



Original Research Article

## 24 Hours Chronomics of Ambulatory Blood Pressure and Heart Rate in Terms of Double Amplitude, Acrophase and Hyperbaric Index in Night Shift Health Care Workers

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### ABSTRACT

**Background:** Night work is associated sleep deprivation, where the person's internal body clock is in conflict with the rotating shift schedule leads to circadian disruption of various physiological rhythms like blood pressure, heart rate, and various hormones. Night shift workers have altered circadian pattern of blood pressure/heart rate. Due to this variation, night shift worker suffers from various cardiovascular and circadian rhythm disorders.

**Objective:** The Present study was aimed to investigate the effects of rotating night shift on 24 hours chronomics of blood pressure and heart rate in terms of double amplitude, acrophase and hyperbaric index.

**Materials and Methods:** 62 healthy nursing professionals, aged 20-40 year, performing day and night shift duties were recruited. This was the prospective observational study. Each month scheduled to continuous 9 days night shift (12 hours in regular 9 nights, from 20:00 to 08:00); after 9 days night shift they perform remaining duties in day shift and 4 days off in each month. Ambulatory BP and HR were recorded at every 30 min intervals in day time and each hour in night time during their day and night shift duties.

**Results:** Highly Significant difference was found in double amplitude (2DA) of blood pressure between night and day shift ( $p < 0.001$ ). In night shift, hyperbaric index (HBI) of mean systolic blood pressure was found to be increased at 00-03 am (midnight) while during day shift, peak was found at 06-09 am.

**Conclusion:** The present study concluded that the desynchronization was appeared during night shift and entrainment of circadian rhythm in the day shift.

**Key Words:** Circadian rhythm, entrainment, rotating night shift.

### INTRODUCTION

Night shift work is associated with a disruption of circadian rhythms, where a person's internal body clock is in conflict with the rotating shift schedule. The circadian rhythm of the human body is

characterized with an alternating sleep-wake cycle. <sup>[1]</sup> Shift work has been associated with increased risk of cardiovascular disease. Among healthy subjects, sleep tends to occur during a particular phase of circadian cycle. <sup>[2]</sup> Those who work in night shift may

attempt to sleep when their body clock is adjusted for the awakening phase. [3] This attempt disturbs the body clock resulting in a contradictory relationship between sleep time and circadian schedule. There is evidence that shift work affects both sleep and awakening by disrupting the circadian regulation which has adverse effects on family and societal life. [4] The average sleep cycle for night shift workers is sleep during the day which may be 2-4 hrs shorter than that of the day worker sleeping at night. Day sleep is light, fragmented, and more likely to be disrupted and hence, the insomnia can be severe in night shift workers. [5] It is possible that the circadian sleep propensity rhythm and hormonal rhythm are under influence of circadian pacemaker as well as sleep habit. [6]

Most rhythms are driven by an internal biological clock located in the hypothalamus, suprachiasmatic nucleus and can be synchronized by external signals such as light-dark cycles. [7] Majority of the circadian rhythms in our body have both an endogenous component regulated by an internal clock, viz. the suprachiasmatic nuclei (SCN), and an exogenous component composed of a light-dark cycle. [1,5] The disruption in natural time pattern, under influence of light dark cycle, acts upon the circadian system to bring it into desynchronization with the new time pattern.

The purpose of this study was to investigate the effects of rotating night shift on 24 hrs chronomics of Blood Pressure and heart rate in terms of Double Amplitude (2DA), Acrophase and hyperbaric.

## **MATERIALS AND METHODS**

### ***Subjects***

Out of 80 volunteers (night shift nursing professionals), 18 were excluded due to non-fulfilments of study protocol. 62 healthy nursing professionals (32 males &

30 females), aged 20-40 year, performing day and night shift duties were recruited for this prospective observational study. The mean age of all participants is  $24.74 \pm 3.81$ . Each study subject had a monthly scheduled of regular 9 night shifts (12 hours night shift, from 20:00 to 08:00) followed by remaining 17-18 day shifts (6 hours day shift, from 08:00 to 14:00) with a total of 4 days off in between. For this study, we have recorded ambulatory blood pressure and heard rate at every 30 minutes in day time (07:00-22:00 pm) and each hour at night time (22:00 pm -07:00 am) during their night shift and again in day shift duties. Subjects were recruited from the Trauma Center, GM and Associated Hospitals, King George's Medical University, Lucknow, UP, India. The duration and pattern of shift work were the same among all the subjects. The study was approved by the institutional ethic committee (Ref. code: XXXIV ECM/B-P3) and written, informed consent was obtained from all the subjects to participate in the study. Subjects with any acute/chronic illness, known patients of diabetes mellitus, other endocrinal disorders, hypertension, coronary artery disease, and chronic renal were excluded from the study.

### **24-hours Ambulatory blood pressure and heart rate monitoring:**

24 hrs chronomics of Blood pressure and heart rate were recorded by ambulatory blood pressure monitor TM-2430 (A&D, Japan) that measured repeated oscillatory blood pressure and heart rate at selected time intervals. Taking serial measurements a several times each day is important to reduce the error associated with a single measurement. The method provides estimates of the rhythm-adjusted mean or MESOR (midline estimating statistic of rhythm, defined as the average value of the rhythmic function fitted to the data), as well as the amplitude (defined as half the extent of rhythmic change in a cycle approximated

by the fitted curve) and acrophase (lag from a defined reference time point of the crest time in the curve fitted to the data) for every fitted component. Taking only one or two measurements in a day, always at awakening and/or at bed time may fail to reveal abnormalities seen only at other times of the day, or abnormalities that apply only to the variability in blood pressure or heart rate. [8] The MESOR is a more precise and more accurate estimate of location than the arithmetic mean. [9]

In this study, the subjects wore an ambulatory blood pressure monitor programmed to automatically measure blood pressure and heart rate at every 30 min intervals while awake and in each sleeping hours during night shift and again recorded when they were shifted to day duties. The data were downloaded after each monitoring span to a local PC via an interface (TM-2421, A&D). Data records were sent to the Halberg Chronobiology Center, University of Minnesota, Minneapolis, MN, USA for further interpretations. Each blood pressure and heart rate profile was analyzed by a sphygmochron, utilizing both a parametric and non-parametric approach. Original oscillometric data from each blood pressure series was first synchronized according to the activity-rest cycle of each individual by recomputing all the records in hours, from bed time to avoid differences among subjects in actual time of daily activity and to express results in circadian time rather than in less meaningful clock hours. In the current implementation of the chronobiological recommendations, reference values have been specified for clinically healthy peers of a given gender and ethnicity in different age groups. [9] An interaction between biorhythms, the biological clock and triggerers, which may be important in the pathogenesis of altered

heart rate variability (HRV) and blood pressure variability (BPV). Day shift workers show typical circadian rhythms with a drop in both systolic and diastolic blood at night. This pattern was reversed in night-shift workers. [10]

**Statistical Analysis:**

All the data were summarized as Mean±SD (Table 1). Groups were compared by applying paired t test. Associations between variables were done by Pearson correlation analysis. A two tailed ( $\alpha=2$ ),  $p<0.05$  was considered just significant,  $p<0.01$  moderate/very significant and  $p<0.001$  highly significant. Statistical analysis was carried out by using INSTAT 3.0 (Graph pad prism software; San Diego, CA).

**RESULTS**

Double amplitude and acrophase of systolic and diastolic blood pressure (SBP, DBP) and heart rate were significantly affected by night shift. Extremely Significant difference was found in double amplitude or predictable change of blood pressure between night and day shift ( $p<0.001$ ) (Table 2). Clinically significant changes in MESOR of blood pressure and heart rate were not appeared in night as well as day shift. Subjects were as normotensive in terms of MESOR.

Table 1: Baseline characteristics of night shift workers.

Baseline Characteristics	Night Shift Workers (n = 62)
Age	24.74 ± 3.81
Weight (kg)	53.21 ± 8.85
Height (cm)	160.44 ± 8.16
Body mass index (BMI)	20.59 ± 2.40
Marital Status	
Married	16 (25.80%)
Unmarried	46 (74.19%)
Diet	
Vegetarian	23 (37.10%)
Non-Vegetarian	39 (62.90%)

n= number of subjects  
Data are presented as means ± SD.

Table 2: MESOR/Double amplitude of Systolic blood pressure, diastolic blood pressure and heart rate (Mean ± SD) during night and day shift.

Measured Variables	Clinical Variables	During night shift (n=62)	During day shift (n=62)	p values
MESOR	SBP	118.16 ± 10.06	115.48 ± 8.42	0.024*
	DBP	72.93 ± 6.07	71.31 ± 4.98	0.040*
	HR	75.06 ± 6.66	74.57 ± 5.81	0.546 <sup>ns</sup>
Double amplitude	SBP	24.50 ± 15.07	35.07 ± 16.01	<0.001***
	DBP	18.96 ± 10.96	24.85 ± 11.70	<0.001***
	HR	14.16 ± 7.95	19.19 ± 8.35	<0.001**

ns-p>0.05, \*-p<0.05, \*\*p<0.01, \*\*\*-p<0.001

**Changes in double amplitude of blood pressure and heart rate-**

Circadian patterns of systolic double amplitude (Night shift: 24.50 ± 15.07 vs Day shift: 35.07 ± 16.01) (p<0.001) was higher in day shift as compare to night shift, diastolic double amplitude (Night shift: 18.96 ± 10.96 vs Day shift : 24.85 ± 11.70) (p<0.001) was also increased in day shift than night shift and were extremely significant between night and day shift. Double amplitude of heart rate (Night shift: 14.16 ± 7.95 vs Day shift : 19.19 ± 8.35) was found moderately significant between night and day shift (p<0.01) (Table 2).

**Alterations in Acrophase (time of overall peak values) of blood pressure and heart rate-**

Chronobiological study needs to evaluate the circadian pattern individually (especially in the case of peak time of variable) and it was interesting when we see interpret time patterns (i.e. time of overall peak values) in individual subjects in different shifts (night and day shift). Very interesting patterns of systolic blood pressure, diastolic blood pressure and heart rate of acrophase were found during night shift, however during day shift incomplete recovery was found in 6 subjects. Ecphasia (odd timing of circadian pattern of blood pressure not of heart rate) was also found in few subjects. (Figure 1A & B)

Figure (1A)

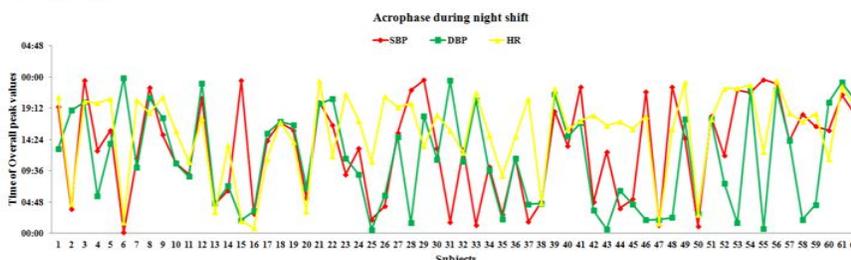


Figure (1B)

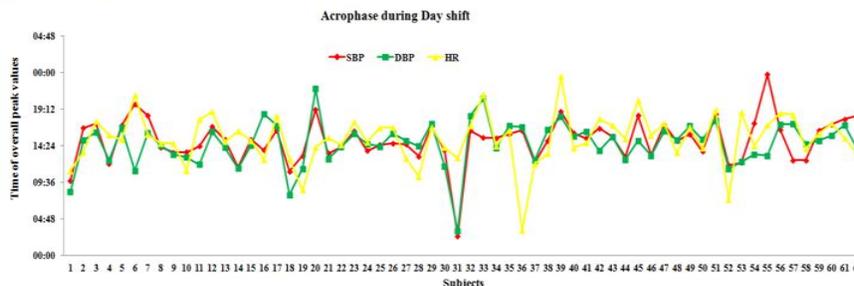


Figure 1A & B: Pattern of Acrophase of blood pressure and heart rate (Time of Overall peak values) exhibits desynchronization during Night shift and entrainment during day shift.

**Elevations in Hyperbaric index (HBI) (upper limit of tolerance interval) of blood pressure and heart rate-**

Hyperbaric index (three hours fractionated time interval/upper limit of tolerance interval), parameter by which we can measure the changes above the tolerance limits. Alteration in HBI of SBP and DBP was found during night and day shift. The mean systolic/diastolic HBI and mean HBI of heart rate in night and day shift have been shown in Figure 2A, 2B & 2C. During night shift, mean HBI of systolic blood pressure was found to be increased at 00-03 am (midnight) however in day shift, peak was found at 06-09 am (early morning). Mean diastolic blood pressure was found to be increased at 06-09 am during night shift and during day shift it was increased at 15-18 pm (evening) however in day shift, peak was

found at 06-09 am (early morning). During night shift mean HBI of heart rate was peak at 18-21 pm while during day shift peak was at 06-09 am. Study results showed that the night shift effect was recovered during day shift. Hyper baric index of Systolic and diastolic blood pressure did not increase continually in 24 hours blood pressure rhythm, indicated that the hypertension was not found among night shift workers.

Table 3: Correlation of SBP, DBP, HR in terms of MESOR and Double Amplitude between Night versus Day shift.

Measured Variables	Night Shift (NS) versus Day Shift (DS)	r ( n=62 )
MESOR	SBP: NS vs DS	0.52***
	DBP: NS vs DS	0.41***
	HR: NS vs DS	0.49***
Double Amplitude	SBP: NS vs DS	0.12 <sup>ns</sup>
	DBP: NS vs DS	0.34**
	HR: NS vs DS	0.01 <sup>ns</sup>

\*-p<0.05, \*\*p<0.01, \*\*\*-p<0.001

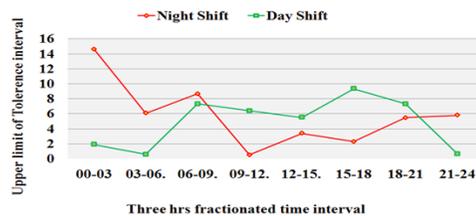


Figure (2A)

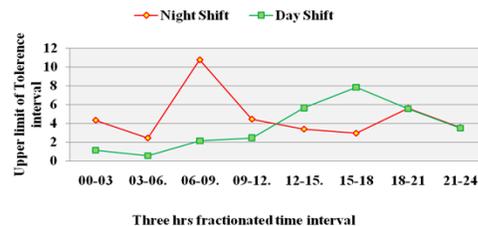


Figure (2B)

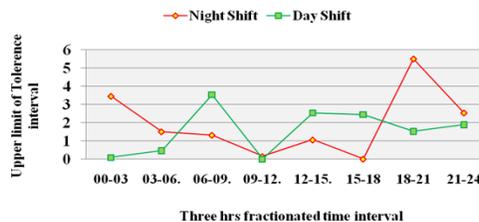


Figure (2C)

Figure 2A, B & C: Mean Hyperbaric index (3 hours fractionated time intervals) of Systolic blood pressure, Diastolic blood pressure and Heart rate during night and day shift.

**Correlation between different variables such as BP/ HR in terms of MESOR and Double Amplitude (DA); circadian rhythm of melatonin-**

The correlations of different variables such as SBP, DBP and HR in terms of MESOR and Double Amplitude

(DA) among night versus day shift are shown in Table 3. We elucidate the pathophysiology of rhythm disorders in night shift workers by the help of correlation analysis of different variables such as BP/ HR in terms of MESOR and Double Amplitude (DA); circadian rhythm of

melatonin. Variables that were significant by paired t test and significantly affected due to night shift were correlated. Associations between variables were done by Pearson correlation analysis. In the present study (n=62), if  $r=0.25$  then  $p<0.05$  (significant), if  $r=0.33$  then  $p<0.01$  (very significant), if  $r=0.41$  then  $p<0.001$  (extremely significant).

Moreover, simple correlation analysis showed that of MESOR (SBP, DBP and HR) of night shift was positively correlated with MESOR (SBP, DBP and HR) of day shift.

This pattern was highly significant. ( $p<0.001$ ) Double amplitude (SBP and HR) of night shift was positively correlated with Double amplitude (SBP and HR) of day shift. However this pattern was insignificant. ( $p>0.05$ ) Very significant and positive correlation was found in the pattern of Double amplitude of DBP between night and day shift. ( $p<0.01$ )

## DISCUSSION

The present study illustrates the effect of rotating night shift on circadian patterns of BP/HR in terms of double amplitude (2DA), acrophase and hyperbaric index (HBI). The results shows the changes in the systolic and diastolic blood pressure double amplitude when subjects completed 8-9 days night shift and came back to day shift. The present observations are in confirmation with the previous report of altered and reversed pattern of blood pressure and heart rate (acrophase) in night shift workers. Day shift workers show typical circadian rhythms with a drop in both systolic and diastolic blood at night. This pattern was reversed in night-shift workers. [11,12] Identical blood pressure and heart rate have been observed among night shift workers. [13] The rapidly rotating shift system including two consecutive night shifts, do not significantly alter the normal circadian rhythm of the body, particularly

performance level, body temperature and hormone release while our study represents significantly alters the blood pressure after eight to nine consecutive night shifts. [14]

Previous findings are similar with the present study shows the odd timing of blood pressure (ecphasia) clearly indicates the non dipping pattern of blood pressure at night during night shift. In general, blood pressure (BP) is also modulated in a circadian rhythm: over a 24-h cycle. The dipping pattern shows high BP in the daytime and low BP at night. It has been suggested that the rhythm closely follows the sleep-wakefulness cycle. [15, 16] Other study on shift workers suggests that night-shift workers are more likely to be classified as non-dippers than are day workers. [17]

In our study, subjects complained of several sleep related problems viz, difficulty in sleep, sleepiness and other problems related to cognitive function like mental fatigue, difficulty in skilled work, problems remembering, decreased alertness and depression during night shift and somewhat similar with previous study. [18] Other studies have also reported higher incidence of poorer sleep and its complications in night shift workers. [18-20] Some studies have demonstrated that shift work is associated with increased cardiovascular morbidity and mortality. [21-24] Devin L Brown et al., 2009 identified rotating night shift work as an independent risk factor for ischemic stroke. [25]

Peak time of blood pressure and heart rate were altered in most of the subjects by night shift schedules and there were individual differences in the circadian time structure of blood pressure during night shift schedule. Similar findings with other study reported that circadian rhythm of blood pressure was rapidly phase delayed by 3.5 h by night shift schedule in healthy human subjects. [26] 12-h night shift work may elevate BP and HR and decrease HRV

which may be associated with delayed blood pressure recovery. [27-30]

The most important physiological mechanisms regarding the night shift work, is the problem of entrainment (resynchronization) of physiological functions after a phase shift of working and sleeping times and has been reported that the resynchronization of circadian rhythm in blood pressure to a night shift schedule occurs much more rapidly than other circadian parameters such as body temperature. [15] This implies that blood pressure circadian rhythm is largely dependent on circadian rhythm in sleep-wakefulness. [13,15,31] Out of 62 nursing professionals, six subjects shows remain altered pattern of Acrophase during night as well as day shift. In these subjects biological rhythm of blood pressure and sleep wakefulness were desynchronized internally.

The results of earlier studies reported that the circadian blood pressure pattern is changed from a dipper to a non-dipper pattern on the first day of the night shift and reverses to a dipper pattern within a few days and suggest that night shift work may have unfavourable effects on blood pressure in patients with hypertension. [32-34]

## CONCLUSION

The altered circadian pattern of blood pressure in terms of double amplitude and acrophase occurred during night shift and it could be contributed to sleep disturbances and adverse effects of night shift schedule. This could probably be due to counteracting effect of an endogenous circadian rhythm and desynchronization during night shift. Entrainment of these rhythms in day shift leads to resynchronization.

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## Conflicts of Interest:

The authors declare there is no conflict of interest.

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