

Study of Dipping and Non-Dipping Patterns in Patients of Type 2 Diabetes Mellitus with Hypertension and Its Association with Microalbuminuria.

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ABSTRACT

Background: Non-dipping of nocturnal blood pressure is common in people with type 2 diabetes with hypertension and is associated with increased risk of cardiovascular and renal morbidity and mortality. This study aimed to identify the pattern of nocturnal non-dipping of BP in people with type 2 diabetes and its association with microalbuminuria. **Methods:** Data was examined from 100 patients with type 2 diabetes with hypertension who had undergone 24hrs ambulatory BP monitoring and it was correlated with urinary ACR, which was done in morning spot urine sample of all the patients. **Results:** Normal dipping was observed in 45%, non dipping in 46%, extreme dipping in 6% and 3% were reverse dippers in patients having type 2 diabetes and hypertension. It was observed that 24 hr dipping pattern of blood pressure and was strongly related to microalbuminuria ($p < 0.001$). Non dippers were significantly older ($p < 0.05$) with a higher prevalence of albuminuria ($p < 0.001$) as compared to dippers. Nocturnal dipping and albuminuria was found significantly associated with glycemic control, duration of diabetes and hypertension. **Conclusion:** Non-dipping of nocturnal BP in people with type 2 diabetes mellitus and hypertension is strongly associated with microalbuminuria.

Keywords: dipping, non-dipping, ambulatory BP monitoring, albuminuria.

INTRODUCTION

Type 2 diabetes patients have a two-threefold increase in cardiovascular risk,^[1] and more than half of patients with type 2 diabetes are having hypertension.^[2] As compared to conventional clinical BP monitoring, Ambulatory BP monitoring more accurately predict cardiovascular mortality^[3,4] and it also detects patients with loss of normal nocturnal dipping of blood pressure.

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Normally, it's seen that BP is lowest in the early morning and rises as the day progress, then it dips down during the night.^[5] During night time, mean BP is approximately 10-20% lower than daytime value.^[5] 'Non-dipping' is attenuation of normal fall in nocturnal BP, it is usually defined as a reduction of both systolic and diastolic ABPM of under 10% of the daytime average (i.e. systolic night/day ratio > 0.90).^[6]

Non-dipping of blood pressure is associated with 25% patients with hypertension^[3,7] with increased prevalence in people with diabetes.^[4,8] Studies by Verdecchia *et al.*^[3] and Sturrock *et al.*^[9] recorded the incidence of non-dipping amongst people with diabetes at 43% and 49%, respectively. There is evidence that non-dipping is associated with increased target organ damage and increased renovascular and cardiovascular risk.^[3,10-12] In previous cross-sectional studies of both hypertensive and normotensive subjects, impaired nocturnal BP reduction was associated with left ventricular hypertrophy,^[13] progressive renal dysfunction,^[14] cerebrovascular disease,^[15] cognitive deterioration^[16] and an increased incidence of fatal and non-fatal vascular events.^[17] The cause of non-dipping remains uncertain. Factors such as levels of activity and arousal during both the day and the night and the depth and quality of sleep may influence nocturnal BP, and non-dipping has been demonstrated in people with autonomic dysfunction^[18] and renal impairment.^[6,9,19] In people with either type 1 or type 2 diabetes, the presence of autonomic neuropathy is associated with a reduced fall in nocturnal blood pressure.^[20] Moreover, studies of hypertensive subjects with^[19] and without^[14]

diabetes have demonstrated a significant correlation between the presence of nocturnal non-dipping of blood pressure and increased urinary albumin excretion.

The results of earlier studies that have examined non-dipping of nocturnal blood pressure in people with diabetes need to be interpreted with some caution. The studies have been quite small, have used variable means of defining non-dipping, and have not included subjects selected at random and no such study has earlier been done in this part of the world. We have studied a randomly selected cohort of people with type 2 diabetes and hypertension and tried to identify the factors associated with nocturnal non-dipping of BP in this study. Nocturnal non-dipping of BP is defined according to the nocturnal systolic and diastolic BP dip. Normal ambulatory blood pressure during the day is <135/<85 mm Hg (hypertension threshold 135/85 mmHg) and <120/<70 mm Hg at night (hypertension threshold 120/70 mmHg) and 24 hrs average <130/80. Levels above 140/90 mm Hg during the day and 125/75 mm Hg at night should be considered as abnormal.^[16] Blood pressure will fall at night in normotensive individuals. People who undergo this normal physiological change are described as 'dippers'.

Range Class:

<0% Reverse Dippers, 0% - 9% Non-Dippers, 10% - 20% Normal Dippers, and >20% Extreme Dippers.

MATERIALS AND METHODS

Data was analysed from 100 randomly selected cases of type 2 diabetes mellitus with hypertension who were admitted in the department of Medicine, Guru Nanak Dev Hospital, Amritsar during 2015 & 2016. Written informed consent was taken, which allowed use of their data for clinical research purposes. Detailed history of patients was taken and routine investigations were done. Patients undergone 24 hrs ambulatory blood pressure monitoring by using ambulatory blood pressure monitor of Meditech Company of model ABPM-05 for all the patients of type 2 diabetes mellitus with hypertension. ABP Monitor was worn by patients for 24 hrs and blood pressure recordings were made at intervals of 0.5 hour from 06.00 to 22.00 hrs and at 1 hourly interval from 22.00 hrs to 06.00 hrs. ABPM recorded all these readings to give 24 hrs data of patient's blood pressure variations. Dippers were defined as those individuals with a mean 24 hr ambulatory BP which dropped >10%. Non-dippers are those individuals with a drop of 0 - 9%. Reverse Dippers are those whose dip is less than 0% and extreme dippers are those individuals whose drop in BP is more than 20%.

For establishing the presence of microalbuminuria, urinary Albumin-Creatinine ratio was done in all the

patients. Morning spot sample of urine was collected and checked for presence of albuminuria. Micro-albuminuria will be defined as an ACR 30 to 299 mg/g. Urinary albumin-creatinine ratio was done by using uChek model of urine analyser of biosense company by using an early morning midstream urine sample. Biosense URS 2AC urine analysis strips were used for albumin to creatinine ratio. The uChek system works on the principle of reflectance photometry which analyses the intensity and colour of light reflected from the reagent areas of the urinalysis reagent strips.

Dipping pattern of BP in Diabetic hypertensive patients was correlated with microalbuminuria and tabulated patterns of dippers and results were tabulated.

Statistical analysis

All statistical analyses were performed using SPSS version 21.0 for Windows. Frequency distribution, Mean and standard deviation were calculated for various qualitative and quantitative variables, respectively. Data was analysed to see the association for various variables using Chi-square test. A p value less than 0.05 was considered to be significant.

RESULTS

After analyzing data in 100 patients with type 2 diabetes and hypertension, the pattern of dipping of blood pressure was observed as – non-dippers were 46%, normal dippers were 45%, reverse dippers were 3% and 6% of the patients were extreme dippers [Table 1]. Nocturnal dipping of blood pressure was found to be significantly related to age of patients ($p < 0.05$) as shown in [Table 2]. It was seen that 24 hr dipping pattern of blood pressure was strongly related to albuminuria ($p < 0.05$). % systolic dipping and % diastolic dipping of blood pressure were associated with 24 hrs nocturnal dipping. Non-dipping of nocturnal blood pressure was found significantly related to duration of diabetes and glycemic control ($p < 0.01$). It was also observed that non-dipping is associated with duration of hypertension. 24 hrs diurnal index was significantly associated with serum cholesterol levels ($p < 0.05$) and S.LDL levels, but not related to S. Triglycerides, S.HDL, S.VLDL levels. There was no significant relation of dipping with gender of patient.

Albuminuria was significantly associated with age of diabetic hypertensive patient (p value < 0.05). Albuminuria was strongly associated with duration of diabetes and HbA1C (p value < 0.05). In this study, it was observed that albuminuria was significantly associated with duration of hypertension (p value < 0.05). No association with gender of study population was seen.

Table 1: Showing Pattern of Diurnal Index in the Study Population.

	All diurnal index of BP	Frequency	Percent	Valid Percent	Cumulative Percent
Reverse dippers	<0	3	3.0	3.0	3.0
Non dippers	0-9	46	46.0	46.0	49.0
Dippers	10-20	45	45.0	45.0	94.0
Extreme dippers	>20	6	6.0	6.0	100.0
	Total	100	100.0	100.0	
Std deviation	0.65782				

Table 2: Age Wise Distribution of Diurnal Index.

Age Groups (yrs)	All Diurnal Index Of BP (%)				Total
	<0	0-9	10-20	>20	
35-50	0	12	17	2	31
51-65	3	26	19	1	49
66-75	0	11	6	3	20
Total	3	46	45	6	100

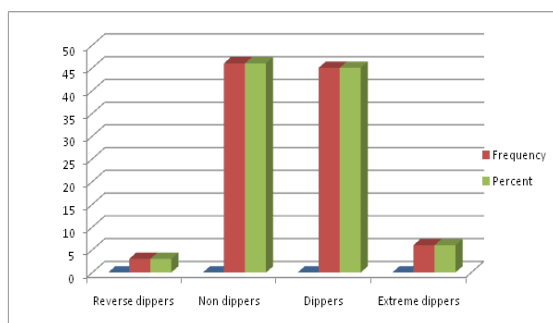
P value 0.040 (<0.05 significant)

Table 3: Showing Correlation of Pattern Of Dipping With Various Parameters.

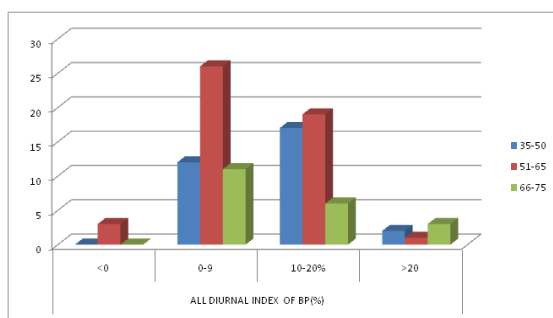
PARAMETERS (MEAN VALUES)	NORMAL DIPPERS (10-20%)	NON-DIPPERS (0-9%)	EXTREME DIPPERS (>20%)	REVERSE DIPPERS (<0%)
URINARY ACR (mg/g)	48	211.35	108.33	300
MEAN AGE(yrs)	55.96	58.73	57.83	61.66
FBS(mg%)	179.33	208.28	197.33	185.66
PPBS(mg%)	276.11	313.91	301.83	365
HbA1C(%)	7.68	8.18	8.28	8.53
DURATION OF DIABETES(yrs)	3.71	7.62	3.83	12.33
DURATION OF HYPERTENSION (yrs)	4.8	8.23	6.66	16.66
S.CHOLESTEROL (mg%)	179.73	205.3	173	223.33
S.TRIGLYCERIDES (mg%)	165.84	178.06	179	168.66
S.HDL(mg%)	43.66	42.02	40.83	42.33
S.LDL(mg%)	103	128	96	147
S.VLDL(mg%)	33	36	36	34
%SYSTOLIC DIPPING	10.62	3.34	19.33	-7.33
%DIASTOLIC DIPPING	15.2	6.39	25.33	-7.0

Table 4: Showing Correlation of Albuminuria with Various Parameters.

PARAMETERS (MEAN VALUES)	NORMALBUMINURIA (0-29 mg/g)	MICROALBUMINURIA (30-299mg/g)	MACROALBUMINURIA (>=300mg/g)
AGE(yrs)	49.16	58.87	60.94
FBS(mg%)	183.33	190.06	215.78
PPBS(mg%)	277.94	296.57	320.21
HbA1C(%)	7.78	7.91	8.35
DURATION OF DIABETES (yrs)	2.33	5.49	9.10
DURATION OF HTN (yrs)	3.44	6.69	10.57
%SYSTOLIC DIPPING	10.77	7.96	1.57
%DIASTOLIC DIPPING	15.5	11.84	4.42



Graph 1: Frequency of Dippers and Non-dippers..



Graph 2: Age Wise Distribution of Diurnal Index.

DISCUSSION

This study demonstrated that non-dipping of nocturnal blood pressure in people with type 2 diabetes was strongly associated with presence of albuminuria and increasing age. Non-dipping of nocturnal blood pressure was found significantly related to duration of diabetes and glycemic control. It is expected that increasing age is associated with increased prevalence of macrovascular complications, but even after adjustment of age, non-dipping status remained significantly associated with presence of albuminuria.

Studies by Nakano *et al*^[17] and Sturrock *et al.*^[9] have shown an association between increasing age and non-dipping status in people with diabetes. Several previous studies of people with type 2 diabetes have also demonstrated an association between nocturnal non-dipping and the presence of nephropathy^[5,9,19] and some have also shown a significant correlation between the presence of nocturnal non-dipping of blood pressure and increased levels of urinary albumin excretion.^[5,14,19] In this study, albuminuria was more prevalent in the non-dipping patients and albumin: creatinine ratios were higher in the patients showing decreased nocturnal dipping. Nakano *et al.* studied 'reversal of circadian rhythm' of blood pressure in people with diabetes and demonstrated an association between loss of circadian rhythm and the presence of all microvascular complications, and also with increased duration of diabetes.^[17] In the present study, there was a tendency for non-dippers to have a longer duration of diabetes and hypertension than

the normal dippers. Determination of the true duration of diabetes is difficult, as type 2 diabetes often remains subclinical for many years before the diagnosis. Previous studies have been relatively small, have used different criteria to define the non-dipping status, and the subjects in these studies have not been chosen at random. We studied a randomly selected cohort of people with type 2 diabetes and hypertension.. In a previous study, glycaemic control correlated with nondipping, with higher levels of glycaemic control observed in non-dippers.^[23] In the present study, glycaemic control was associated with nondipping of nocturnal BP.

The number of cardiovascular medications was also significantly greater in the non-dippers. In theory, this may reduce the severity of the albuminuria and other target organ complications and might, therefore, have weakened any association between non-dipping and nephropathy. The fact that an association is still identified would support this finding. The total cholesterol level and low density lipoprotein was significant in the non-dipping population, but triglyceride, very low density lipoprotein and high-density lipoprotein levels were not significantly different between the two groups. Non-dipping of nocturnal blood pressure is of prognostic importance. Evidence suggests that a blunted reduction in the normal nocturnal blood pressure fall may play a pivotal role in the development of target organ damage^[3,10-12] and is a powerful predictor of cardiovascular mortality.^[25]

CONCLUSION

The present study demonstrated a high prevalence of albuminuria amongst people with type 2 diabetes and non-dipping of nocturnal blood pressure. Nocturnal non-dipping antedates the development of microalbuminuria and nephropathy; this finding might be useful as a potential marker of impending nephropathy and might provide a rationale for treating susceptible persons before the onset of microalbuminuria. So its very important in patients of type 2 diabetes and hypertension to strictly control hyperglycemia to reduce associated morbidity and mortality.

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