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Correlation of twenty-four hours ambulatory blood pressure pattern with severity of stable coronary artery disease in hypertensive patients- A single centre cross sectional observational study

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Abstracts

Background & objectives:

Hypertension is one of the most widely prevalent diseases throughout the world, which is emerging as one of the leading causes of premature morbidity and mortality globally. Nocturnal blood pressure readings measured by ABPM also provide prognostic data. 24 hr Ambulatory BP and specifically nocturnal blood pressure has been found to be associated with superior predictive and prognostic value for target organ dysfunction and CVD events either symptomatic or asymptomatic. Purpose of our study is to find out the prevalence of dipper, non-dipper, reverse dipper and extreme dipper in patients with stable CAD and their association with severity of CAD.

Methods:

This study was conducted in NH- Rabindranath Tagore Institute, Kolkata. Study lasted for 18 months. This study is a single centre cross sectional observational study. All patients who met inclusion criteria were included in this study after a thorough informed consent. Once the patient was recruited, he was admitted for an elective angiogram. Routine clinical history, baseline demographics like age, sex, height, weight, Body Mass Index (BMI), and comorbidities like diabetes hypertension and history of smoking were recorded. During the admission the patient underwent a 24-hr ambulatory BP monitoring after significant coronary artery disease was diagnosed on an elective diagnostic coronary angiogram. All data was anonymized and entered into Microsoft excel spread sheets and computed with SPSS version 20 for measures of statistical significance. Patients were classified into non-dipper& (with a nocturnal drop of mean BP less than 10%), dipper (nocturnal drop of mean BP 10%), extreme dipper (nocturnal drop of mean BP), or reverse dipper (nocturnal elevation of mean BP). Coronary artery disease was classified angiographically into single vessel and multi-vessel coronary artery disease.

Results:

In this present study population, mean age was 57.7±10.55 years, 88.5% were males, while 11.5% were females. 52.5% diabetic, while 34.8% was overweight and, 16.5% was obese. A total of 62.6 % had multi-vessel coronary artery disease and

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37.4% patients had single vessel involvement. In multivessel group vs single vessel group dipper were less (25.29% vs 44.23% p=0.02) and non-dipper were more (50.57% vs 3077% p=0.02), which is statistically significant. Comparison of individual parameters of BP between the multivessel and single vessel CAD, average night SBP (116.15±17.27 vs 109.17±14.91 p<0.05) and average night DBP (63.82±8.65 vs 60.87±7.77 p=0.01) were higher and statistically significant in multivessel group as compare to single vessel group.

Conclusion:

There is a statistically significant association was seen between CAD burden and nocturnal dipping pattern. Multivessel coronary artery disease have more blunted nocturnal blood pressure as compare to single vessel coronary artery disease. Correlation between BMI, smoking, age and DM with circadian pattern was not observed.

INTRODUCTION

Hypertension is one of the most widely prevalent diseases throughout the world, which is emerging as one of the leading causes of global premature morbidity and mortality.(1) Its prevalence is on the rise not only worldwide but in India as well, with crude prevalence of 25.3%, according to data collected from 2012 to 2014.(2)

It is the most important risk factor for cardiovascular morbidity and mortality. It has affected approximately 234 million adults in India.(3)With an ageing population and increasing Body mass index (BMI) the prevalence of hypertension is likely to increase. Hypertension is classified as either primary (essential) or secondary.

Essential hypertension itself constitutes 90%-95% of cases. It is multifactorial in aetiology comprising of genetic, lifestyle and behavioural components and is diagnosed when all underlying causes have been excluded. Only a small number of cases will have an identifiable cause for their hypertension.(4)(5)

As there is close relationship between blood pressure (BP) and cardiovascular risk, defining hypertension is difficult. According to a meta-analysis that collected data from a million of people, that mortality from stroke or myocardial infarction doubled for each 20mmHg rise in systolic BP (SBP) or 10mmHg rise in diastolic BP (DBP) above the reference value.(6) Values of a SBP >140mmHg and/or a DBP >90mmHg have been taken as the cut off level to define hypertension.(7)

As per the 2020 International society of hypertension, global hypertension practice guidelines. Following table provides different parameters that will define and stage the hypertension.(8)

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Table 1. Classification of Hypertension Based on Office Blood Pressure (BP) measurement. Systolic (mm Hg) Normal BP

Category	Systolic (mm Hg)		Diastolic (mm Hg)
Normal BP	<130	And	<85
High-normal BP	130–139	and/or	85–89
Grade 1 hypertension	140–159	and/or	90–99
Grade 2 hypertension	≥160	and/or	≥100

However, the optimal target BP is more controversial. Wide discrepancies are seen between the blood pressure readings at home and at the clinician's office (i.e. "white coat" hypertension/ Mask hypertension) in clinical practice. Hence ABPM is being increasingly recommended for clinical practice.[(9),(10)]

Nocturnal blood pressure readings measured by ABPM also provide prognostic data.[(11)] The importance of these issues is now well known, and hence it follows that managing hypertension without ABPM is no longer acceptable.

24 hr Ambulatory BP and specifically nocturnal bloodpressure has been found to be associated with superior predictive and prognostic value fortarget organ dysfunction and CVD events either symptomatic or asymptomatic. Whilethere is dearth of data in favour of association of ABPM with Heartfailure, Strokeand chronic kidney disease, however thesame for stable coronary artery disease (CAD) is lacking.

Purpose of our study is to find out the prevalence of dipper, non-dipper, reverse dipperand extreme dipper in patients with stable CAD and their association with severity ofCAD.

MATERIALS AND METHODS

This study was conducted in NH- Rabindranath Tagore Institute, Kolkata. Study lasted for 18 months. This study is a single centre cross sectional observational study. All patients who met inclusion criteria were included in this study after a thorough informed consent. Once the patient was recruited, he was admitted for an elective angiogram. Routine clinical history, baseline demographics like age, sex, height, weight, Body Mass Index (BMI), and comorbidities like diabetes hypertension and history of smoking were recorded. During the admission the patient underwent a 24-hr ambulatory BP monitoring after significant coronary artery disease was diagnosed on an elective diagnostic coronary angiogram.

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The Position Paper made the general recommendation that in clinical practice a satisfactory ABPM recording should have ≥70% of expected measurements. Blood pressure was measured by ABPM with minimum daytime (7am-9pm) measurement of 20 (every half hourly), minimum measurements of 10 (every hourly) at night throughout the entire 24-hour period.[12]

Based on above measurement, severity wise they were classified into "non-dipper" (with a nocturnal drop of mean BP less than 10%), a "dipper" (nocturnal drop of mean BP > 10%), "extreme dipper" (nocturnal drop of mean BP >20%), or a "reverse dipper" (nocturnal elevation of mean BP)

Severity of CAD was categorized as follows:

Multi-vessel coronary artery disease defined[13] by the presence of ≥50 % diameter stenosis of two or more epicardial coronary arteries.

Single vessel coronary artery disease [14]- the presence of at least a ≥70% stenosis of a major coronary artery (left anterior descending, left circumflex, or right coronary arteries) or one of their respective major branches (diagonal, obtuse marginal, posterior descending, or posterior left ventricular arteries).

Inclusion criteria

All of the following criteria must be met

- Age more than 18 years
- Hypertensive patients diagnosed by at least one 24-hour ABPM measurement within last 1 year as part of planned care, irrespective of medication and duration
- CAG shows significant atherosclerotic coronary artery disease.

Exclusion criteria

- Patient is in HFrEF beyond NYHA functional CLASS- II
- Previous Stroke
- Chronic kidney disease
- Patient refusal.
- Patients with ACS and unstable angina
- Patients with secondary HTN

RESULTS

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During study period of one and half years (June 2018 to December 2019), 160 patients were included in this study. Out of these 139 patients are finally included in the study 21 patient's data could not interpreted due to inadequate BP measurement and the results were analysed.

Individual parameters were compared between ≤ 60 years age group and > 60 years age group. All blood pressure parameter (12 hr day and night systolic and diastolic blood pressure and 24 hr systolic and diastolic blood pressure) was higher in >60 years age group as compare to ≤ 60 years age group. Among those 60 years and below of age, study revealed that maximum no. i.e., 40.79% patients were non dipper, while dipping was seen in 30.26% of study population, reverse dipping was seen in about 21.05% population, and a small subset about 7.89% were found to have extreme dipping. While among population (>60 years) as much as 46.03% population was non- dipper, about 34.92% patients fell under dipper category, while reverse dipper accounted for about 12.7%, and 6.35% were found to be extreme dipper. Overall, both groups were matched for their circadian differences in 24 hour blood pressure.

Table no- 2: Age distribution:

	<60 YEARS	**>60 YEARS**	**TOTAL**	**p Value**
REVERSE DIPPER, N (%)	16(21.05)	8(12.7)	24(17.27)	>0.05
NON-DIPPER, N (%)	31(40.79)	29(46.03)	60(43.17)	>0.05
DIPPER, N (%)	23(30.26)	22(34.92)	45(32.37)	>0.05
EXTREME DIPPER, N (%)	6(7.89)	4(6.35)	10(7.19)	>0.05
Total	76(100)	63(100)	139(100)	>0.05

OUT of 139 Patients, 11.5% were female and 88.5% were male. Among female, reverse dipper and non-dipper accounted for equal no. i.e., 31.25% also dipper and extreme dipper had equal prevalence of about 18.75%. While male population had 44.72% population as non-dipper, dippers were 34.15%, 15.45% population was found to be reverse dipper and extreme dipper were confined to 5.69%. The result was statistically insignificant. Individual ABPM parameter analysis was done between male and female which was statistically insignificant. However. the representation of females in this study is inadequate to draw any causal relationship. Possible reasons being under-reporting/atypical symptoms in females and is not contrary to previously done trials in coronary artery disease .[15]

Table no-3: Gender distribution:

	FEMALE	**MALE**	**Total**	**P Value**

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REVERSE DIPPER, N (%)	5(31.25)	19(15.45)	24(17.27)	>0.05
NON-DIPPER, N (%)	5(31.25)	55(44.72)	60(43.17)	>0.05
DIPPER, N (%)	3(18.75)	42(34.15)	45(32.37)	>0.05
EXTREME DIPPER, N (%)	3(18.75)	7(5.69)	10(7.19)	>0.05
Total	16(100)	123(100)	139(100)	>0.05

Among the population under study, out of 139 patients 87 had multi-vessel coronary artery disease and 52 patients had single vessel involvement. Out of 87 multi-vessel CAD patients. 50.57%, 25.29% ,19.54% and 4.6% patients were non dipper, dipper, reverse dipper and extreme dipper respectively. In 52 single-vessel CAD patients. 44.23%,30.77% ,13.46% and 11.54% patients were dipper, non-dipper, reverse dipper and extreme dipper respectively. In multivessel group vs single vessel group dipper were less (25.29% vs 44.23% p=0.02) and non-dipper were more (50.57% vs 3077% p=0.02). They are statistically significant.

Table no - 4 : Circadian pattern of BP and Coronary artery disease.

	Single vessel	**Multi vessel**	**Total**	**pValue**
REVERSE DIPPER N(%)	7(13.46)	17(19.54)	24(17.27)	0.36
NON-DIPPER N (%)	16(30.77)	44(50.57)	60(43.17)	0.02
DIPPERN(%)	23(44.23)	22(25.29)	45(32.37)	0.02
EXTREME DIPPER N(%)	6(11.54)	4(4.6)	10(7.19)	0.17
Total	52(100)	87(100)	139(100)	

DISCUSSION

Present study was conducted in NH- Rabindranath Tagore Institute, Kolkata. Study lasted for 18 months. It was an observational prospective study. 160 patients were included in this study. Out of these 21 patient's data could not interpreted due to inadequate BP measurement. In this present study population, mean age was 57.7±10.55 years. And 88.5% of total population under study were males. A total of 42.4% of study population was smoker, 62.6 % had multi-vessel coronary artery disease and 37.4% patients had single vessel involvement.

In individual ABPM parameter analysis it was found that as the age increases, average day & night SBP & DBP and 24 hr SBP & DBP increases, these

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observations are similar to the study of Upendra Kaul et al[16] who also noted that higher individual parameter of ABPM in elderly and burden of non-dippers increases with increasing age. This might be due to a steeper increase in night time BP with age as compared to the age-related increase in daytime BP.

In this present study we found that number of non-dippers were more in males this is mainly because of higher prevalence of coronary artery disease among the males and that is why more males undergo cardiac catheterization.[17,] although this result was not found to be statistically significant. Our study was supported by finding of the B.F.K Lialestaniet et al[18,] study, who also found no correlation between circadian rhythm and gender distribution.

Our study had an observation that multivessel coronary artery disease group having more non dipper (50.57% vs 30.77% p=0.02) and less dipper (25.29% vs 44.23% p=0.02) as compare to single vessel coronary artery disease. which was statistically significant. In individual ABPM analysis multivessel disease group having higher day time and night SBP & DBP and 24 SBP & DBP. Our current finding were similar to study by Soto R.M et al[19,] who conducted study in 60 patients and found that reverse dipper and non-dipper were significantly associated with the presence of coronary disease in two or more vessels. Liang T et al [20,] also came to a similar conclusion that the prevalence of double-vessel and triple-vessel disease was significantly higher in non-dipper than that in normal dipper blood pressure pattern. Tarek Mousa et al [21,] conducted a study in 68 cases and they found that a larger proportion of patients with CAD were non-dippers as compared to control subjects.

In various literature non-dipper had more severe CAD it may be because:[22,] 1-Nocturnal ischemia could be related to increase of myocardial oxygen demand (increase in heart rate and BP due to disturb or rapid eye movement sleep, postural changes and raised LV diastolic pressure). 2-Persistent hypertension during the night time could be associated with a more severe vascular dysfunction, endothelial dysfunction resulting in increased coronary tone and vasospasm. These two mechanisms (i.e., increased oxygen demand and decreased oxygen supply) may be involved in the pathogenesis of increased nocturnal ischemia in non-dipper hypertensive patients. Our study remains unique in the fact that it adds to the current evidence that severe multi- vessel disease is common in patients who are non-dippers suggestive of abnormal unabated autonomic activity which may result in abnormal neurohormonal balance and cause deleterious effects on the heart. However, it remains underpowered to establish a causal relationship between abnormal circadian BP patterns. comorbid and severity of CAD.

Conclusion:

There is a statistically significant association was seen between CAD burden and nocturnal dipping pattern. Multivessel coronary artery disease have more blunted nocturnal blood pressure as compare to single vessel coronary artery disease.

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Correlation between BMI, smoking, age and DM with circadian pattern was not observed.

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