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# Circadian blood pressure variations in normotensive and hypertensive Indian adults: An exploratory study

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**Abstract**
**Background and Objectives:** Though 24hours BP monitoring is a useful tool that provide insights in masked and white coat hypertension as well as can be used as a marker of allostatic load (by monitoring circadian variations) and applicable in chronotherapy, is still sparingly used clinically. Hence, the objective of present study is to explore the pattern of circadian variation of blood pressure in normotensive and hypertensive Indians to pave the way for future chronobiological research and predictive medicine.
**Materials and Methods:** In this cross-sectional study, total 125 volunteers, referred from the medicine OPD/IPD, enrolled. All the volunteers underwent 24 hour ambulatory blood pressure monitoring. BP recording of 100 participants (37 female and 63 male, mean age = 43.15±14.47 years) was used for final analysis. On the basis of guidelines provided for diagnosis of hypertension by European Society of Heart, individuals were grouped as i) normotensives (n=37) and ii) hypertensives (n=63). For descriptive analysis, different blood pressure parameters from three segments *viz*. overall, awake period and asleep period were used. Between groups comparison was done using Mann-Whitney and ANNOVA test. P-value < 0.05 had been considered as significant.
**Observation and Results:** A significance difference in circadian systolic, diastolic and mean arterial BP was observed between groups. Although a higher percentage of non-dippers (65%) was observed in hypertensives but 38% of normotensives have also shown non- dipping status that indicates altered circadian rhythm or allostatic load.
**Conclusion:** We observed altered circadian blood pressure pattern in both groups though higher percentage of non-dipping status in hypertensive patients. In normotensives it could subserve as an early marker of disease process, in hypertensives, it may be useful for application of Chrono-pharmacology.

**Keywords:** Allostatic load, ambulatory blood pressure monitoring, chronopharmacology, circadian rhythm, dippers, hypertension and non-dippers

## Introduction
More than 25% of all cause mortalities were due to cardiovascular diseases that India has witnessed in past few years [1]. Hypertension an established independent risk factor for acute and chronic cardiovascular conditions contributes approximately 13% of all cause cardio-vascular deaths [2]. Therefore, early diagnosis and effective management of hypertension is considered as an important cornerstone for reducing global burden of cardiovascular morbidity and mortality. However, in clinical situations usually the patient reaches to physicians when some symptoms of hypertension appear or accidentally diagnosed, nonetheless the hypertension is quite established till that time. Therefore, though simple in theory but early diagnosis of hypertension practically is still a medical challenge.
Clinically the most common method used to diagnose hypertension is spot measurement of blood pressure recorded at three different times in sitting position after giving appropriate rest to patient. However, there are many fallacies observed with spot measurement for example, it provides single point evaluation of blood pressure that may show false higher values (white coat hypertension) or false lower values (masked hypertension) [3]. It also fails to record the daily circadian fluctuations in blood pressure.

Insights in pathophysiology of hypertension has also evolved over decades and what we understand now is that it's a multi-factorial systemic disorder where right from alterations in baroreceptors sensitivity to alterations in functioning of renal nephrons and secretions of renal hormones or generalized progressive sympathetic overdrive or accumulation of allostatic load (neuro-adrenergic theory of hypertension as proposed by Grassi 2013 *et al*.) [4] that changes system's physiology from pre disease state to clinically overt hypertension and if uncontrolled then gradual progression towards complications of hypertension [4]. Therefore, early detection of hypertension on this disease continuum is a real challenge. In this context there are some leads from chronobiology research, where it is highlighted that it is the loss of circadian blood pressure variation especially non-dipping of systolic and diastolic blood pressure during night can be a very early change that may precedes the clinically overt hypertension.

Moreover, regarding the clinical management of hypertension, the ABPM technique carries its own importance in terms of the implication of chronotherapy and disease prognosis. Chronotherapy is the attainment of the synchronization of disease pattern or symptoms variations with maximum drug effectiveness. Many drug trials have proved that this synchrony can be achieved effectively by planning a chronotherapy in hypertensive individuals after observing their own circadian rhythm. For instance, ACE inhibitors and thiazide diuretics have been shown as more effective therapeutic agent when given in the evening especially to non-dippers whereas beta blockers are more effective when given in the morning [5, 6].

With this scientific insight application of 24 hour BP monitoring attracted attention of clinical fraternity and gained recognition as an assessment tool. 24 hour ambulatory blood pressure measurement shows much larger picture of blood pressure variability. This technique measures the BP several times, with customized interval ranging from five minutes to 1 hour throughout 24 hours thus captures the circadian variations in the BP [7]. Various studies have observed a characteristics day night pattern in BP fluctuation, the blood pressure values show a distinct 24 hour rhythm along with other cardiovascular parameters such as cardiac output and heart rate.

In the last few years, many renowned health agencies such as American Heart Association, National institute for Health and Care, UK and also the European Society of Cardiology offered some changes in terms of diagnosis & management of hypertension [8]. For accurate diagnosis of hypertension, it has been recommended to measure the BP by ambulatory method once after getting higher values on examination by OBPM [9].

In a survey study conducted on physicians by the Cardiological society of India, it was found that ABPM is practiced only in a few patients (< 5%) by most of the physicians (71.93%) [10].

Though the 24 hour BP measurement carries the substantial benefits in terms of diagnosis, management and prognosis of hypertension its time consuming procedure with more economic burden makes the physicians hesitant for recommending it to their patients. However, several issues regarding the false positive or false negative BP recordings can be ruled out easily with the help of ABPM technique that will result in comparatively lesser burden on the healthcare costs. The scarcity of relevant data and published literature provide an additive effect for non-recommendations, especially in Indian scenarios.

Hence, in order to develop a better understanding towards the blood pressure's circadian variability and it's application in chronotherapy in Indians, we have done a comparative study of BP fluctuations in normotensive and hypertensive individuals.

## Materials and Methods

It is a cross sectional study. A total number of 125 volunteers either known hypertensives patients or newly diagnosed based on spot measurements and their relatives without known history of hypertension and normal BP on spot measurement, between February 2016 to February 2021 referred from the medicine OPD and IPD of Smt. Kashibai Navale Medical College and General Hospital, Pune was enrolled for the study. Informed consent was taken. The study received approval from Institutional Ethics Committee. Personal information and relevant medical history was taken. All individuals (n=125) underwent 24-hour ambulatory blood pressure monitoring using Schiller BR- 102 PLUS ABP monitor. As per physicians' instruction the anti-hypertensive medications were withheld for 24 hours prior to recording. The recording interval of 30 minutes was chosen for all recordings. After completion of 24 hours reports were generated using MT-300 BPR software. The validation of Schiller BR-102 has been done according the international protocol introduced by the working group on Blood pressure monitoring of the European Society of the Hypertension [11, 12]. Based on the criteria recommended by European Society of Heart for ABP monitoring, individuals were divided into normotensives and hypertensives (awake BP ≥ 135/85 mmHg, asleep BP ≥ 120/70 mmHg, overall 24 hour BP ≥ 130/80 mmHg has been considered as hypertensives). All the hypertensive patients were on anti-hypertensive medications. Moreover, as per their guidelines based on percentage fall in the blood pressure during night, individuals were further classified into dippers, non-dippers and reverse dippers categories.

The parameters recorded and reported by the ABP device are: 1) Mean blood pressure with its minimum and maximum, 2) Mean systolic and diastolic blood pressure with their minimum and maximum, 3) Mean heart rate with its minimum and maximum, 4) Mean pulse pressure with its minimum and maximum values.

All of the above mentioned parameters were reported three times: 1) Overall for complete 24 hour duration 2) Awake for approximately 15 hours of awakening duration 3) Asleep for approximately 9 hours of sleep duration.

**Inclusion criteria:** All volunteers referred by medicine OPD & IPD.

**Exclusion criteria:** Having less than 70% successful blood pressure readings recorded out of complete record of 24 hours.(2) out of 125 only 100 recordings were more than 70% therefore included for final analysis.

**Statistical analysis:** Mean and SD of all the mentioned parameters ware computed. Dipping status of individuals was measured in Percentage. Between groups comparisons were done using Mann-Whitney test. ANNOVA was

applied for multiple group comparison. P-value < 0.05 was considered as significant.

**Observation and Results**

Table no. 1 shows the demographic profile Age and Gender distribution between groups. In normotensive group, 22 were males and 15 were females. In Hypertensive group, 41 were males and 22 were females. The mean age of normotensives was 48.42±14.06 years whereas the mean age of hypertensives was 40.15±13.95 years.

The mean age for hypertensive group was surprisingly less compared to normotensive group, we think this finding is of concern.

Table No. 2 shows descriptive statistics of all the parameters of ambulatory blood pressure monitoring. All the parameters of blood pressure systolic, diastolic, mean arterial and pulse pressure) are higher in hypertensive than normotensive group in all three segments of recording. The heart rate parameters are also higher in hypertensive group

Table No 3 shows the significance of differences between the two groups. Majority of parameters of ambulatory blood pressure shows that the difference between the normotensives and hypertensives group is significant in all three stages (p-value < 0.05) except a few like Max. MAP of overall state, Max. HR of awake state, Min. HR of asleep state and minimum pulse pressure of asleep state.

The frequency distribution of dipping status (fairly good indicator to circadian fluctuation) has been calculated (Figure No. 1 A & B). 52% (n=19) of normotensives were dippers, 38% (n=14) were non-dippers and 11% (n= 4) were reverse dippers as against to 27% (n=17) of hypertensives as dippers, 65% (n=41) as non-dippers and 8% (n=5) reverse dippers.

The percentage nocturnal fall in the systolic blood pressure (systolic dip) is less compared to fall in diastolic blood pressure (diastolic dip) in both the groups.

Furthermore, the ABP parameters were analyzed in hypertensive group according to their dipping status. No significant difference in all ABP parameters among dippers, non-dippers and reverse dippers during overall 24 hours and awake state was observed, however except heart rate almost all other ABP parameters have shown significant difference during asleep state as depicted in Table No. 4.

**Discussion**

The present study was an observational study to explore the circadian variations in blood pressure in volunteers. We have analyzed blood pressure in three phases i) overall (24 hours) ii) awake (approx. 16 hours) & iii) asleep(approx. 8 hours). Means of systolic, diastolic, mean arterial blood pressure, pulse pressure and heart rate with their minimum and maximum values were the recorded parameters. As per guidelines of European Society of Heart for diagnosis of hypertension on basis of 24 hour ambulatory BP monitoring, individuals were classified into two groups i) normotensive and ii) hypertensive.

37 individuals were found normotensive and 63 were found hypertensive with the mean age of 48.42±14.06 years and 40.15±13.95 years respectively. While recording in all three stages, the majority of parameters were found significantly higher in the hypertensive group as compared to the normotensive (p-value < 0.05).

**Dipping status**

Physiologically Blood pressure falls during sleep. A 10% or more nocturnal fall (of the awake) in the systolic and diastolic blood pressure is considered as the normal dipping. Prescence of normal dipping in the blood pressure indicates normal homeostatic and allostatic control Allostasis is "maintaining stability, or homeostasis, through change i.e. a process of adaptation to acute stress, involving the acute and chronic mechanisms (sympathetic and HPA activation) that act to restore homeostasis in the face of a challenge (Sterling and Eyer 1988). However restoration to baseline for physiological parameters like Blood pressure, Glucose, once the stressful stimulus is abolished is nearly impossible, as no biological system is hundred percent efficient. Therefore over a period of time the amount of error built up that shifts the resting baseline to higher normal levels that is referred as allostatic load. So, in nutshell "Allostatic load" refers to the price the body pays for being forced to adapt to adverse psychosocial or physical situations, and it represents either the presence of too much stress or the inefficient operation of the stress hormone response system [26].

In case of blood pressure, the allostatic load indicates less than 10% or absence of nocturnal fall in the blood pressure (non-dipping) or higher blood pressure during sleep compared to awake state (reverse dipping).

In the present study, 38% of normotensive individuals and 65% of hypertensive were found as non-dippers, whereas, 11% of normotensive and 8% of hypertensive were found as reverse dippers. Nishtha Vaidya *et al*. In their study on circadian variability in young normotensive individuals found 24% of young normotensives as non-dippers [14]. The lesser frequency of non-dipper normal individuals compared to our study may be due to the differences in age range (18-35 years v/s 48.42±14.06). In an extensive study performed on 27,472 individuals, Kaul U *et al*. observed the age related changes in the parameters recorded by ABPM. They found the prevalence of dipping status decreases from 42.5% to 17.9% as the age advances from youngest to the oldest age group of the study population [28]. Choudhary N. *et al*., observed the recordings of ABPM in obese normotensive IAF personnel (mean age of 40.4±4.38 yrs) and found 20% of them as non-dippers [15]. Salagre S.B. *et al*. evaluated clinical utility of ABPM monitoring in newly diagnosed stage I hypertensive individuals. They observed 41% of their study population as non-dippers [16].

A Japanese study demonstrated that a diminished decline in nocturnal blood pressure leads to increased cardiovascular risk irrespective of 24 hour overall blood pressure load [17]. Other researchers found that non-dipping status is common in patients of coronary artery disease with or without the presence of hypertension [18, 19]. In a longitudinal study, Hermida *et al*. investigated that the non-dipping pattern of circadian rhythm is the better predictor of CVD as compared to overall ambulatory blood pressure load. They found that non-dippers with normal awake and asleep blood pressure showed the same hazard ratio of CVD events as dippers with elevated overall blood pressure [20].

Andrew Sherwood *et al*. found the correlation of sympathetic overdrive with the non-dipping status in normal individuals (32% were non dippers) by means of measuring the fall in nor-epinephrine and epinephrine excretion rates during asleep. The normotensive individuals with hyper active sympathetic nervous system were more likely to be associated with the family history of hypertension. Debra J.

Barksdale *et al*. observed the non-dipping status (in 30% of normal individuals) can be correlated with higher levels of cortisol in one hour after awakening and family history of hypertension [21, 22].

In addition to non-dipping status, the reverse dipping also is a kind of abnormal circadian variability. In this study, such difference in the frequency of reverse dipping might be due to the fact that the group of normotensive individuals was significantly older than the group of hypertensive. In a pioneering Japanese study, Ohkubo and colleagues found 3% prevalence of RD in general population with higher prevalence in older people [23]. In a detailed review, Cesare Cuspidi *et al*., mentioned that reverse dipping pattern is more harmful phenotype of circadian variability that emerged as a powerful marker of adverse cardiovascular prognosis in many studies [7].

Thus, the abnormal patterns seen in circadian rhythm of Blood pressure regulation can be an early indicator of allostatic load that will be manifested as hypertension in later stages.

Since the abnormal activation of HPA axis, sympathetic overdrive, metabolic dysfunctions and abnormal reflex are the patho-physiological basis found behind the abnormal dipping status of the individuals, many studies reported a close association between non-dipping status and advanced target organ damage [17].

Hence the present study, in line with the literature, suggests that 24 hour ABPM is important to evaluate the patterns of circadian rhythm which can be the early sign of the onset of hypertension and cardiovascular derangements.

## Chronopharmacotherapy

With the higher prevalence of non-dipping status among hypertensives (65%), the applications of chronotherapy can show more potential benefits in the treatment of hypertension as compared to the conventional treatment plans. Two decades back, in one of the initiating studies, Uzu *et al*. observed that the value of nocturnal BP fall was significantly increased in non-dippers as compared to dippers with the help of short term diuretic treatment plan [24]. In the Hypertension and Lipid Trial (HALT) study, 118 hypertensives with different nocturnal BP patterns (18 extreme dippers, 46 dippers, 48 non-dippers, and 6 reverse dippers) were administered doxazosin on nighttime. The hypotensive effect of doxazosin on nocturnal systolic BP was greatest in reverse dippers (−18 mm Hg), intermediate in non-dippers (−12 mm Hg), and lowest in dippers (−1 mm Hg) and extreme dippers (+4 mm Hg) [25]. Hermida *et al*. investigated the efficacy of many anti-hypertensive drugs ingested during the bedtime and compared that with the conventionally prescribed ingestion in the morning in diabetic hypertensive patients. They found that treatment with ≥ 1 medication during bedtime has resulted in improved ambulatory blood pressure control by decreasing the asleep mean blood pressure without the loss of awake blood pressure lowering efficacy of the drugs [5]. Potucek P *et al*. reviewed many randomized controlled trial (RCT) studies and concluded that timing of administration of anti-hypertensive drugs is helpful in controlling hypertension effectively not only because of reduced blood pressure load per se but also by restoring the normal circadian rhythm [6].

Thus, the normalization of circadian rhythm may be considered as one of the important targets of hypertension treatment plan because the normal dipping profile is clinically more impactful as compared to the reduction in mean BP alone.

**Table 1:** The demographic distribution of the study population

| | Normotensives (n=37) | | Hypertensives (n=63) | |
|---|---|---|---|---|
| Gender | Males | Females | Males | Females |
| | (n = 22) | (n = 15) | (n = 41) | (n = 22) |
| Mean age (Years) | 46.71±14.48 | 51.41±13.16 | 40.6±15.23 | 40.36±11.83 |
| | 48.42±14.06 | | 40.15±13.95 | |

p-Value = 0.01* Significant

**Table 2:** Mean & SD of Systolic/ Diastolic / Mean arterial blood pressure/Heart rate/Pulse Pressure measured from three segments (Overall, Awake, Asleep)

| Parameters | Overall | | Awake | | Asleep | |
|---|---|---|---|---|---|---|
| | Groups | | Groups | | Groups | |
| | Normotensive (n=37) | Hypertensive (n=63) | Normotensive (n=37) | hypertensive (n=63) | Normotensive (37) | Hypertensives (n=63) |
| Mean SBP±SD (mmHg) | 120.16±7.9 | 139.31±9.2 | 124.27±8.52 | 143.14±9.44 | 113.24±8.24 | 132.88±11.006 |
| Max SBP±SD (mmHg) | 153.64±15 | 170.98±15.6 | 151.97±14.88 | 169.85±14.97 | 134.91±14.42 | 155.9±14.68 |
| Min SBP±SD (mmHg) | 85.08±13.9 | 102.04±15.3 | 91.4±16.1 | 110.52±17.35 | 92.67±12.71 | 109.95±14.04 |
| Mean DBP±SD (mmHg) | 72.48±5.4 | 85.5±7.6 | 76.45±6.07 | 88.76±7.8 | 65.91±6.19 | 79.9±8.68 |
| Max DBP±SD (mmHg) | 104.35±16 | 114.8±16.8 | 101.91±15.21 | 113.76±16.23 | 88.18±16.64 | 99.55±12.65 |
| Min DBP±SD (mmHg) | 44.4±8.13 | 54.20±12.39 | 49.29±10.42 | 60.03±14.42 | 49.81±7.76 | 61.57±10.74 |
| Mean MAP±SD (mmHg) | 94±6.8 | 110.63±7.8 | 98.05±7.67 | 112.82±15.07 | 87.05±7.42 | 104.33±9.39 |
| Max MAP±SD (mmHg) | 125.97±14.9 | 142.39±14.4 | 124.48±13.33 | 141.68±14.39 | 108.83±14.45 | 126.73±12.92 |
| Min MAP±SD (mmHg) | 63.32±9 | 77.63±13.2 | 68.91±13.05 | 84.77±14.75 | 69.54±8.95 | 83.39±11.54 |
| Mean HR±SD | 75.48±11.06 | 80.33±9.64 | 79.21±11.27 | 84.41±9.91 | 69.21±12.38 | 73.92±10.34 |
| Max HR±SD | 114.86±24.12 | 113.31±20.7 | 112.7±20.83 | 110.9±24.46 | 87.86±22.08 | 95.41±16.04 |
| Min HR±SD | 56.91±10.88 | 60.69±8.46 | 60.72±10.14 | 65.61±9.28 | 58.59±11.58 | 62.07±9.28 |
| Mean PP±SD (mmHg) | 47.59±6.05 | 53.84±8.28 | 47.97±6.61 | 54.61±8.67 | 47.37±5.85 | 53.07±8.39 |
| Max PP±SD (mmHg) | 74.43±15.62 | 83.88±18.58 | 72.91±16.37 | 82.47±18.33 | 63.64±7.7 | 70.38±14.27 |
| Min PP±SD (mmHg) | 23.35±8.31 | 28.95±12.45 | 24.13±8.38 | 29.68±12.67 | 46.91±10.63 | 49.09±15.68 |

(SBP: Systolic blood pressure, DBP: Diastolic blood pressure, MAP: Mean arterial pressure, HR: Heart rate, PP: Pulse pressure)

**Table 3:** Test for significance between group comparison using Mann-Whitney test

| | Overall | | Awake | | Asleep | |
|---|---|---|---|---|---|---|
| **Parameters** | **p-value** | **z-score** | **p-value** | **z-score** | **p-value** | **z-score** |
| Mean SBP | 0.0001** | -0.9451(N) | 0.0001** | -0.9223 (N) | 0.001** | 0.8962 (N) |
| | | 0.5551 (H) | | 0.5417 (H) | | 0.5263(H) |
| Max SBP | 0.001** | -0.6232 (N) | 0.0001** | -0.6546 (N) | 0.0001** | -0.7457 (N) |
| | | 0.3660 (H) | | 0.3845 (H) | | 0.4380 (H) |
| Min SBP | 0.001** | -0.6334 (N) | 0.0001** | -0.6270 (N) | 0.0001** | -0.6849 (N) |
| | | 0.3720 (H) | | 0.3682 (H) | | 0.4022 (H) |
| Mean DBP | 0.001** | -0.8794 (N) | 0.0001** | -0.8298 (N) | 0.0001** | -0.8506 (N) |
| | | 0.5165 (H) | | 0.4873 (H) | | 0.4995 (H) |
| Max DBP | 0.002** | -0.3830(N) | 0.0005** | -0.4441 (N) | 0.0001** | -0.4708 (N) |
| | | 0.2249 (H) | | 0.2608 (H) | | 0.2765 (H) |
| Min DBP | 0.0001** | -0.5164 (N) | 0.0001** | -0.4819 (N) | 0.0001** | -0.6578 (N) |
| | | 0.3033 (H) | | 0.2830 (H) | | 0.3863 (H) |
| Mean MAP | 0.0001** | -0.9528 (N) | 0.0001** | -0.6346 (N) | 0.0001** | -0.9019 (N) |
| | | 0.5596 (H) | | 0.3727 (H) | | 0.5297 (H) |
| Max MAP | 0.09# | -0.6224 (N) | 0.0001** | -0.6666 (N) | 0.0001** | -0.7045 (N) |
| | | 0.3655 (H) | | 0.3915 (H) | | 0.4138 (H) |
| Min MAP | 0.001** | -0.6571 (N) | 0.0001** | -0.6226 (N) | 0.001** | -0.6950 (N) |
| | | 0.3859 (H) | | 0.3656 | | 0.4082 (H) |
| Mean HR | 0.008** | -0.2932 (N) | 0.01** | -0.3064 (N) | 0.04* | -0.2620 (N) |
| | | 0.1722 (H) | | 0.1800 (H) | | 0.1539 (H) |
| Max HR | 0.04* | 0.0445 (N) | 0.7 NS | 0.0490 (N) | 0.05* | -0.2534 (N) |
| | | -0.0261(H) | | -0.0288 (H) | | 0.1488 (H) |
| Min HR | 0.05* | -0.2492 (N) | 0.01* | -0.3127 (N) | 0.1 (NS) | -0.2135 (N) |
| | | 0.1464 (H) | | 0.1836 (H) | | 0.1254 (H) |
| Mean PP | 0.0001** | -0.4860 (N) | 0.0001 | -0.4886 (N) | 0.0004** | -0.4481 (N) |
| | | 0.2854 (H) | | 0.2869 (H) | | 0.2632 (H) |
| Max PP | 0.01* | -0.3299 (N) | 0.01 | -0.3316 (N) | 0.009** | -0.3354 (N) |
| | | 0.1938 (H) | | 0.1948 (H) | | 0.1970 (H) |
| Min PP | 0.01* | -0.3098 (N) | 0.01 | -0.3026 (N) | 0.45 NS | -0.0979 (N) |
| | | 0.1820 (H) | | 0.1777 (H) | | 0.0575 (H) |

N: Normotensives, H: Hypertensives NS: Not Significant, * Significant, ** highly significant

**Table 4:** Mean values of all parameters (Asleep state) in Dippers, Non-dippers and Reverse dippers among hypertensives.

| **Parameters** | **Dipping status in hypertensives** | | | **p - value** |
|---|---|---|---|---|
| | **D (17)** | **ND (41)** | **RD (5)** | |
| SBP(Mean±SD) | 123.41±7.5 | 135.48±9.7 | 143.8±9.6 | 0.001** |
| Max SBP (Mean±SD | 149.35±12.22 | 157±13.9 | 169.2±19.84 | 0.01* |
| Min SBP (Mean±SD | 98.29±11.1 | 113.36±12.68 | 121.6±9.34 | 0.001** |
| Mean DBP (Mean±SD | 74.7±5.5 | 81.19±8.3 | 87±12.7 | 0.004** |
| Max DBP (Mean±SD | 96.23±8 | 100.34±12.17 | 104.4±25.68 | 0.3 (NS) |
| Min DBP (Mean±SD | 53.23±8.46 | 63.7±9.23 | 72.4±12.7 | 0.001** |
| Mean MAP (Mean±SD | 97.23±7.55 | 106.07±8.18 | 114.2±10.2 | 0.0001** |
| Max MAP (Mean±SD | 122.94±11.36 | 126.6±12.34 | 140.6±15.8 | 0.02* |
| Min MAP (Mean±SD | 74.05±11.11 | 85.87±9.59 | 94.8±7.39 | 0.001** |
| Mean HR (Mean±SD | 74.52±10.1 | 73.78±10.53 | 73±11.72 | 0.9 (NS) |
| Max HR (Mean±SD | 97.94±15.02 | 94.43±15.55 | 94.8±25.16 | 0.7 (NS) |
| Min HR (Mean±SD | 61.76±9.34 | 62.21±9.52 | 62±8.88 | 0.98 (NS) |
| Mean PP (Mean±SD | 48.82±5.82 | 54.39±8.13 | 56.8±13.4 | 0.03* |
| Max PP (Mean±SD | 70.23±15.64 | 70.04±13.81 | 73.6±16.07 | 0.8 (NS) |
| Min PP (Mean±SD | 46.52±21.05 | 49.07±12.9 | 58±15.77 | 0.3 (NS) |

(D: Dippers, ND: Non-dippers, RD: Reverse dippers, NS: Non significant** highly significant, * significant)

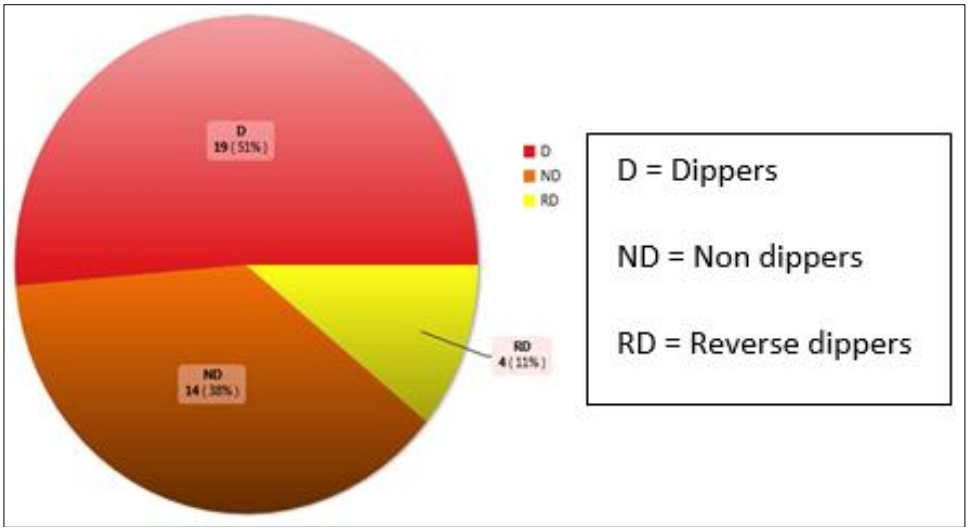


**Fig 1A:** Distribution of normotensive individuals according to their dipping status

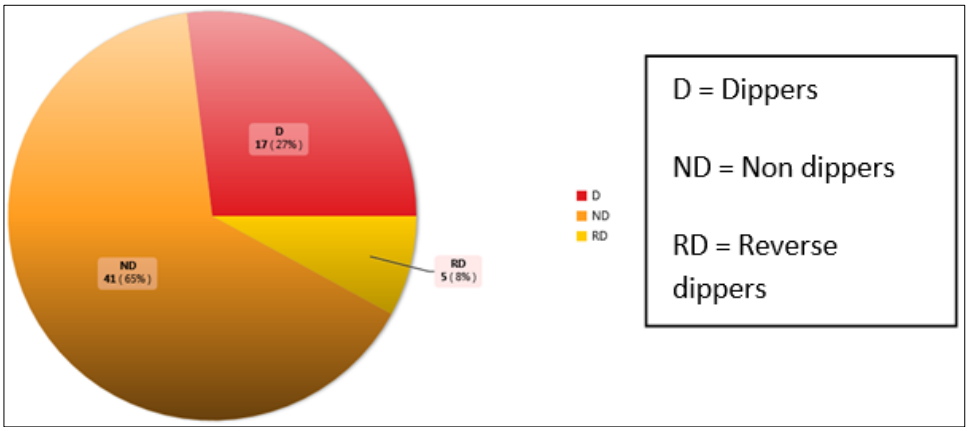


**Fig 1B:** Frequency distribution of hypertensive individuals according to their dipping status.

## Conclusion

Abnormal circadian blood pressure variability as indicated by non-dipping and reverse dipping status, was observed in both normotensive and hypertensive individuals. The abnormal circadian variability in normotensive individuals is a sensitive marker for early prediction of homeostatic derangements or allostatic load may be useful for implementation of lifestyle modification or suitable pharmacotherapy (preventive medicine). The abnormal circadian variability in hypertensive individuals on medication emphasized the implementation of chrono-pharmacotherapy for better control. Our study further corroborates the significance of 24 hour ambulatory blood pressure monitoring in overall management of hypertension.

## Conflicts of interests

The authors declare that there are no conflicts of interest.

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