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Ambulatory Blood Pressure Monitoring in Normotensive Patients with Type 2 Diabetes Mellitus

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ABSTRACT

Background: One of the primary risk factors for the beginning and development of chronic problems in type 2 diabetes mellitus is hypertension (DM).

Aim and objectives: The aim of this study was early detection of BP abnormalities in people with type 2 diabetes mellitus over the course of 24 hours.

Subjects and methods: The present study was carried out on 135 patients who presented to Cardiology Department at Zagazig University Hospitals and Cardiology Department at Matrtouh Cardiac Center in the duration between Janurary 2021 and Augest 2022. The patients were classified into three groups according to blood pressure dipping. Group 1 (Non-dippers): (n= 65), group 2 (dippers) included 53 cases and group 3 reversed dippers (n= 17).

Results: Significant positive correlation was detected between ratio of BP dipping and height (r=0.209, p-value =0.015) as well as night BP (r=0.287, p-value =0.001) while there was significant negative correlation between ratio of BP dipping and TG (r=-0.217, p-value =0.011) as well as day BP (r=-0.363, p-value <0.001),

Conclusion: Insightful information is provided by the study on the prevalence of aberrant ABP patterns and the limits of office blood pressure readings for either diagnosing hypertension or evaluating blood pressure control in people with type 2 diabetes.

Keywords: Ambulatory, Blood pressure, Monitoring, Normotensive, Type 2 Diabetes mellitus.

INTRODUCTION

One of the major risk factors for the beginning and development of chronic problems in type 2 diabetes mellitus (DM) is hypertension [(1)].

Compared to office-based blood pressure data, ambulatory blood pressure monitoring (ABPM) has a better correlation with abnormalities of the target organ. The ability to check a variety of blood pressure parameters, including the 24-hour, daytime, and overnight systolic and diastolic BP means, BP loads, and the absence of a nocturnal decrease in blood pressure, as well as the detection of white-coat and masked hypertension, is also provided [(2)].

Compared to non-DM patients, DM patients had higher daytime and nocturnal BP means. Additionally, one-third of type 2 DM patients with normotensive blood pressure have concealed hypertension, which is linked to an increase in albuminuria and a thickening of the left ventricular wall. We still don't know how common or dangerous white-coat hypertension is in people with type 2 diabetes. In the absence of nocturnal declines in blood pressure, the 24-hour, daytime, and overnight blood pressure measurements do not provide further information, but the midnight blood pressure readings seem to be significant in DM retinopathy [(3)].

In pre-hypertensive stages, white-coat settings, or lone clinics, ambulatory blood pressure monitoring has emerged as a critical method for the diagnosis of hypertension. Nowadays, those with high blood pressure (BP) when checked in a medical facility but normal readings elsewhere are referred to as having hypertension, such as at home or with a 24-hour ambulatory BP monitor [(4)]. Early detection of BP abnormalities in people with type 2 diabetes mellitus over the course of 24 hours was the goal of this investigation (ABPM).

SUBJECTS AND METHODS

This cross-sectional study was carried out between January 2021 and August 2022 at Cardiology Departments, Zagazig University Hospitals and Matrtouh Cardiac Center.

Inclusion Criteria

Age > 18, both sexes and patients with type-2 diabetes mellitus not known to be hypertensive.

Exclusion Criteria

Heart failure, coronary heart disease, stroke history, renal dysfunction (serum creatinine > 2 mg/dl or macroalbuminuria > 300 mg/24 h), significant valvular or pericardial disease, rhythm disturbances that make it challenging to interpret echocardiographic findings (like right or left bundle-branch block and atrial fibrillation), patients who work at night, and individuals with already low left ventricular ejection fraction are all risk factors (LVEF).

All patients were subjected to the following: Complete physical examination, thorough history taking (clinical symptoms, related diseases, drug use, past medical history, and family history), and regular laboratory tests including tests for kidney function, an ambulatory blood pressure monitor, an echocardiogram, and a complete blood count.

All patients were classified according to the results.

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Ethical Approval:

The study was given the go-ahead by Zagazig University Ethics Council, and the patients were given all the trial-related information they needed. After being fully informed, each study participant gave their signed consent. When conducting this human study, the World Medical Association's code of ethics known as the Declaration of Helsinki was observed.

Statistical analysis

The collected data were statistically analysed using SPSS version 24 (Statistical Program for Social Science). To check if the data distribution was normal, the Shapiro Walk test was used. For the purpose of displaying qualitative data, frequencies and relative percentages were used. The difference between the qualitative variables was ascertained using the chi square test (2) and Fisher exact, as shown. Using the independent T test and the Mann Whitney U test, respectively, the differences in quantitative variables in two groups with normally distributed and non-normally distributed data were compared.

RESULTS

The present study was carried out on 135 patients who were classified into three groups according to blood pressure dipping. Group 1 (Non-dippers): (n= 65), group 2 (dippers) included 53 cases and group 3 reversed dippers (n= 17). The mean age was 45.6 ± 7.9 years. Therewere 100 males (74.1%) and 35 females (25.9%). 58 (43.0%) cases were smokers. Regarding anthropometric measurements. The mean weight, height and BMI was 85.7 ± 8.8 Kg, 173.1 ± 7.8 cm and 27.6 ± 3.6 Kg/m^2 (table 1).

Table (1): Characteristics of the studied population (N= 135)

		Total N=135
AGE		45.6±7.9
Gender	Female	35 (25.9%)
	male	100 (74.1%)
Smoking	Non	77 (57.0%)
	smoker	58 (43.0%)
Hight		173.1±7.8
Wight		85.7±8.8
BMI		27.6±3.6

Data expressed by median (range), mean±SD or n (%) as appropriate.

The mean age in non-dippers and dippers was 44.2 ± 8.4 years and 47.7 ± 6.6 years respectively. Age was significantly higher in dippers compared to non-dippers (p-value was 0.014). The mean weights of dippers and non-dippers were 86.98.1 kg and 83.89.4 kg, respectively, and their respective mean BMIs were 28.03.5 kg/m^2 and 26.93.7 kg/m^2. Non-dippers had significantly higher weight and BMI than dippers (p-value was 0.021 & 0.047 respectively). Gender, smoking, and height did not significantly differ between the two study groups (p-value >0.05) (Table 2).

Table (2): Comparison of clinico-demographic data between both study groups

		Dippers		Total N=135	Test	P
		Non-dippers N=82	Dippers N=53			
Age (years)		44.2±8.4	47.7±6.6	45.6±7.9	-2.47	**0.014**
Gender	Female	22 (26.8%)	13 (24.5%)	35 (25.9%)	0.09	0.766
	Male	60 (73.2%)	40 (75.5%)	100 (74.1%)		
Smoking	Non	46 (56.1%)	31 (58.5%)	77 (57.0%)	0.08	0.784
	smoker	36 (43.9%)	22 (41.5%)	58 (43.0%)		
Height (cm)		173.2±8.4	173.0±6.9	173.1±7.8	-0.02	0.987
Wight (kg)		86.9±8.1	83.8±9.4	85.7±8.8	-2.31	**0.021**
BMI (kg/m^2)		28.0±3.5	26.9±3.7	27.6±3.6	-1.88	**0.047**

Quantitative variables were expressed as mean±SD and compared using Independent T test, while qualitative variables were expressed as numbers and percentages and compared using Chi-square X^2 test.

The mean HbA1c in non-dippers and dippers were 8.1 ± 1.5 and 8.5 ± 1.6 respectively. The mean LDL in non-dippers and dippers were 191.4 ± 178.1 mg/dl and 170.6 ± 41.2 mg/dl respectively. While, the mean TG in non-dippers and dippers was 169.9 ± 46.3 mg/dl and 171.9 ± 51.3 mg/dl respectively. No significant differences were observed between the two groups concerning HbA1c, LDL and TG (P-value =0.072, 0.802 & 0.647 respectively) as illustrated in table (3).

Table (3): Comparison of Lab. result between both study groups

	Dippers		Total N=135	T-Test	P
	Non-dippers (N=82)	Dippers (N=53)			
	Mean±SD	Mean±SD	Mean±SD		
HBA1c	8.1±1.5	8.5±1.6	8.2±1.5	-1.80	0.072
LDL mg/dl	191.4±178.1	170.6±41.2	183.2±141.2	-0.25	0.802
TG mg/dl	169.9±46.3	171.9±51.3	170.7±48.1	-0.46	0.647

There is no significant difference between dippers and non-dippers groups regarding ambulatory BP result & circadian rhythm (P-value =0.097 & 0.244 respectively) as illustrated in table (4).

Table (4): Comparison of Ambulatory BP result & Circadian rhythm data between both study groups

		Dippers		Total N=135	X^2 Test	P
		Non-dippers N=82	Dippers N=53			
		N (%)	N (%)	N (%)		
Ambulatory BP result	border line HTN	4 (4.9%)	1 (1.9%)	5 (3.7%)	7.87	0.097
	Dramatic rise\sever HTN	5 (6.1%)	0 (0.0%)	5 (3.7%)		
	isolated systolic HTN	0 (0.0%)	2 (3.8%)	2 (1.5%)		
	Latent HTN	34 (41.5%)	27 (50.9%)	61 (45.2%)		
	Normal	39 (47.6%)	23 (43.4%)	62 (45.9%)		
Circadian rhythm	Impaired	44 (53.7%)	23 (43.4%)	67 (49.6%)	1.36	0.244
	Normal	38 (46.3%)	30 (56.6%)	68 (50.4%)		

The results showed that ratio of dipping was significantly lower in dippers than non-dippers (p-value was 0.039) as the median (IQR) ratio of dipping was 0.915 (0.810-1.09) in non-dippers and 0.910 (0.810-1.09) in dippers. Meanwhile, ratio of dipping diameter was significantly higher in dippers than non-dippers (p-value was 0.009) as the median (IQR) ratio of dipping diameter was 7.6 (0.4-92.3) in non-dippers and 8.0 (0.0-26.1) in dippers as illustrated in table (5).

Table (5): Comparison of BP measures between both study groups

	Dippers		Total N=135	Test	P
	Non-dippers (N=82)	Dippers (N=53)			
Heart Rate	77.5±10.5	74.9±7.4	76.5±9.5	-1.50	0.132
Office SBP	123.3±10.6	125.3±11.5	124.1±11.0	-1.10	0.273
Office DBP	78.2±7.7	79.2±7.0	78.6±7.4	-0.55	0.579
24 h Average systolic	134.7±15.2	138.8±11.5	136.3±14.0	-1.58	0.115
24 h Average diastolic (mmhg)	85.9±12.8	86.6±11.5	86.2±12.3	-0.18	0.859
Night BP	130.8±12.6	132.0±12.1	131.3±12.4	-1.94	0.052
day BP	139.2±15.9	144.2±10.3	141.2±14.2	-0.56	0.573
Ratio of dipping sys	6.7 (0.1-19.7)	5.3 (0.2-18.8)	6.0 (0.1-19.7)	-0.36	0.722
Ratio of dipping diameter (average day Night)%	7.6 (0.4-92.3)	8.0 (0.0-26.1)	7.8 (0.0-92.3)	-2.63	**0.009**
ratio of dipping	0.915 (0.810-1.09)	0.910 (0.810-1.09)	0.910 (0.810-1.09)	-2.07	**0.039**

Using the Chi-square X2 test, qualitative variables were compared with numerical and percentage expressions. The Independent T test is used to compare ordinarily disturbed continuous data, and the Mann-Whitney test is used to compare non-normally disturbed continuous variables. Continuous variables are expressed as mean and standard deviation (SD) for ordinarily disturbed variables.

Table (6) displayed correlations between the ratio of BP dipping and several examined parameters for the entire group. Significantly negative connection was found between ratio of BP dipping and TG (r=-0.217, p-value =0.011) and day BP, whereas significantly positive correlation was found between ratio of BP dipping and height (r=0.209, p-value =0.015) and night BP (r=0.287, p-value =0.001) (r=-0.363, p-value <0.001).

Table (6): Correlations between Ratio of BP dipping and certain studied parameters in the whole group

	Ratioof BP dipping	
	r	P
AGE	-0.113	0.192
Hight	0.209	**0.015**
Wight	0.154	0.075
BMI	-0.093	0.285
Heart Rate	-0.133	0.123
Office SBP	0.020	0.818
Office DBP	0.020	0.815
HA1C	0.004	0.964
LDL	-0.149	0.084
TG	-0.217	**0.011**
24 h Average systolic	-0.161	0.062
24 h Average diastolic (mmhg)	-0.104	0.231
Night BP	0.287	**0.001**
Day blp	-0.363	**<0.001**

r (Correlation Coefficient)

Univariate logistic regression analysis of potential predictors of BP dipping. The results revealed that age was associated with BP dipping with relative risk of 1.062 with lower bound of 1.013 & upper bound of 1.112 (P = 0.012) as shown in table (7).

Table (7): Univariate logistic regression of potential predictors of BP dipping

	B	S.E.	Sig.	RR	95% C.I.for RR
AGE	0.060	0.024	0.012	1.062	1.013-1.112
Gender (F vs M)	-0.121	0.405	0.766	0.886	0.401-1.961
Hight	-0.004	0.023	0.872	0.996	0.953-1.042
Wight	-0.042	0.022	0.055	0.959	0.919-1.001
BMI	-0.087	0.050	0.084	0.917	0.831-1.012
Smoking	0.098	0.357	0.784	1.103	0.548-2.219
Heart Rate	-0.030	0.020	0.129	0.971	0.934-1.009
Office SBP	0.017	0.016	0.301	1.017	0.985-1.050
Office DBP	0.018	0.025	0.467	1.018	0.970-1.070
HA1C	0.191	0.116	0.098	1.211	0.965-1.518
LDL	-0.002	0.003	0.496	0.998	0.993-1.004
TG	0.001	0.004	0.812	1.001	0.994-1.008

β: regression coefficient; SE: standard error; RR: relative risk; 95%CI: 95% confidence interval, p< 0.05 is significant.

Multivariate analysis showed that age, and HbA1c were independent predictors for BP dipping. Age had relative risk of 1.063 with lower bound of 1.012 & upper bound of 1.117 (P = 0.014). While, HA1c had relative risk of 1.308 with lower bound of 1.019 & upper bound of 1.679 (P = 0.035) as shown in table (8).

Table (8): Multivariate logistic regression of potential predictors of BP dipping

	B	S.E.	Sig.	RR	95% C.I.for RR
AGE	0.061	0.025	0.014	1.063	1.012-1.117
Wight	-0.052	0.028	0.063	0.95	0.899-1.003
BMI	-0.013	0.062	0.833	0.987	0.873-1.115
HA1C	0.268	0.127	0.035	1.308	1.019-1.679

a Variable (s) entered on step 1: AGE, Wight, BMI, HA1C. All variable with p <0.1 in univariate analysis were entered in this regression model

β: regression coefficient; SE: standard error; RR: relative risk; 95%CI: 95% confidence interval, p< 0.05 is significant.

DISCUSSION

There is strong evidence that people with disguised hypertension are more likely to experience cardiovascular events, have poor metabolic profiles, and have target organ damage than people with normotension [(5).] This study sought to determine early BP changes in people with type 2 diabetes mellitus over a 24-hour period (ABPM). 135 patients who visited the Cardiology Clinics at Matrtouh Heart Center and Zagazig University Hospitals participated in this cross-sectional study. The patients were divided into two groups based on blood pressure drops: Group 1 (Non-dippers) had 82 occurrences, of which non-dippers (n=65) and reversed (n=17) instances made up the remainder, while group 2 (Dippers) had 53 cases.

The mean age was 45.6 ± 7.9 years. There were 100 males (74.1%) and 35 females (25.9%). 58 (43.0%) cases were smokers. Regarding anthropometric measurements, the mean weight, height and BMI were 85.7 ± 8.8 Kg, 173.1 ± 7.8 cm and 27.6 ± 3.6 Kg/m^2. In comparison with our findings, a cross-sectional study of **Najafi *et al*.** [(6)] was conducted in the Vali-Asr Hospital's diabetes clinic, which is a part of Tehran University of Medical Sciences. There were 192 participants in all (mean age 58.1), 87 of whom were men and 105 of them were women. Furthermore, the study of **Hemant *et al*.** [(7)] determined that 167 of the 291 patients with T2DM who visited the hospital throughout the study period were qualified to take part in the study. All of the participants were 56.7 ± 7.8 years old on average. There were a total of 93 patients, or 62% men, and 57 patients, or 38% women. The average time from diabetes diagnosis was 5.2 ± 4.7 years. 40 people in all (27%)

were either smokers or used tobacco in any other way. 39 people in total (26%) drank alcohol.

In the current study, the mean ages of dippers and non-dippers were 44.2 ± 8.4 and 47.7 ± 6.6 years, respectively. There were noticeable age disparities between dippers and non-dippers (p-value was 0.014). Dippers and non-dippers had mean weights of 86.9 ± 8.1 kg and 83.8 ± 9.4 kg, respectively, and mean BMIs of 28.0 ± 3.5 kg/m^2 and 26.9 ± 3.7 kg/m^2, respectively. Non-dippers' weight and BMI were substantially higher than in dippers' (p = 0.021 & 0.047 respectively). Height, smoking, and gender between the two study groups did not substantially differ (p-value > 0.05). According to the study by **Karaagac *et al.*** [(8)], there were 26 female and 9 male patients in the dipper group, with a mean age of 55 ± 11 years, which is identical to our findings. The non-dipper group had 25 female patients and 10 male patients, with a mean age of 56 ± 11 years. There was no obvious difference between the two groups in terms of essential features. Non-dipper hypertensive patients had larger thoracic aortic diameters (35.6 ± 2.4 and 33.2 ± 31.1, p = 0.01) than dippers. HbA1c, LDL, and TG were assessed in the study's dipper and non-dipper groups. The mean HbA1c was 8.1 ± 1.5 in non-dippers and 8.5 ± 1.6 in dippers, respectively. In contrast to the mean TG in non-dippers and dippers, which was 169.9 ± 46.3 mg/dl and 170.6 ± 41.2 respectively. The mean LDL in non-dippers and dippers was 191.41 ± 78.1 mg/dl and 170.6 ± 41.2 mg/dl, respectively. For TG, LDL, and HbA1c, no statistical differences between the two groups were found (P-value =0.072, 0.802 & 0.647 respectively). Our findings are in agreement with the study of **Akçay *et al.*** [(9)], which included 41 healthy individuals as a control group and 114 successive hypertensive patients without diabetes. The classification of 58 patients into non-dipper and 56 patients into dipper groups throughout the course of a 24-hour period was made possible by ambulatory blood pressure monitoring. Age, gender, cholesterol levels, and BMI did not differ significantly between the groups. Dippers with hypertension and control participants' HbA1c levels did not significantly differ (5.18 ± 0.43 vs. 5.36 ± 0.39, p=0.121). The HbA1c values of the non-dipper patients were substantially higher than those of the controls (5.54 ± 0.48 vs 5.18 ± 0.43 p = 0,001). The difference was not statistically significant, despite the fact that non-dippers tended to have higher HbA1c levels than dippers (5.54 ± 0.48'e 5.36 ± 0.39 p= 0.07).

There was no discernible difference between the dipper and non-dipper groups in the current study's ambulatory blood pressure results or circadian rhythm (P-values = 0.097 & 0.244, respectively). **Sommerfield *et al.*** [(10)] analysed data from 100 type 2 diabetics who underwent ambulatory blood pressure monitoring, which is consistent with our findings.

Dippers showed a systolic nighttime blood pressure reduction of almost 15%, compared to non-dippers who had a systolic evening blood pressure drop of less than 5%. Between the groups that engaged in dipping (142.9 mmHg) and those that did not (142.0 mmHg), the mean awake systolic blood pressure did not significantly differ (p=0.77). According to the current study, people with type 2 diabetes were more likely than healthy people to have masked phenomena, nocturnal systolic hypertension, and non- or reverse-dipping. **Draman *et al.*** [(11)] study is in line with us where 55% non-dipping outcome of the current investigation showed that type 2 diabetes had a significant incidence of abnormal circadian BP cycles. **De la Sierra** [(12)] observed in a sample of 34,563 treated and 8384 untreated hypertension patients that there was a clear relationship between type 2 diabetes mellitus and non-dipping.

Regarding heart rate, night BP, day BP, office SBP, office DBP, 24 h average systolic, and 24 h average diastolic, there were no differences between the dipper and non-dipper groups. In line with our findings, **Gunawan *et al.*** [(13)] reported that 31 persons, including seven (23%), had aberrant circadian BP rhythms with non- or reverse-dipping patterns. Among these, 5 (16%) were reverse dippers and 26 (84%) were non-dippers. In contrast to the 10 (38%) non-dippers who only did it during systole, 16 (62%) of the 26 non-dippers did it during either systole or diastole. For both systole and diastole, reverse dipping was seen in all five (100%) reverse dippers. Five patients (20%) had extreme patterns, while 20 patients (80%) displayed extreme or medium dipping patterns. One (20%) of the five extreme dippers only dipped often during systole and excessively only during diastole, two (40%) dipped excessively during both systole and diastole and two (40%) dipped excessively only during systole while dipping normally during diastole. All (100%) of the usual dippers experienced normal systole and diastole dipping. A substantial positive association between the ratio of BP dipping and height (r=0.209, p-value =0.015) and night BP (r=0.287, p-value =0.001) was found in addition to the data mentioned above.

According to research by **Nakano *et al.*** [(14)]**,** people with diabetes who are older are more likely to have non-dipping status. Previous research by **Lindsay *et al.*** [(15)] in individuals with type 2 diabetes has also shown a link between nocturnal non-dipping and the presence of nephropathy. Some of these studies have also revealed a statistically significant link between nocturnal non-dipping of blood pressure and higher levels of urinary albumin excretion. Prior research employed different criteria to establish the non-dipping status, were very limited in size, and did not randomly select their subjects.

We looked at a cohort of type 2 diabetics without hypertension who were randomly chosen. In a previous study of **Björklund *et al.*** [(16)], Glycaemic control and non-dipping were associated with non-dippers having better levels of glycaemic control. Contrarily, age was related with BP dipping in the current study, with a relative risk of 1.062, with lower and upper bounds of 1.013 and of 1.112 (P-value=0.012) in univariate logistic regression analysis of putative predictors of BP dipping. While, regarding multivariate analysis, we showed that age, and HA1c were independent predictors for BP dipping. Age had relative risk of 1.063 with lower bound of 1.012 & upper bound of 1.117 (P-value=0.014) while HA1c had relative risk of 1.308 with lower bound of 1.019 & upper bound of 1.679 (P-value=0.035). In comparison with our findings, **Spallone *et al*.** [(17)] observed that nighttime sleep or variations in daily activity can impact blood pressure monitoring. Day and night periods in this study were based on individual schedules for going to bed and waking up rather than fixed intervals. Also, patients underwent ABPM while they were in the hospital, allowing for a better consistency of recording circumstances, particularly with reference to physical activity.

Nevertheless, **Eguchi *et al.*** [(18)] found that nightly blood pressure variation is strongly related to irregular diurnal blood pressure readings rather than a higher risk of cardiovascular illness in patients with type 2 diabetes in particular. Remarkably, both people with and without a known history of hypertension had the same average 24-hour systolic ABP. This may be explained by the cohort's high prevalence of nocturnal hypertension and the presence of masked phenomenon, but given the small sample size, it's also plausible that this was just a coincidental discovery.

CONCLUSION

The study offers proof of the prevalence of aberrant ABP patterns as well as the limits of office blood pressure for either diagnosing hypertension or evaluating blood pressure control in people with type 2 diabetes. The overall results of this study support the therapeutic efficacy of ABPM in type 2 diabetes, despite the fact that they are not very novel. They further contend that, regardless of the degree of blood pressure control identified by office visits, type 2 diabetes patients may gain diagnostic advantage from 24-hour ABP monitoring BP measurement.

DECLARATIONS

- **Consent for publication:** I attest that all authors agreed to submit the work.
- **Availability of data and material:** Available
- **Competing interests:** None
- **Funding:** No fund
- **Conflicts of interest:** no conflicts of interest.

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