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Circadian variation of blood pressure obtained by ambulatory blood pressure monitoring in hypertensive individuals in Mexico City

Comportamiento circadiano de la presión arterial obtenida por monitoreo ambulatorio de presión arterial en individuos hipertensos en la Ciudad de México

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Palabras clave:
ritmo circadiano, presión arterial, hipertensión, monitoreo ambulatorio de presión.

ABSTRACT

Introduction: the circadian rhythm of blood pressure has been associated with various vascular and metabolic effects contributing to increased mortality among individuals with hypertension. Thus, elucidating relevant variables could enhance understanding and potentially decrease mortality rates in this population. **Objective:** this retrospective study aimed to determine the circadian pattern of blood pressure in hypertensive individuals using Ambulatory Blood Pressure Monitoring (ABPM) in Mexico City. **Material and methods:** an observational, descriptive, cross-sectional study was conducted by reviewing PDF files of ABPM reports from a cardiology outpatient clinic. The study encompassed all individuals undergoing follow-up at a specialized clinic in Mexico City. **Results:** among the 648 patients included in the study, the physiological dipper pattern, considered normal, was present in 72.6% of hypertensive individuals. Additionally, 19% exhibited a non-dipper pattern, 22.5% displayed an inverse dipper pattern, and 12% showed an extreme dipper pattern. No significant differences were observed between genders. **Conclusions:** the circadian rhythm of blood pressure, characterized by the physiological dipper pattern, was observed in only 72.6% of hypertensive individuals, even among those with normal average blood pressure. The inverse dipper pattern represented the second most prevalent group at 22.5%. Minor differences were noted between men and women regarding the timing of peak hypertension.

RESUMEN

Introducción: *el comportamiento circadiano de la presión arterial se ha vinculado a múltiples efectos vasculares y/o metabólicos que incrementan la mortalidad en individuos hipertensos, por lo que el esclarecimiento de las variables relacionadas podría ayudar al mejor entendimiento, con el objetivo de fortalecer el descenso de la mortalidad de pacientes portadores de hipertensión arterial.* ***Objetivo:*** *establecer el comportamiento circadiano de la presión arterial en individuos hipertensos mediante la utilización del monitoreo ambulatorio de presión arterial (MAPA) en la Ciudad de México.* ***Material y métodos:*** *estudio observacional, retrospectivo, descriptivo y transversal, se realizó la revisión de los archivos en formato PDF de los reportes de MAPA realizados de la consulta externa de cardiología, se incluyeron todos aquellos individuos en seguimiento en una clínica de especialidades de primer contacto en la Ciudad de México.* ***Resultados:*** *de un total de 648 pacientes se encontró que el fenómeno dipper fisiológico considerado como normal ocurre en 72.6% de la población hipertensa, mientras que el no dipper ocurre en 19%, dipper inverso en 22.5% y finalmente el dipper extremo ocurre en 12% del total de la población. No existen diferencias significativas entre hombres y mujeres.* ***Conclusiones:*** *el comportamiento circadiano de la presión arterial considerado como fisiológico dipper sólo ocurre en 72.6% de las personas hipertensas aun en individuos con cifras de presión arterial promedio normal. El dipper inverso es el segundo grupo con mayor valor porcentual en la población estudiada con 22.5% de la población. Existen pequeñas diferencias entre hombres y mujeres con respecto al horario de mayor hipertensión.*

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Abbreviations:
ABPM = Ambulatory Blood Pressure Monitoring.
BMI = Body Mass Index.

INTRODUCTION

Blood pressure levels are intricately linked to various pathophysiological phenomena that underlie multiple diseases, predominantly of vascular origin. Investigating the circadian behavior of blood pressure holds promise in elucidating diagnostic and treatment challenges within the hypertensive population of Mexico City. Non-communicable diseases, particularly arterial hypertension, continue to dominate global mortality statistics, likely owing to their multifaceted modifiability. In Mexico, the prevalence of hypertension, as defined by the criteria established in the 2014 «Eighth Joint National Committee (JNC 8)»[1] American Hypertension Guidelines, was documented in the National Health Survey (ENSANUT) of 2022. The survey revealed a diagnosis of systemic arterial hypertension in 43.9% of adults, with a prevalence of 29.4% among individuals aged over 20, slightly higher in males at 31.3% and females at 27.7%.[2] However, some experts argue that these figures underestimate the true prevalence, prompting methodological refinements in various statistical trials better to capture the incidence and prevalence of arterial hypertension. This challenge was exemplified in 2005 by the «*Re-encuesta Nacional de Hipertensión Arterial (RENAHTA): Consolidación Mexicana de los Factores de Riesgo Cardiovascular. Cohorte Nacional de Seguimiento*» which, unfortunately, failed to demonstrate significant deviations from the earlier findings of ENSANUT.[3]

The complexities of hypertension extend beyond frequency and prevalence to encompass diagnostic criteria and optimal follow-up and treatment paradigms, as evidenced by a study published by García Zamora et al. In their analysis of the «PROSPERO» registry, encompassing four studies involving 29,820 patients with intensive arterial hypertension treatment, they found that despite intensive treatment, mortality rates remained unaltered. Specifically, the relative risk (RR) was found to be 0.89 with a 95% Confidence Interval (CI 95%): 0.68-1.07; p = 0.16, with no impact on total mortality (p = 0.45) for any of the evaluated causes.[4]

Currently, the established indications for Ambulatory Blood Pressure Monitoring (ABPM) remain relatively unchanged and fundamentally address three conditions.[5] Firstly, patients with elevated arterial hypertension readings in outpatient office settings termed the «white coat phenomenon». Secondly, individuals with blood pressure readings within the normal range during office visits but with a history of elevated pressure during daily activities are known as «masked hypertension».[6] Finally, continuous blood pressure monitoring is recommended to evaluate the nocturnal blood pressure behavior in cases of «isolated nocturnal hypertension».[7,8] However, the pathogenic aspects of the latter indication remain poorly understood,[9] as evidenced by various conditions associated with the nocturnal behavior of arterial hypertension, such as periodic limb movement. It seems that sympathetic discharges are the etiological cause with greater support. One study aimed at demonstrating the relationship between arterial hypertension and periodic limb movement took place in Cordova, a province of Spain. In this study, 11 individuals with a previous diagnosis of periodic limb movement were compared with seven control individuals using polysomnography. The patients with periodic limb movement had an average age of 57 ± 14 years, whereas the control group had an average age of 64 ± 6 years. However, the age difference between the two groups was not statistically significant (p = 0.284).

Contrary to the expected hypothesis, the results showed intriguing findings regarding blood pressure. The average blood pressure obtained over 24 hours by ambulatory blood pressure monitoring was lower in the periodic limb movement group compared to the control group. Specifically, the systolic pressure was 114.2 ± 11 mmHg in the periodic limb movement group versus 123 ± 11 mmHg in the control group, with a p-value of 0.095. Similarly, the diastolic pressure was 65.7 ± 5 mmHg in the periodic limb movement group and 74.4 ± 11 mmHg in the control group, with a p-value of 0.027.[10] These

unexpected findings raise questions about the underlying mechanisms and their implications for hypertension management. This prompts further investigation into whether circadian patterns of blood pressure behavior are linked to extravascular complications.[11] Multiple studies have sought to address this question. In 2018, a study in Cuba attempted to establish a link between the circadian behavior of blood pressure and specific conditions like left ventricular hypertrophy and insulin resistance among 46 hypertensive patients. Surprisingly, the initial hypothesis suggesting a direct relationship between insulin resistance and blood pressure behavior was not supported by the study's findings.

Nevertheless, the study shed light on the nocturnal behavior of blood pressure, uncovering significant anomalies. Among the participants, 58% exhibited abnormal nocturnal blood pressure patterns. This included 15% with the non-dipper phenomenon, 7% with Extreme dippers, and an additional 5% with Reverse dippers.[12] These findings underscore the existence of potential independent vascular risk factors within the hypertensive population, although their precise nature remains unclear.

MATERIAL AND METHODS

In an observational, retrospective, descriptive, and cross-sectional study, PDF files of Ambulatory Blood Pressure Monitoring (ABPM) reports obtained from the cardiology outpatient clinic were meticulously reviewed. This encompassed all individuals undergoing follow-up in a specialized first-contact clinic in Mexico City, dedicated to the control and monitoring of arterial hypertension, as well as the management of various cardiovascular pathologies, receiving referrals from health centers across the city. Evaluation of accepted indications for ABPM in the cardiology clinic was not conducted, adhering strictly to the prevailing normative criteria for specialty outpatient care in the institution.

Between June 1, 2018, and October 15, 2023, ambulatory blood pressure monitoring was conducted using a Schiller model BR 102 plus device. The device was programmed to record blood pressure at 30-minute intervals during daytime hours from 08:00 to 22:00 and during nighttime hours from 22:00 to 08:00 the following day. The decision to perform ABPM was solely based on clinical criteria and the follow-up protocol established by the responsible cardiologist.

A comprehensive database was constructed from the total ABPM records in PDF format, capturing essential variables such as age, sex, height, weight, body mass index (BMI), overall blood pressure averages, daytime, and nighttime blood pressure averages, as well as maximum blood pressure readings at various times and the corresponding hours of those peaks. An analysis of variance was conducted for multiple quantitative variables, and a Student's t-test was employed to determine differences between groups in independent variables, with a significance level set at $p < 0.05$.

RESULTS

A total of 768 ABPM reports obtained between June 1, 2018, and October 15, 2023, were scrutinized. However, 42 studies were excluded due to incomplete information for analysis. Among these, 26 lacked nighttime blood pressure recordings during ABPM, eight lacked weight and height measurements, and eight lacked age records in the ABPM report, rendering them unsuitable for analysis. Additionally, 78 ABPM studies performed to establish the diagnosis of arterial hypertension were set aside, constituting 10% of the total sample, as these patients were suspected to have the «white coat phenomenon and masked hypertension».

The groups of patients with previously diagnosed hypertension and established prior treatment totaled 648 individuals, who were further subdivided into two groups: those with information on office blood pressure measurements for comparison with ABPM averages.

Of the 648 studies conducted on hypertensive patients in follow-up, 425 corresponded to women (65.5% of the total records), while 223 corresponded to men (34.5%). Multivariate analysis revealed four

variables with statistically significant differences when comparing men and women *(Table 1)*.

1. The average body mass index for men was 28.77, and for women was 28.49, with a p-value of 0.03.
2. The time of maximum diastolic pressure for men was at 12:59 hours, and for women was at 12:23 hours, with a p-value of 0.0003.
3. The time of maximum nocturnal systolic pressure for men was at 21:56 hours, and for women was at 22:22 hours, with a p-value of 0.0001.
4. The time of maximum nocturnal diastolic pressure for men was at 22:39 hours, and for women was at 21:55 hours, with a p-value of 0.0004.

The remaining variables showed no statistical significance. Notably, no significant differences were found in the subgroup of patients with office blood pressure

Table 1: Comparative multivariate analysis of males and females.

	Males	Females	p
Age	65.03	64.13	0.3985
Weight	78.95	65.43	91.3993
Height	165.13	154.62	55.2257
BMI	28.77	28.49	0.0374
Global SP	122.53	121.66	0.3805
Global DP	73.61	68.67	12.1982
Global MAP	93.47	91.60	1.7500
Diurnal SP	124.36	123.32	0.5370
Diurnal DP	74.75	70.15	10.5721
Diurnal MAP	94.68	93.04	1.3551
Nocturnal SP	118.60	116.42	2.3760
Nocturnal DP	69.97	63.77	19.2136
Nocturnal MAP	89.62	87.22	2.8794
Reduction in SP	4.82	5.44	0.1975
Reduction in DP	6.09	8.88	3.8988
Maximum SP	154.08	154.99	0.4140
Time of maximum SP	12:33:48	12:50:48	6.9686
Maximum DP	100.75	98.95	1.6126
Time of maximum DP	12:59:12	12:23:18	0.0003
Maximum diurnal SP	152.90	156.34	5.9316
Time of maximum diurnal SP	12:58:07	13:02:11	3.9878
Maximum diurnal DP	99.68	97.76	1.8376
Time of maximum diurnal DP	13:33:33	13:37:20	3.4467
Maximum nocturnal SP	137.52	135.58	1.8890
Time of maximum nocturnal SP	21:56:55	22:22:56	0.0001
Maximum nocturnal DP	86.31	80.42	17.3725
Time of maximum nocturnal DP	22:39:56	21:55:46	0.0004
Mean HR	69.66	71.79	2.2714
Maximum HR	104.32	109.22	11.9851
Minimum HR	51.93	54.36	2.9567
In office SP	135.02	138.01	4.4588
In office DP	76.59	69.98	21.8460

BMI = Body Mass Index. DP = Diastolic Pressure. HR = Heart Rate. MAP = Mean Arterial Pressure. SP = Systolic Pressure.

Table 2: Nocturnal blood pressure variability: stratified by sex.

	Male N = 223 n (%)	Female N = 425 n (%)	Both N = 648 n (%)	p (T ≤ T) two-tailed
Inverse dipper –1 a –20%	53 (23.7)	93 (21.8)	146 (22.5)	0.3755
Non-dipper 0%	7 (3.1)	12 (2.8)	19 (2.9)	0.4842
Dipper 1 A 20%	159 (71.3)	312 (73.4)	471 (72.6)	0.0873
Extreme dipper 20%	4 (1.7)	8 (1.8)	12 (1.8)	0.4873

readings compared to the average values obtained in ABPM.

The circadian rhythm of systolic blood pressure allowed patients to be categorized into four distinct groups based on their nocturnal blood pressure behavior. These groups include:

1. **Inverse dipper:** patients exhibiting an increase in blood pressure during the night ranging from 0 to 20%.
2. **Non-dipper:** patients with no significant modifications in blood pressure values during nighttime.
3. **Dipper:** patients displaying a nocturnal reduction in systolic blood pressure of up to 20%.
4. **Extreme dipper:** patients with a substantial nocturnal reduction in systolic blood pressure exceeding 20%.[13]

Statistical analysis revealed small but significant differences in blood pressure behavior between men and women, with a calculated p-value of 0.059. Specifically, it was observed that 71.3% of women exhibited a dipper response, compared to 73.4% of men. The next most common group consisted of patients with inverse dipper patterns, accounting for 23.7% of women and 21.8% of men. Non-dipper behavior was less prevalent, accounting for 3.1% of men and 2.8% of women. Additionally, extreme dipper patterns were found in 1.7% of men and 1.8% of women. However, none of these individual percentages demonstrated statistically significant differences between genders *(Table 2)*.

In the gender-based analysis, notable disparities were observed in systolic and diastolic blood pressure values, primarily revolving around the timing of maximum peaks of hypertension. Additionally, a slight discrepancy in body mass index was identified between the inverse dipper and non-dipper groups, with values of 29.04 and 29.06, respectively, yielding a statistically significant p-value of 0.00018. Among men exhibiting dipper and extreme dipper responses, a marginal age difference was noted, with the first group averaging 64.05 years and the latter 64.5 years, resulting in a p-value of 0.09.

In cases where ABPM served as a diagnostic tool for arterial hypertension, no significant demographic distinctions were observed among the 79 individuals studied, comprising 58 women and 20 men. However, statistically significant differences were evident in the timing of maximum blood pressure values. For women, the hour with the highest systolic pressure was approximately 12:53 pm, while for men, it occurred around 2:09 pm, with a p-value of 0.001. Similarly, the hour of maximum nocturnal diastolic hypertension for women was recorded at 11:08 pm, whereas for men, it was at 10:10 pm, with a p-value of 0.0008. Notably, despite these temporal variations, average blood pressure values remained quite similar across genders.

The average blood pressure behavior among hypertensive patients in the study was slightly higher in men, with readings of 122/73 mmHg compared to 121/68 mmHg in women. During daytime hours, men exhibited an average blood pressure of 124/74 mmHg, whereas women recorded 123/70 mmHg. Nighttime blood pressure averaged 118/69 mmHg in men and 116/63 mmHg in women. Although men displayed a slightly greater reduction in systolic

blood pressure (4.8 mmHg) and diastolic pressure (6 mmHg) during nighttime, these differences did not reach statistical significance by gender. Moreover, no notable disparities were found between office blood pressure and average ABPM readings for hypertension diagnosis, as illustrated in *Table 3*.

DISCUSSION

The impact of abnormal circadian blood pressure patterns on vascular and metabolic diseases has been extensively documented in various studies, hinting at a common underlying etiology.[14] A recent systematic review delved into the cardiometabolic implications of circadian rhythm disruptions in the North American population, particularly associated with occupational factors. This review explored the interplay between meal timing, work schedules, and their correlation with body mass index, diabetes prevalence, hypertension, and cerebrovascular diseases. The findings revealed alarming statistics, including a 23% prevalence of obesity and overweight, a 14% increase in diabetes mellitus, and a metabolic syndrome prevalence ranging from 11% to 35% among individuals with disrupted circadian rhythms. Notably, hypertension exhibited a 10% prevalence but with a staggering 30% elevated risk of occurrence, underscoring the profound impact of circadian rhythm changes on health.[15]

The daily patient record was not consulted for the preparation of this study. However, the significance of this study potentially lies in its revelation that blood pressure behavior may deviate from expected norms even among individuals without significant changes in their daily activities. Surprisingly, only 71.5% of men and 73.4% of women exhibited a normal blood pressure pattern (dipper) despite their average blood pressure values falling within the normal range. Various efforts have been made to elucidate these phenomena, such as the research published by Murray E.C. et al., which investigated vascular response phenotypes in early hypertension. Their study, involving 73 newly diagnosed hypertensive individuals without standard treatment, compared with a control group of 79 hypertensive individuals matched for demographic characteristics, found that all newly diagnosed hypertensive individuals displayed vascular stiffness but not endothelial dysfunction.[16] This finding aligns with previous multicenter studies associating the duration of hypertension with vascular intima necrosis and greater endothelial dysfunction.

However, our study reveals gender-specific behavioral differences among individuals without a prior hypertension diagnosis. This aspect is particularly noteworthy as the timing of peak hypertension could unveil underlying factors yet to be fully understood between men and women. Despite similar systolic and diastolic pressure values, distinct differences in the times of peak hypertension were observed. These findings underscore the complexity of blood pressure regulation and the need

Table 3: Summary of blood pressure dynamics.

Study groups	Overall global blood pressure (mmHg)	Average diurnal blood pressure (mmHg)	Average nocturnal blood pressure (mmHg)	Systolic/diastolic reduction (%)
Overall blood pressure dynamics (M: 223/F: 435)	M: 122/73 F: 121/68	M: 124/74 F: 123/70	M: 118/69 F: 116/63	M: 4.8/6 F: 5.4/8.8
ABPM in hypertension diagnosis (M: 20/F: 58)	M: 121/72 F: 124/75	M: 123/74 F: 126/77	M: 112/64 F: 116/68	M: 7.3/11.1 F: 7.9/12.6
In office blood pressure records (M: 155/F: 314)	M: 123/74 F: 121/68	M: 125/75 F: 123/70	M: 118/69 F: 111/61	M: 4.5/5.9 F: 5.3/9.0

ABPM = Ambulatory Blood Pressure Monitoring. F = Female. M = Male.

Table 4: Individuals with indicated ambulatory blood pressure monitoring for hypertension diagnosis without prior diagnosis of arterial hypertension.

	Female	Male	Variance
N	58	20	722.00
Age	52.05	45.5	21.46
Weight	75.29	82.2	23.85
Height	155.20	166.4	62.64
BMI	30.30	29.65	0.20
Global SP	121.17	124.3	4.89
Global DP	72.70	75.35	3.49
Global MAP	93.79	95.2	0.98
Durnal SP	123.08	126.8	6.89
Diurnal DP	74.60	77.9	5.43
Diurnal MAP	95.74	97.5	1.54
Nocturnal SP	112.12	116.55	9.80
Nocturnal DP	64.98	68.45	6.01
Nocturnal MAP	85.53	87.75	2.45
SP reduction	7.37	7.9	0.13
DP reduction	11.18	12.6	0.99
Maximum SP	151.46	149.5	1.93
Time of maximum SP	13:12:40	14:33:18	0.00
Maximum DP	103.67	103.05	0.19
Time of maximum DP	13:39:00	13:27:00	0.00
Maximum diurnal SP	153.75	149.3	9.93
Time of maximum diurnal SP	12:53:43	14:09:18	0.00
Maximum diurnal DP	102.55	101.85	0.24
Time of maximum diurnal DP	14:16:22	12:57:00	0.00
Maximum nocturnal SP	129.05	134.15	12.99
Time of maximum nocturnal SP	13:03:37	12:55:30	0.00
Maximum nocturnal DP	81.10	84.7	6.46
Time of maximum nocturnal DP	11:08:48	10:10:30	0.00
Mean HR	73.13	71.95	0.70
Maximum HR	110.75	112.65	1.78
Minimum HR	54.75	52.6	2.32
In office SP	132.03	132.45	0.08
In office DP	71.96	79.45	28.04

BMI = Body Mass Index. DP = Diastolic Pressure. MAP = Mean Arterial Pressure. SP = Systolic Pressure.

for further investigation into gender-specific mechanisms influencing blood pressure patterns *(Table 4)*.

CONCLUSION

The circadian behavior of blood pressure, characterized by the physiological dipper pattern, was observed in only 72.6% of hypertensive individuals, even among those with normal average blood pressure values. The inverse dipper pattern emerged as the second most prevalent group in the studied population, comprising 22.5% of individuals. Minor disparities were noted between men and women regarding the timing of peak hypertension.

The group of researchers is developing work on the behavior of obstructive sleep apnea in cardiovascular disease, which could further enrich knowledge about this disease and its growing prevalence.

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Declaration of confidentiality and patients consent: the authors declare they have followed their workplace protocols for using patient data. Also, they certify that the patient has received sufficient information and has given written informed consent for his/her/their images and other clinical information to be reported in the journal, without names or initials, to protect the right to privacy.

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