Original Article

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Ambulatory Blood Pressure Monitoring in Normotensive Type 2 Diabetes Mellitus: An Observational Study

Internal Medicine Section

CHARAN NEERADI[1], BHAVANI MADDULURI[2], R VENKATESHWARAN[3], RATHINAM PALAMALAI SWAMINATHAN[4]

ABSTRACT

Introduction: Hypertension (HTN) is a major cause of cardiovascular morbidity and mortality, particularly in diabetic people. Because HTN and Type 2 Diabetes Mellitus (T2DM) frequently co-exist, HTN is a significant risk factor for chronic problems masked HTN affects around a one third of T2DM patients who have normal Blood Pressure (BP) readings in the clinic. T2DM patients frequently have normal office BP (BP) and no nocturnal BP falling. The non dipping BP pattern raises the risk of cardiovascular events and damage to target organs. Multiple BP recordings can be obtained with Ambulatory BP Monitoring (ABPM). By providing variability of BP, and diurnal variation in BP, it assists the treating physician in the diagnosis and management of HTN.

Aim: To elucidate the prevalence of non dipping pattern in T2DM and the characteristics of diabetics who have non dipping pattern using ambulatory monitoring.

Materials and Methods: This was an observational study carried out in the Department of Medicine at JIPMER, Puducherry, India. Between January 2016 and December 2017, 110 patients with T2DM were visited to Medicine Outpatient Department (OPD) and the Diabetic Clinic. Out of 110, a total of 62 patients, with an average age of 46.67 years, were included in the study. Sun Tech Oscar 2' 24 hour[R] ABPM system was used for the study of ambulatory BP of patients, at specified times.

Results: Sixty two normotensive T2DM patients, mean age of 46.67 years were analysed in the 24 months. A total of 62 patients, the non dipping pattern was seen in 47 (76%) of the 62 individuals evaluated for ABPM, while the dipping pattern was seen in 15 (24%) of the normotensive T2DM patients. A non dipping pattern was associated with a higher Body Mass Index (BMI) (p-value=0.03). A non dipping habit was also substantially associated with high Postprandial Blood Sugar (PPBS) values (p-value=0.02).

Conclusion: Patients with a history of HTN and smoking had a higher chance of non dipping patterns, which may lead to end-organ damage and future cardiovascular events. ABPM can be used as a screening tool to predict cardiovascular events in T2DM.

Keywords: Cardiovascular events, Hypertension, Non dipping pattern

INTRODUCTION

Co-morbidities such as HTN and T2DM are very common. In diabetic patients, HTN is twice as common as in non diabetic ones, and it is a prominent risk factor for the development of chronic problems in T2DM patients [1-3]. On 24-hour ABPM, many diabetic individuals who are normotensive on regular clinic BP tests show aberrant BP profiles [4]. In hypertensives, ABPM has been demonstrated to have a stronger connection with target organ damage than clinical BP monitoring. ABPM provides 24-hour BP profiles, encompassing daytime and night-time measurements, as well as the fluctuation in BP over a 24-hour period [5,6]. In the present study, standard deviation of average 24-hour, night-time, or daytime BP measurements was used to calculate 24 hour BP variability. This BP fluctuation is typically elevated in diabetics and it is an indirect predictor of disordered autonomic circulation control. The BP pattern is also provided by ABPM in the early morning hours. Morning HTN is more common in diabetic patients than in non diabetics and it predicts diabetic nephropathy development rate [7]. The patient profile of non dippers and its prevalence in diabetics helps to consider early antihypertensive therapy and to assess the ABPM as a screening tool in T2DM in order to predict further development of HTN.

To date, no study has evaluated the prevalence of non dipping patterns in normotensive T2DM in India. The present study was undertaken to identify the prevalence of non dipping pattern in diabetic patients. If the non dipping pattern prevalence is high in diabetics, then screening with ABPM can be recommended to detect non dippers, so that lifestyle modification and therapy for preventing HTN-related complications can be initiated.

MATERIALS AND METHODS

This was an observational study carried out at JIPMER's Department of Medicine on patients with T2DM who visited the Medicine OPD and the Diabetic Clinic between January 2016 and December 2017. The Institutional Ethics Committee (IEC) had approved the study (JIP/IEC/SC/2016/26/861). A total of 62 patients were included in present study. Consent from the participants was taken and confidentially of the data was maintained.

Inclusion criteria: Age >30 years, T2DM, normotensive patients (<140/90 mm Hg on two occasions atleast one week apart) were included in the study.

Exclusion criteria: Already on antihypertensive therapy or on drugs that are known to affect BP, known cases of systemic HTN, established coronary artery disease, heart failure, endocrinopathies other than diabetes, established nephropathy (macroalbuminuria >300 mg/24 hours, with albumin creatinine ratio of >34 mg/mmol), pregnancy were excluded from the study.

Study Procedure

Clinical and laboratory data were collected for all included patients using a standardised data collection form. The following data were collected- demographic data; clinical details like duration of diabetes, symptoms of hypothyroidism, snoring, history of smoking, treatment details for diabetes, family history of diabetes and HTN, BMI, waist to hip ratio, clinic BP at presentation, fundus examination for retinopathy; laboratory parameters like fasting and postprandial blood glucose, HbA1c, total cholesterol, Low Density Lipoprotein (LDL), High Density Lipoprotein (HDL), Thyroid function test, urine albumin.

Measuring method: The Sun Tech Oscar 2ABPM[R] device was used. Oscilometry with step deflation to monitor BP. The measurements of BP were started between 8 am and 10 am and ended 24 hours later. Three sphygmomanometer readings and three single measurements with the ABPM recorder was taken to ensure that the difference between the two was no greater than 5 mmHg. The subjects were carefully instructed regarding the measurement protocol. Minimal physical activity was allowed, vigorous physical activity and caffeine intake was prohibited. They were advised to cease activity and keep the arm still at the onset of cuff inflation. For the 24-hour ABP recording, the recorder was programmed as follows: patient's name, age, hospital number, height and weight, starting time and ending time were entered.

For each of the three measurement periods (24 hour, day and night), the systolic and diastolic means were calculated. The systolic and diastolic percentage dipping (normal >10%) were calculated. Individuals were classified as dippers based on the percentage of dipping if both systolic and diastolic dips were at least 10% [8].

Results of the ABPM recording were derived by using the following formula:

$$\text{Dipping percentage} = \frac{\text{Day mean BP} - \text{Night mean BP}}{\text{Day mean BP}}$$

The ABPM recorder was linked to all of the patients for 24 hours. The mean 24-hour Systolic Blood Pressure (SBP), Diastolic Blood Pressure (SBP), mean daytime SBP, DBP and mean night-time SBP, DBP were recorded.

STATISTICAL ANALYSIS

Categorical variables were expressed as number and percentage and compared across the groups using Pearson's Chi-square test for independence of attributes of categorical variables and student's unpaired t-test to compare two groups and p-value <0.05 was considered as level of significance.

RESULTS

The patients' mean age (SD) was 46.67±6.7 years, with 30 (48%) of them being men [Table/Fig-1].

Characteristics	N (%)
Age group (years)	
25-35	02 (3)
36-50	44 (71)
>50	16 (26)
Mean±SD	46.67±6.7 years
Sex	
Male	30 (48)
Female	32 (52)

[Table/Fig-1]: Demographic characteristics of the patients.

At the time of presentation, the mean duration of diabetes was 3.5±3.1 years. At the time of enrollment, 50 (81%) patients were taking oral hypoglycaemic agents. A family history of diabetes was found in 33 (53%). A family history of HTN was found in 11 (18%) The mean SBP in the clinic was 113 mmHg, while the mean DBP was 75 mmHg. The mean BMI was 23.6 kg/m^2 and the mean waist-to-hip ratio was 1.0 [Table/Fig-2].

Characteristics	N (%)
Duration of DM, years*	3.5±3.1
Antidiabetic therapy	
OHA only	50 (81)
Insulin only	3 (5)
OHA and Insulin	9 (14)
Family history of DM	33 (53)
Family history of HTN	11 (18)
Snoring	02 (3)
Smoking	18 (29)
SBP (mmHg)*	113±10.6
DBP (mmHg)*	75±8
BMI (kg/m^2)*	23.6±3.5
Waist to hip ratio*	1.0

[Table/Fig-2]: Clinical characteristics of included patients.
DM: Diabetes mellitus, HTN: Hypertension, OHA: Oral hypoglycaemic agents, SBP: Systolic blood pressure, DBP: Diastolic blood pressure; *Data presented as mean±SD

[Table/Fig-3] summarises the findings of laboratory research. The fasting blood sugar level was 169±74 mg/dL, while the postprandial blood sugar level was 276±97 mg/dL. LDL cholesterol levels averaged 116±30.4 mg/dL. LDL levels were higher than 100 mg/dL in 43 (69%) of the individuals.

Laboratory parameter	Values
Fasting blood sugar (mg/dL)*	169±74
Postprandial blood sugar (mg/dL)*	276±97
HbA1c	
<6%	4 (6)
6-7%	11 (18)
7-8%	16 (26)
>8%	31 (50)
Total cholesterol (mg/dL)*	194±42
LDL cholesterol (mg/dL)*	116±30.4
LDL cholesterol (mg/dL)	
<100	19 (31%)

[Table/Fig-3]: Laboratory findings.
*Data presented as mean±SD; all other data presented as n (%)

The clinical and analytical findings of the dipper and non dipper groups were compared [Table/Fig-4,5]. A non dipping pattern was associated with a higher BMI (p-value=0.03). A non dipping habit was also substantially associated with high PPBS values (p-value=0.02).

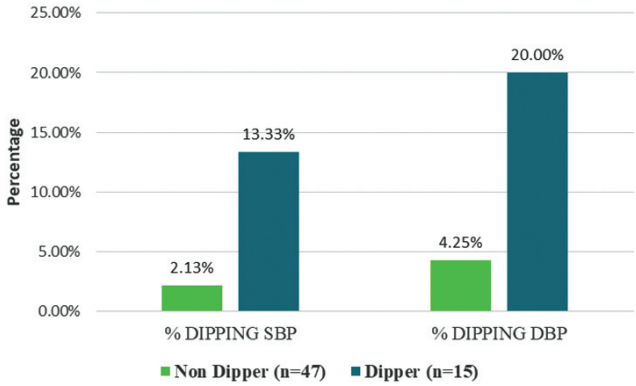
Characteristic	Non dipper (n=47)	Dipper (n=15)	p-value
Age, years*	46±6.4	47±7.8	0.6
Male gender	22 (47)	8 (53)	0.66
Duration of DM, years*			
Mean	3.7	3	0.13
<5	29 (62)	11 (73)	
5-10	17 (36)	03 (20)	
>10	01 (02)	01 (07)	
Antidiabetic therapy			
OHA	36 (77)	14 (93)	0.720
Insulin OHA and	03 (6)	0	
Insulin	08 (17)	1 (07)	
Family history of DM	27 (57)	06 (40)	0.23
Family history of HTN	11 (23)	0	0.052
Snoring	02 (4)	0	0.7
Smoking	16 (34)	02 (13)	0.12
SBP (mmHg)*	112±10.9	114±10	0.63
DBP (mmHg)*	75±7.7	75±9.1	0.8
BMI (kg/m^2)*	24.1±3.8	21.9±1.7	0.03
Waist to hip ratio*	0.88±0.08	0.87±0.06	1.0

[Table/Fig-4]: Comparison of clinical characteristics between non dipper and dipper groups.
*Data presented as mean±SD; all other data presented as n (%)

Laboratory parameters	Non dipper (n=47)	Dipper (n=15)	p-value
Fasting blood sugar (mg/dL)*	162±69	191±87	0.18
Postprandial blood sugar (PPBS, mg/dL)*	324±122	264±84	0.02
HbA1c			
<6%	03 (06)	01 (07)	0.38
6-7%	08 (17)	03 (20)	
7-8%	12 (26)	04 (27)	
>8%	24 (51)	07 (46)	
LDL cholesterol (mg/dL)*	116 ±32	117 ±25	0.95
LDL cholesterol (mg/dL)			
<100	15 (32)	04 (27)	0.70
>100	32 (68)	11 (73)	

[Table/Fig-5]: Comparison of laboratory findings between non dipper and dipper groups.
*Data presented as mean±SD; all other data presented as n (%)

SBP and DBP dipping percentages in the non dipper group were lower than in the dipper group which was 1 (2.13%) and 2 (4.25%) of non dipper in % Dipping SBP and DBP, respectively [Table/Fig-6].



[Table/Fig-6]: Comparison of dipping percentage between non dipper and dipper groups.

Clinical features and dipping pattern are related: BMI and Postprandial Blood Sugar (PPBS) were shown to be substantially linked with non dipping pattern in univariate analysis (p-value 0.05). The correlation between these variables (BMI, PPBS) and dipping pattern was investigated using multivariate analysis employing multiple logistic regression methods, but no significant relationship was found. [Table/Fig-7] summarises the results of multivariate analysis.

Variables	Beta (B)	Standard error (SE)	Significance (P)	Exp (B)	95% CI for Exp (B)	
					Lower	Upper
Postprandial blood sugar	0.006	0.003	0.083	1.006	0.999	1.013
BMI	0.308	0.166	0.064	0.0735	0.531	1.018

[Table/Fig-7]: Multivariate analysis results.

DISCUSSION

One of the most important risk factors for the onset and progression of chronic complications in T2DM is HTN. ABPM has a better correlation with target organ lesions than office-based BP monitoring. It also allows for the assessment of various BP parameters such as 24-hour, daytime, and night-time systolic and diastolic BP means, BP loads, and the absence of nocturnal BP drops, as well as the detection of white-coat and masked HTN. The present observational study was conducted at a tertiary care centre in a south-Indian community. This study demonstrated ABPM to determine the prevalence of the non dipping pattern in normotensive T2DM patients. It also identified the non dipping pattern predictors.

Prevalence of non dipping pattern: The clinical outcomes seen in this study were similar to those seen in earlier trials. The non dipping pattern was seen in 47 (76%) of the 62 individuals evaluated for ABPM, while the dipping pattern was seen in 15 (24%) of the patients. Cuspidi C et al., reported a 58% incidence in normotensive middle-aged T2DM patients [9].

According to Pistrosch F et al., 70% of hypertensive type 2 diabetics do not dip [10]. The non dipping trend was observed in 75% of hypertensive diabetics in the present study. The present study revealed a considerably higher prevalence of known dipping pattern than previous studies. The study done by Spallone et al. stated that decreasing vagal tone and increasing cardiac output can lower BP during the night in people with type 2 diabetic autonomic neuropathy [11]. Hyperinsulinaemia was one of the other reasons for the non dipping trend. The average age of the non dippers was 46±6.4 years in the present study. The mean duration of DM at presentation did not differ significantly between the non dipping and dipping groups. A higher BMI was found to be connected with a non dipping habit. These findings were in line with earlier research. Kotsis V et al., found the incidence of non dipping BP to be as high as 71.4% in obese patients [12]. Oxidative stress is the pathophysiological process behind postprandial hyperglycaemia and non dipping [13]. By producing reactive oxygen species, postprandial hyperglycaemia plays a critical role in acute and chronic inflammatory processes, endothelial dysfunction and diabetic end organ damage. Multivariate analysis revealed that fasting blood glucose and HbA1c are not statistically significant predictors of non dipping pattern in this study. Smoking cigarettes decreases the circadian pattern of BP [11]. Smoking is the greatest cause of atherosclerotic vascular disease, which results in non dipping BP. The present study found that just 4% of non dippers experienced symptoms of OSA. Ambulatory monitoring can rule out white coat high BP, preventing people from being prescribed BP-lowering drugs which they don't need. It can also detect masked HTN, allowing people to receive the necessary BP medications. The present study also demonstrated that family history of HTN and smoking were associated with increased risk of developing a non dipping pattern. So these patients should be routinely screened for end-organ damage. As the prevalence of non dipping is high even in normotensive T2DM, ABPM can be recommended as a screening method for identifying the non dipping pattern in diabetic patients.

Limitation(s)

Firstly, though on univariate analysis higher BMI and higher PPBS were shown to have a significant association with the non dipping, they were not found to be significant predictors on multivariate analysis, which might be because of the inadequate sample size. Secondly, during the study recordings of ABPM were not repeated to see the reproducibility.

CONCLUSION(S)

In normotensive T2DM patients, the prevalence of non dipping pattern was 76%, which could lead to end-organ damage and future cardiovascular events. As a result, ABPM can be utilised as a screening tool for T2DM patients to anticipate cardiovascular events. This study also discovered a link between on-dipping and a higher BMI, as well as postprandial hyperglycaemia. Current research also found that patients with a history of HTN and smoking have a higher chance of non dipping patterns.

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PARTICULARS OF CONTRIBUTORS:
1. Assistant Professor, Department of General Medicine, ESIC Medical College, Hyderabad, Telangana, India.
2. Junior Resident, Department of General Medicine, Jawaharlal Institute of Post Graduate Medical Education and Research, Puducherry, India.
3. Assistant Professor, Department of General Medicine, Jawaharlal Institute of Post Graduate Medical Education and Research, Puducherry, India.
4. Professor, Department of General Medicine, Jawaharlal Institute of Post Graduate Medical Education and Research, Puducherry, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Charan Neeradi,
Puducherry, Hyderabad, Telangana, India.
E-mail: shwetaagrawalniar@gmail.com

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