Ambulatory Blood Pressure Monitoring as Predictor of Diabetic Cardiovascular Complications

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ABSTRACT

Background: Blood pressure (BP) readings taken at a doctor's office or clinic have historically served as the foundation for the diagnosis, treatment, and estimation of mortality risk for patients with hypertension.
Objective: The present study aimed to measure the relative predictive value of office-based BP versus ambulatory BP for cardiovascular complications in diabetes patients.
Patients and methods: This cohort study included 48 adult diabetic patients from Cardiology Department, Zagazig University. The examined cases had at least two consecutive BP clinic measures with a validated automatic oscillometric instrument or the conventional approach using a sphygmomanometer.
Results: Office systolic blood pressure ranged from 107 to 138 mmHg with a mean of 126.88 mmHg. Office diastolic blood pressure ranged from 53 to 79 mmHg with a mean of 71.98 mmHg. Mean 24-hour systolic blood pressure ranged from 105 to 147 mmHg with a mean of 122.69 mmHg. Mean 24-hour diastolic blood pressure ranged from 51 to 90 mmHg with a mean of 70.5 mmHg. There was statistically significant positive correlation between office SBP and both daytime and night ambulatory systolic blood pressure. There was statistically significant positive correlation between office DBP and both daytime and night ambulatory diastolic blood pressure. There was statistically significant positive correlation between office MBP and both ambulatory mean 24-hour systolic and diastolic blood pressure
Conclusion: Ambulatory blood pressure monitoring (ABPM) is linked to the development of cardiovascular problems from diabetes and diabetic retinopathy at a mean ambulatory BP level of less than 122.5/70.5 mmHg.
Keywords: Blood pressure monitoring, Diabetes patients, Cardiovascular complications.

INTRODUCTION

Blood pressure (BP) is measured using the auscultatory method with a sphygmomanometer and stethoscope. According to the American College of Cardiology/American Heart Association (ACC/AHA), normal systolic and diastolic blood pressure for adults is <120 mm Hg and <80 mm Hg, respectively [(1)]. Changes in blood pressure (BP) occur frequently during aging and during normal physiologic responses to stress and exercise. An increase in BP becomes a clinical disorder when this change causes a threat to biologic functions and during this time is defined as a pathologic elevation in BP or systemic hypertension [(2)].

In patients 65 years of age and older, the target blood pressure is <130/80 mmHg. Higher blood pressures earn the progressively severe labels of elevated blood pressure, stage I hypertension, stage II hypertension, and hypertensive crisis [(3)]. This increase in BP is due to complex and varied components, which are not only due to aging factors but also to unique environment and lifestyle factors. With advanced age, microscopic and macroscopic changes to the heart, vascular system, and autonomic nervous system may occur, which can dramatically affect blood pressure [(4)].

Ambulatory BP has been known to help start treatment of hypertension in patients with differential cardiovascular risks, which may include low-risk patients with white coat hypertension, or with high risk, including sustained hypertensive patients [(5)]. With better understanding of the dynamic changes in blood pressure, health care providers now emphasize appropriate blood pressure techniques and have established medical diagnoses such as "white coat and masked hypertension," which reflect blood pressure measurements that do not represent the true patient status [(6)].

This study aimed to measure the relative predictive value of office-based BP versus ambulatory BP for cardiovascular complications in diabetes patients.

PATIENTS AND METHODS

A Cohort study that was conducted at Cardiology Department, Faculty of Medicine, Zagazig University.
Inclusion criteria: Patients with diabetes (HbA1c value ≥ 6.5%) or previous criteria for fasting glucose (≥ 126 mg/dL) or 2-hour glucose (≥ 200 mg/dL) in age above 18 years.

Exclusion criteria:
Patients had BP measurements over140/80 mmHg, age < 18 or >80years old, pregnant female, patients had evidences of acute stroke or myocardial infarction within the past 6 months and patients who had evidence of disease or conditions responsible for secondary hypertension.

All patients were subjected to the following:

I- Office BP Assessment

Trained investigators were observed at least two consecutive clinic BP measurements using a traditional method by sphygmomanometer or validated automatic oscillometric device after the participants were rested in a seating position for ≥ 10 min. Systolic blood pressure (SBP), diastolic blood pressure (DBP) and Mean blood Pressure (MBP) were recorded.

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II- ABPM Assessment

Ambulatory BP were recorded over 24 hours and set to measure every 30 min at daytime (from 7:00 AM to 11:00 PM) and every 60 min at nighttime (from 11:00 PM to 7:00 AM) lasting 24 hours automatically. The monitor will be installed on the non-dominant arm between 7:00 AM and 9:00 AM and removed 24 hours later. The patients were asked to take activities as usual and avoid daytime napping and sleep for 6 h to 12 h. The occurrence of unusual events or poor sleep will be noted for further evaluation. Values from the 24-h BP profiles: mean 24-h systolic and diastolic values, daytime SBP and DBP, nighttime SBP and DBP. The normal day-night dipping of BP were defined for SBP as 10%–20% reduction in mean BP values at night compared to the daytime values.

BP patterns of patients in our study were divided into dipper (10% to 20% SBP fall), non-dipper (0% to 10% SBP fall), extreme-dipper (> 20% SBP fall) and reverse-dipper (< 0% SBP fall), according to the range of the nocturnal SBP dip [(7)].

❖ **The following tests were done including**

1. Fasting blood sugar [FBS], 2 hr post-prandial blood sugar [PPBS] and Haemoglobin A1c [HbA1c].
2. Total cholesterol, triglyceride [TGs], low density lipoprotein [LDL] and high density lipoprotein [HDL].
3. Serum Creatinine, urea and uric acid.
4. BMI measurement and Waist to hip ratio.

❖ **Echocardiography:**

2D echocardiography was performed by experienced physician-echcardiographer, patients were imaged in the left lateral position using GE vivid 7 echocardiography system (GE-Vingmed Ultrasound AS, Horten, Norway), standard images were obtained using 3.5-MHz transducer in the parasternal and apical views, the frame rates of acquired images were between 82 and 95 frames/ sec. Standard 2D and color Doppler data of at least three consecutive cardiac cycles, triggered to QRS complex, were saved in a cine loop format at a breath hold at shallow expiration. 2D echocardiography was used to assess conventional echocardiographic parameters:

- Aortic Orifice [AO] dimension,
- Left Atrial [LA] dimension,
- Left Atrial [LA] volume,
- Right Ventricular [RV] dimension,
- Interventricular Septum [IVS] thickness,
- Left Ventricular Posterior Wall [LVPW] thickness,
- Left Ventricular End Systolic Dimension [LVESD],
- Left Ventricular End Diastolic Dimension [LVEDD],
- Ejection Fraction [EF] and Fractional Shortening [FS],
- Left Ventricular [LV] mass,
- Left Ventricular [LV] diastolic dysfunction (grading and how to asses).

❖ **ECG:**

Assessment of LVH (by Romhilt-Estes criteria and by voltage citeria).

- ➢ Amplitude of largest R or S in limb leads ≥ 20 mm = 3 points
- ➢ Amplitude of S in V1 or V2 ≥ 30 mm = 3 points
- ➢ Amplitude of R in V5 or V6 ≥ 30 mm = 3 points
- ➢ ST and T wave changes opposite QRS without digoxin = 3 points
- ➢ ST and T wave changes opposite QRS with digoxin = 1 point
- ➢ Left Atrial Enlargement = 3 points
- ➢ Left Axis Deviation = 2 points
- ➢ QRS duration ≥ 90 ms = 1 point
- ➢ Intrinsicoid deflection in V5 or V6 > 50 ms = 1 point
- ➢ If the score equals 4, LVH is present with 30% to 54% sensitivity, if the score is greater than 5, LVH is present with 83% to 97% specificity.

Ethical Consideration: An approval of the study was obtained from Zagazig University Academic and Ethical Committee. Written informed consents of all the participants were obtained. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Statistical analysis

Data were analyzed using Microsoft Excel software. Data were then imported into Statistical Package for the Social Sciences (SPSS) version 20.0 software for analysis. According to the type of data qualitative were represented as number and percentage, quantitative continues group were represented as mean ± SD. Differences between quantitative independent multiple were tested by ANOVA or Kruskall Wallis. P value was set at ≤ 0.05 for significant results & <0.001 for highly significant results.

RESULTS

The study included 48 diabetic patients with age range from 4 to 75 years with a mean of 50.63 years. Half of them were males. Body mass index ranged from 20.3 to 36 kg/m^2 with a mean of 27.09 kg/m^2. Waist to hip ratio ranged from 0.6 to 0.95 with a mean of 0.839. The largest percentage of patients were obese (83.3%) and had high waist to hip ratio (68.8%) **(Table 1).**

Table (1): Distribution of the studied patients according to demographic and clinical data

	N=48	%
Age: **Mean ± SD** **Range**	50.63 ± 12.17 4 – 75	
Gender: **Female** **Male**	24 24	50% 50%
BMI: **Mean ± SD** **Range** **Obese**	27.09 ± 3.15 20.3 – 36.0 40 (83.3%)	
Waist to hip ratio: **Mean ± SD** **Range** **Abnormal**	0.839 ± 0.069 0.6 – 0.95 33 (68.8%)	

Office systolic blood pressure ranged from 107 to 138 mmHg with a mean of 126.88 mmHg. Office diastolic blood pressure ranged from 53 to 79 mmHg with a mean of 71.98 mmHg. Office mean arterial blood pressure ranged from 71 to 97.67 mmHg with a mean of 90.28 mmHg **(Table 2).**

Table (2): Office blood pressure measurement among the studied patients

	Mean ± SD	Range
Systolic blood pressure	126.88 ± 6.65	107 – 138
Diastolic blood pressure	71.98 ± 4.64	53 – 79
MAP	90.28 ± 4.66	71 – 97.67

Day time systolic blood pressure ranged from 105 to 146 mmHg with a mean of 126 mmHg. Day time diastolic blood pressure ranged from 52 to 91 mmHg with a mean of 72.5 mmHg.

Night systolic blood pressure ranged from 100 to 149 mmHg with a mean of 118.77 mmHg.

Night diastolic blood pressure ranged from 49 to 88 mmHg with a mean of 67.88 mmHg. Mean 24-hour systolic blood pressure ranged from 105 to 147 mmHg with a mean of 122.69 mmHg. Mean 24-hour diastolic blood pressure ranged from 51 to 90 mmHg with a mean of 70.5 mmHg **(Table 3).**

Table (3): Ambulatory blood pressure measurement among the studied patients

	Mean ± SD	Range
Daytime Systolic blood pressure	126.0 ± 7.07	105 – 146
DaytimeDiastolic blood pressure	72.5 ± 6.63	52 – 91
Night Systolic blood pressure	118.77 ± 11.62	100 – 149
Night Diastolic blood pressure	67.88 ± 8.29	49 – 88
Mean 24 hour SBP	122.69 ± 8.29	105 – 147
Mean 24 hour DBP	70.5 ± 6.78	51 – 90

Regarding blood pressure phenotypes, 27.1%, 47.9%, 4.2% and 20.8% had dipper, non-dipper, extreme dipper and reverse dipper respectively **(Table 4).**

Table (4): Distribution of the studied groups according to blood pressure phenotypes

	N=48	%
Dipper	13	27.1%
Non-dipper	23	47.9%
Extreme dipper	2	4.2%
Reverse dipper	10	20.8%

There was a statistically significant positive correlation between office SBP and both daytime and night ambulatory systolic blood pressure **(Table 5).**

Table (5) Correlation between office SBP and ambulatory blood pressure

	Office SBP	
	R	P
Day time SBP	0.58	<0.001**
Night time SBP	0.434	0.002*

r Pearson correlation coefficient *p<0.05 is statistically significant **p≤0.01 is statistically highly significant

There was a statistically significant positive correlation between office DBP and both daytime and night ambulatory diastolic blood pressure **(Table 6).** There was a statistically significant positive correlation between office MBP and both ambulatory mean 24-hour systolic and diastolic blood pressure **(Figures 1, 2)**.

Table (6) Correlation between office DBP and ambulatory blood pressure

	Office DBP	
	r	**P**
Day time DBP	0.714	<0.001**
Night time DBP	0.754	<0.001**

r Pearson correlation coefficient *p<0.05 is statistically significant **p≤0.01 is statistically highly significant

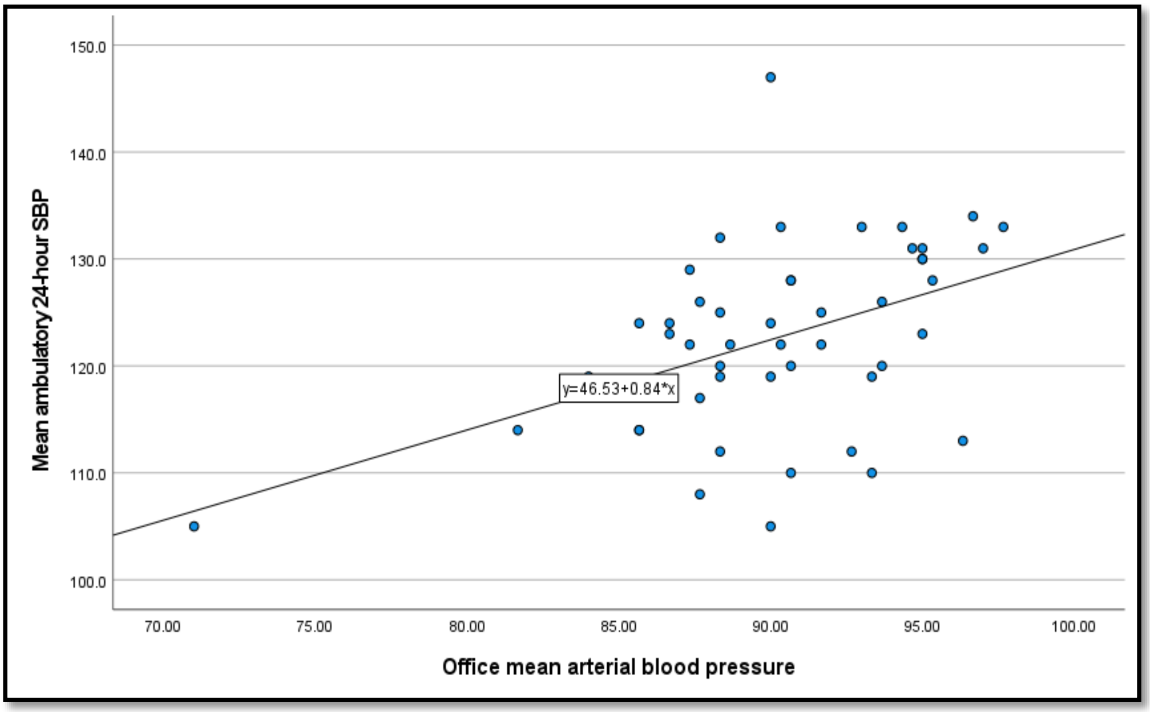

Figure (1): Scatter dot showing significant positive correlation between mean arterial blood pressure and mean ambulatory 24-hour SBP.

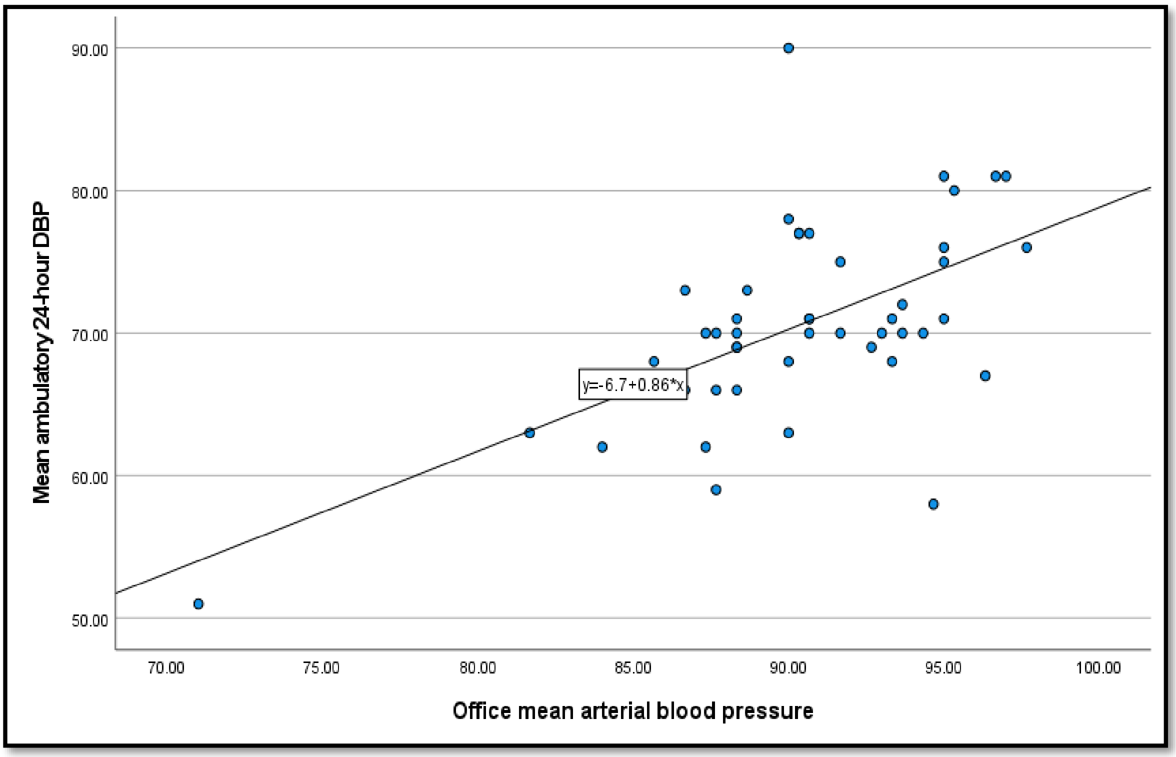

Figure (2): Scatter dot showing significant positive correlation between mean arterial blood pressure and mean ambulatory 24 hour DBP.

DISCUSSION

Ambulatory blood pressure monitoring is a technique with several important advantages over office blood pressure [8].

The correlation between blood pressure level and the risk of target organ damage and cardiovascular events is much greater for ambulatory blood pressure monitoring in both the general population and in patients with diabetes [9].

This cohort study selected 48 adult diabetic patients that were recruited from the cardiology department at Zagazig University. The examined cases had at least two consecutive BP clinic measures with a validated automatic oscillometric instrument or the conventional approach using a sphygmomanometer.

Regarding demographic and clinical data, it was found that the mean age of the included diabetic patients was 50.63 ±12.17years and half of them were males. Their body mass index mean was 27.09 ± 3.15 kg/m^2 where 83.3% were obese and 68.8% had high waist to hip ratio. These findings are in agreement with an Egyptian cross-sectional study aimed to assess the use of ambulatory BP monitoring in diabetic patients, which showed that the mean age of enrolled cases was 47.5 ± 13.2 years and 48% of them were males [10]. According to a cross sectional study aimed to investigate the association between diabetic complications and both diurnal and nocturnal variability in BP, it was reported that the mean age of participated diabetic patients was 58.1 years and 45.3% were men [11]. **Gunawan *et al.*** [12] in a cross sectional study showed that the involved diabetic patients were older (mean age 67 ± 10 years) and similarly to our study 50% of them were males. In addition, **Salles *et al.*** [13] reported in a prospective cohort study included diabetic patients that mean age was 60.4 ± 9.5 years, 37.5% were males with BMI 29.5 ± 4.8 kg/m^2 and 48% were on insulin.

Regarding office BP measurement, it was revealed that the mean SBP was 126.88 ± 6.65 mmHg, the mean DBP was 71.98 ± 4.64 mmHg and the mean arterial BP was 90.28 ± 4.66 mmHg. **Cardoso *et al.*** [14] and **Salles *et al.*** [13] who conducted a cross-sectional study among 550 type 2 diabetic patients demonstrated higher office BP measurements than reported in our study where mean SBP was 148 ± 25 and mean DBP was 85±13. This difference can be attributed to variations in clinical characteristics of the studied patients, duration of follow up and small sample size. In the same line, a cross sectional study reported that average day SBP was 131.4 ± 19.5 mmHg and DBP was 81.4 ± 13.1 mmHg, while at night SBP was 116 ± 19.6 mmHg and DBP was 70.6 ± 11.9mmHg with all over average SBP was 124.01 ± 19.4 mmHg and DBP was 76.2 ± 12.3 mmHg [10]**.** In addition, **Najafi, *et al.*** [11] who investigated ambulatory BP measurements in type 2 diabetic patients and found that the mean of 24 h SBP was 124.9 ± 13 mmHg and that of DBP was 75.1 ± 8.1mmHg with mean awake SBP of 126.6 ± 13 mmHg and DBP of 75.8 ± 8.4 mmHg while a sleep SBP was 121.1 ± 14.7 mmHg and DBP was 72.8 ± 8.7 mmHg. In contrast **Dahle *et al.*** [15] revealed that the mean clinic systolic and diastolic BP (153/77) were higher than the mean ambulatory 24-h BP (131/68 mmHg). In addition, **Gunawan *et al.*** [12] who used ambulatory BP technique in diabetic patients and demonstrated that 29% masked phenomenon, but only 7% demonstrated white coat effect. This clarify the role of ambulatory BP in detecting both false positive and false negative results. This difference could be referred to variation in the studied population and used devices.

The usefulness of ambulatory BP monitoring in diabetes is related not only to the possibility of assessing the features of BP elevation over 24 h, but also to its ability to identify BP patterns reflecting an important pathophysiological mechanism underlying the cardiovascular effects of diabetes, namely autonomic dysfunction [16].

Regarding blood pressure phenotypes, it was shown that most of studied diabetic patients were categorized as non-dippers (47.9%) followed by 27.1% classified as dipper, 20.8% were reverse dipper and only 4.2% were extreme dipper. There was a statistically significant relation of blood pressure phenotypes especially reverse dipper and non-dipper with occurrence of decompensated CHF. This is in agreement with a cross-sectional study, where eligible patients with T2 DM underwent 24- hour ambulatory BP measurements under standardized conditions, resulted that non-dipping and nocturnal systolic hypertension were prevalent in 55% and 57% patients, respectively where nocturnal systolic hypertension had a significant association with composite microvascular complications independent of daytime systolic BP control (OR= 1.72(CI 1.41-4.25) [12]**.** Similarly, **Cardoso *et al.*** [14] reported that 53% had non-dipper pattern. Conversely, a cross-sectional data from patients with type 2 diabetes, aged 55–66 years demonstrated that 65.3% were classified as dippers and 34.7% had a nocturnal non-dipping pattern [17]**.**

The prevalence of the non-dipper pattern in diabetes reported in the medical literature is highly inconsistent, ranging from 30% to 73%, possibly because of disparities between the different studies in the populations studied (treated vs untreated patients, patients with different clinical severity, etc.), relatively small sample sizes, the use of a single and therefore poorly reproducible 24 h ABPM, and inadequate definition of the activity and resting periods using pre-defined time intervals for all the patients studied [9, 18].

Non-dipping status (< 10% decrease) and reverse-dipping status (when the average nighttime BP is greater than the daytime BP) are associated with worse outcomes in adults with type 2 diabetes [19]**.**

Ambulatory BP is particularly important for the management of hypertension in diabetic patients, since hypertension is a major risk factor for cardiovascular disease in these patients. Diabetic patients are more likely to be non-dippers, and therefore office BP measurements do not reflect the real cardiovascular risk [20].

CONCLUSION

Ambulatory blood pressure monitoring is linked to the development of cardiovascular problems from diabetes and diabetic retinopathy at a mean ambulatory BP level of less than 122.5/70.5 mmHg.

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