**Figure 1. Comparison of SD1, a Poincare plot measure between hypertensives and normotensives**



**Figure 2. Comparison of SD2, a Poincare plot measure between hypertensives and normotensives**

**Figure 3. Comparison of SD1/SD2 ratio, a Poincare plot measure between hypertensives and normotensives**



**Figure 3. Comparison of SD1/SD2 ratio, a Poincare plot measure between hypertensives and normotensives**

## Discussion

The heart rate variability captures the modulatory activity of the parasympathetic and sympathetic nervous systems. The pathophysiology of hypertension affects the modulatory activity of the autonomic nervous system. Researchers used various analytical approaches to study modulation associated with hypertension, including time and frequency domain analysis and nonlinear methods. The physiological systems are complex and have inherent nonlinear interactions; thus, nonlinear methods may prove helpful in extracting more information. Khandoker et al. used Poincare plots to describe the autonomic activity of the parasympathetic and sympathetic systems.[10]

The present study measured Poincare parameters, including SD1, SD2, and SD1/SD2 ratio. The SD1 and SD2 were significantly reduced in the hypertensive subjects. The decrease in SD1 correlates with the decreased parasympathetic tone, while a decrease in SD2 correlates with an increased sympathetic tone. Similarly, the SD1/SD2 ratio has been significantly decreased in the hypertensive subjects compared to controls. The SD1/SD2 ratio provides information about overall sympathovagal balance. Given the above, decreased SD1/SD2 ratio may be due to a decrease in SD1, an increase in SD2, or both. In the present study, SD1 and SD2 were significantly decreased, implying a decreased parasympathetic and increased sympathetic activity.

Velusami et al., in a study, analyze the cardiac autonomic status of prehypertensive individuals using Poincare analysis. Researchers found a decrease in SD1 and SD2 among prehypertensives in both males ( $p=0.0001$  and  $0.001$  for SD1 and SD2, respectively) and females ( $p=0.056$  and  $0.048$  for SD1 and SD2, respectively) [11] Karmakar et al. used Complex Correlation Measure (CCM) from Poincare plots to assess changes

during atropine infusion,  $70^\circ$  head-up tilt, and scopolamine administration in healthy human subjects. CCM was found to be most sensitive compared to SD1 and SD2. The CCM was decreased with the decrease in parasympathetic activity during atropine infusion and  $70^\circ$  head-up tilt phase. In contrast, CCM values increased with increased parasympathetic activity during scopolamine administration.[12] The present study's findings are similar to the study conducted by Goit et al. where SD1, SD2, and SD1/SD2 decreased in hypertensives compared to normotensives.[13]

Pushpanathan et al. found the effect of yoga in hypertensives and observe blood pressure and Poincare parameters before and after the intervention. They found significant improvement in blood pressure and an increase in SD1 and SD2 after performing yogic exercises.[14] The Poincare analysis can be an alternate metric to extract information on the nonlinear process in complex physiological systems. [15]

**Conclusion:** The present study endorsed the use of Poincare analysis as an independent prognostic tool to predict autonomic dysfunction in newly diagnosed hypertensives. Further, the Poincare methods can be used to observe the effects of various interventions.

### Research Quality and Ethics Statement:

The present study was per the ethical standards of the responsible committee on human experimentation (institutional or regional) and with the Helsinki Declaration of 1975, revised in 2000. The approval of the Institutional Ethical Committee, SMS Medical College, Jaipur was through letter no 3433/MC/EC/2017 dated 7 Oct 2017.

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