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Sympathetic Hyperactivity and Its Relationship with Obesity in Diabetic Hypertensive Patients: A Study of 122 Cases

Khaoula Bourzeg [a*], Rim Zerhoudi [a], Joumana El massrioui [a], Abdelkarim Aityahya [a], Mohamed El Jamili [a], Saloua El Karimi [a] and Mustapha El Hattaoui [a]

[a] Cardiology Department, Mohammed VI University Hospital, Marrakesh, Morocco.

Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Introduction: The circadian rhythm of heart rate reflects the balance of activity in the autonomic nervous system. The relationship between sympathetic activity and the presence of hypertension (HTN) or diabetes has been a subject of significant study for many years.
Methods and Results: We conducted a descriptive retrospective study including 122 diabetic and hypertensive patients who underwent ambulatory blood pressure monitoring over a period of 4

**Corresponding author: E-mail: khaoulabour95@gmail.com;*

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years. The mean age was 60.9 ± 13.3 years, ranging from 19 to 95 years. Women comprised 62.3% of the sample. Among the patients, 31.97% were obese and 44.26% were overweight. The average heart rate was 69.50 ± 8.6 beats per minute. A similar profile to the reverse dipper blood pressure pattern, defining sympathetic hyperactivity, was observed in our series. In bivariate analysis, obesity was present in 43.75% of patients with sympathetic hyperactivity compared to 41.56% in those with normal circadian rhythm (p >= 0.999). This finding was reinforced in multivariate analysis, which showed a significant correlation between body mass index (BMI) and sympathetic hyperactivity (OR=0.582 [0.232; 1.46], p=0.7297).

Discussion: Insulin resistance is associated with obesity, particularly central obesity. Recent studies have shown the involvement of insulin resistance in the development of hypertension (HTN), which explains the high rate of obese individuals in our series, although this may not be directly related to sympathetic hyperactivity. Currently, the role of sympathetic dysfunction in the genesis or exacerbation of cardiovascular and metabolic disorders is well-established. Research has demonstrated the influence of circadian rhythm on gene and protein expression in cardiac cells, affecting cardiac contraction and electrophysiology. These findings underscore the importance of always exploring the autonomic nervous system in the etiological assessment of metabolic syndrome broadly, and specifically in hypertension and diabetes.

Keywords: The circadian rhythm; obesity; hypertension; diabetes; sympathetic hyperactivity.

1. INTRODUCTION

The circadian rhythm of heart rate reflects the balance of the autonomic nervous system activity. The relationship between sympathetic activity and the presence of hypertension or diabetes has been a significant subject of study for many years. Indeed, a significant correlation between sympathetic hyperactivity and various cardiovascular or metabolic risk factors (BMI, waist circumference, blood pressure, heart rate, triglycerides, HDL cholesterol) has been established.

2. MATERIALS AND METHODS

We conducted a retrospective descriptive study involving 122 diabetic and hypertensive patients who underwent ambulatory blood pressure monitoring over a period of 4 years. This was a descriptive, retrospective study with cross-sectional data collection from the MORTARA ambulo 2400 Holter registry at the Cardiology and Vascular Diseases Unit of the Mohammed VI University Hospital in Marrakech. We collected ambulatory blood pressure monitoring data from all diabetic patients from January 2019 to December 2022, covering a 4-year period. The variables studied included demographic data (age, sex), clinical data such as diabetes history, BMI, blood pressure, heart rate, and dipper profile. Quantitative variables were represented as mean, standard deviation, and extremes. Bivariate analysis was presented in tabular form, using the Mann-Whitney test to compare means of quantitative variables, and Fisher's exact test or Chi-square test for qualitative variables.

A multivariate linear logistic regression analysis was used to assess the relationship between BMI (the variable of interest) and sympathetic hyperactivity. Data multicollinearity was checked using the Belsley-Kuh-Welsch technique. Heteroscedasticity and normality of results were evaluated using the Breusch-Pagan test and the Shapiro-Wilk test, respectively. A p-value of 0.05 was considered statistically significant. Statistical analysis was conducted using Easy Med Stat software (version 3.21.5; www.easymedstat.com).

3. RESULTS

During our study period, ambulatory blood pressure monitoring was conducted on a total of 122 diabetic patients. The average age was 60.9 ± 13.3 years with a range from 19 to 95 years. 71% of our patients were over 60 years old. The sex ratio favored women in our series, accounting for 62.3%.

In our study population, type 2 diabetic patients were predominant at 95.1%, while type 1 diabetics accounted for 4.9%. A history of hypertension was found in 75.4% of our series.

Moderate obesity accounted for 25.4% (31), overweight for 44.3% (54), morbid obesity for 7.4% (9), and 22.9% (28) had a normal BMI.

Table 1. Patient dipper profile

Dipper profile	Effectif	Pourcentage
Dipper	24	19,7%
Non-dipper	77	63,1%
Reverse dipper	18	14,7%
Hyperdipper	3	2,5%

Table 2. Heart rate profile of patients studied

		DT/HTA+ N (%)	DT/HTA-N (%)
Heart rate	**<75**	55 **(75,3)**	34 **(69,4)**
	75-80	11 **(15,1)**	7 **(14,3)**
	≥80	7 **(9,6)**	8 **(16,3)**

The average heart rate was 69.5 ± 8.5 bpm with extremes ranging from 32 to 123 bpm. 15 patients (12.3%) had a heart rate over 80 bpm, 18 patients (14.7%) had a heart rate between 75 and 80 bpm, and 89 patients (73%) had a heart rate below 75 bpm. A similar profile to the reverse dipper defining sympathetic hyperactivity in our series was found in 20 patients (16.4%).

In bivariate analysis, obesity was observed in 43.75% of patients with sympathetic hyperactivity compared to 41.56% in patients with a normal circadian rhythm (p >= 0.999).

This observation was reinforced in multivariate analysis, which showed a significant correlation between BMI and sympathetic hyperactivity (OR=0.582 [0.232; 1.46], p=0.7297).

4. DISCUSSION

Obesity is defined by the WHO as an abnormal increase in total fat mass, specifically an increase in adipocyte size, commonly subdivided into two subcategories: abdominal (central) obesity and subcutaneous (peripheral) obesity [1]. Lifestyle, geographical variations, and cultural characteristics are factors that can influence the association between health culture and nutritional status [2].

Also, obesity-related hypertension is defined as hypertension accompanied by obesity. It accounts for 65% to 75% of essential hypertension, is characterized by increased salt sensitivity and is frequently the cause of resistant hypertension [3].

diabetes and hypertension are closely interlinked because of similar risk factors, such as endothelial dysfunction, vascular inflammation, arterial remodelling, atherosclerosis, dyslipidemia, and obesity [4].

Due to the significant role of the sympathetic nervous system (SNS) in mobilizing energy reserves and regulating food intake, it has been suggested that an imbalance in this system may be linked to the development of obesity. Indeed, the study by Arone et al. indicated that overeating tends to increase SNS activity, whereas under-eating or fasting tends to decrease it [5]. Additionally, Grassi et al. demonstrated that normotensive obese patients exhibit significantly higher sympathetic activity compared to lean subjects. Among obese individuals, those with central obesity show higher sympathetic hyperactivity than those with peripheral obesity [6].

A longitudinal study conducted among young non-obese Japanese individuals who were either normotensive or borderline hypertensive showed that an increase in plasma noradrenaline (NA) levels precedes the onset of hyperinsulinemia and elevated blood pressure [7,8]. This supports the hypothesis that sympathetic hyperactivity may be a cause of insulin resistance development.

The role of sympathetic dysfunction in the onset or worsening of cardiovascular and/or metabolic disorders is currently well-established.

Thus, several studies have demonstrated that the circadian rhythm influences the gene and proteomic expression of cardiac cells, which has implications for the contraction and electrophysiology of the heart [9,10]. These results encourage systematic exploration of the autonomic nervous system in the etiological evaluation of metabolic syndrome in general, as well as arterial hypertension and diabetes in particular.

5. CONCLUSION

Multiple studies have highlighted sympathetic hyperactivity in the early stages of metabolic

syndrome. For patients with diabetes and obesity, ambulatory blood pressure monitoring (ABPM) should be performed at least once to better stratify the risk of hypertension. Early detection of nocturnal hypertension is crucial for preventing cardiovascular events.

DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc) and text-to-image generators have been used during writing or editing of manuscripts.

CONSENT

As per international standards or university standards, patient(s) written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

As per international standards or university standards written ethical approval has been collected and preserved by the author(s).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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