

Hydration status and hypertension in occupational health service users

Estado de hidratação e hipertensão em utilizadores de um serviço de saúde ocupacional

Maria Francisca Pereira de Melo Gomes

**ORIENTADO POR: PROF^ª. DOUTORA PATRÍCIA PADRÃO
COORIENTADO POR: PROF. DOUTOR JOÃO BREDAS E MESTRE ANTÓNIO TEIXEIRA**

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Abstract

Background: Hypohydration is responsible for deleterious impacts on physiological functions, and it seems to be linked with cardiovascular diseases, the primary cause of death and disability in the WHO European Region. This study aims to quantify the association between hypohydration and hypertension, according to sociodemographic and lifestyle characteristics. **Methods:** Baseline sociodemographic, lifestyle and clinical data from the randomized control trial iMCSalt, including 114 occupational health service users were analysed. Urinary biomarkers were assessed through a 24h-urine collection and volume, osmolality, creatinine, sodium and potassium were quantified. Free Water Reserve was used to assess hydration status. A hypertension diagnosis was made by the responsible doctor. A multivariable binary logistic regression model, adjusted for confounders, was used to estimate the association between hydration status and hypertension. **Results:** Among the 107 (51.4 % women) eligible participants, hypohydration was found in 30.9% of women and 25.0% of men, whereas 29.1% of women and 50.0% of men were reported hypertensive. Hypohydration was associated with a 5-fold increased risk of hypertension, in women (adjusted model: OR=5.423; 95% CI: [1.217-24.176]). No such association was observed in men. **Conclusions:** Hypohydration is suggested to significantly increase the risk for hypertension, in women, but further research is needed to better understand the mechanisms behind this association. Raising people's awareness of the importance of hydration at all ages is recommended.

Keywords: hydration status, hypohydration, hypertension, cardiovascular diseases, free water reserve

Resumo

Contexto: O estado de hipohidratação prejudica as funções fisiológicas e parece estar associada ao desenvolvimento de doenças cardiovasculares, a principal causa de morte e incapacidade na Região Europeia da Organização Mundial de Saúde. Este estudo pretende quantificar a associação entre hipohidratação e hipertensão, considerando características sociodemográficas e de estilo de vida.

Metodologia: Dados sociodemográficos, clínicos e de estilo de vida, recolhidos no momento inicial do ensaio de controlo randomizado iMCSalt, provenientes de 114 utilizadores de um serviço de saúde ocupacional, foram analisados. Biomarcadores urinários, como volume, osmolalidade, creatinina, sódio e potássio foram obtidos através de uma colheita de urina de 24h; o estado de hidratação através do método Free Water Reserve; e o diagnóstico de hipertensão foi feito pelo médico. Um modelo de regressão logística binária multivariada, ajustado para os confundidores, foi usado para estimar a associação entre o estado de hidratação e hipertensão. **Resultados:** Dos 107 (51,4% mulheres) participantes elegíveis, das mulheres e homens, respetivamente, 30,9% e 25,0% estavam hipohidratados, e 29,1% e 50,0% eram hipertensos. A hipohidratação associou-se a um risco 5 vezes superior de hipertensão, nas mulheres (modelo ajustado: OR=5,423; 95% CI: [1,217-24,176]). Nos homens não se verificou associação. **Conclusão:** A hipohidratação parece aumentar significativamente o risco de hipertensão em mulheres, mas mais estudos são necessários para compreender melhor estes resultados. Recomenda-se a consciencialização sobre a importância da hidratação em todas as idades.

Palavras-chave: estado de hidratação, hipohidratação, hipertensão, doenças cardiovasculares, reserva de água livre

List of abbreviations

AVP	Arginine vasopressin
BMI	Body mass index
CI	Confidence intervals
EFSA	European Food Safety Authority
FWR	Free water reserve
OR	Odds ratio

Contents

Abstract	ii
Resumo	iii
List of abbreviations	iv
Introduction	1
Aim.....	2
Participants and Methods	3
<i>Study design and sampling</i>	3
<i>Sociodemographic, Lifestyle and Clinical Data</i>	3
<i>Urinary Biomarkers and Hydration Status</i>	4
<i>Data Analysis</i>	5
Results.....	6
Discussion	10
Conclusion	15
References.....	16

Introduction

Water is the most abundant component of the human body, accounting for about 60% of the body mass, depending on the individual's body composition⁽¹⁾. It plays a vital role in various physiological processes including metabolism, substances' transport across membranes, cellular balance maintenance, body temperature regulation, and circulatory function⁽²⁾. Therefore, the preservation of water balance is crucial for human survival. As it is constantly being challenged by urinary, sweat, fecal, and other insensible losses⁽³⁾, and as metabolic water production only compensates for a small part of them, water intake is fundamental to well-being^(3, 4). However, among European countries, 5% to 35% of the population still presents inadequate water intake⁽⁵⁾.

Generally, despite large discrepancies in daily water consumption, the human body can maintain these variations within a narrow range^(3, 4) through highly sensitive osmotic mechanisms that activate on one hand the sensation of thirst to stimulate fluid intake and, on the other hand, to reduce water loss, the release of arginine vasopressin (AVP) on the renal collecting ducts, via vasopressin V2 receptors, diminishing renal water excretion⁽³⁾. However, despite being tightly regulated, short-term states of hyperhydration or hypohydration can be faced⁽⁴⁾. In fact, about 16.3% of Portuguese older adults are either hypohydrated or at risk of hypohydration⁽⁶⁾.

Dehydration refers to the process of body water loss⁽⁴⁾, resulting in hypohydration when acute or chronic⁽⁷⁾. Evidence suggests that sudden and significant hypohydration can seriously impact physiological functions, namely compromise cognitive function, alter thermoregulation mechanisms, reduce

physical performance, worsen mood, and impair glycemic regulation⁽⁷⁾. In addition, chronic systemic hypohydration is suggested to be linked to cardiovascular events such as stroke, coronary heart disease, venous thromboembolism, and hypertension⁽⁷⁾.

High blood pressure is the leading preventable risk factor for cardiovascular diseases such as stroke, heart attack, heart disease⁽⁸⁾ and myocardial infarction⁽⁹⁾, as well as kidney failure⁽¹⁰⁾. It plays a significant role in early mortality, cognitive decline, physical disability, and the financial burden on healthcare systems⁽¹⁰⁾, being responsible for an estimated 9.4 million deaths annually⁽¹¹⁾. In the WHO European Region, cardiovascular diseases are the primary cause of death, premature mortality, and disability⁽⁹⁾. In Portugal, not only is stroke the leading mortality cause but also is high blood pressure the third major mortality and disability risk factor⁽¹²⁾.

Despite the mentioned importance for health, research on the association between short and long-term hypohydration, blood pressure regulation and vascular function is limited⁽⁷⁾.

Aim

The present study aimed to quantify the association between hypohydration and hypertension, in a sample of Portuguese adults, according to sociodemographic and lifestyle characteristics.

Participants and Methods

Study design and sampling

The current study was undertaken considering data collected from the randomized controlled trial iMCSalt, which aimed to assess the impact of an intervention to reduce salt consumption, in occupational health service users from the University of Porto⁽¹³⁾.

The data analysed in this paper was collected from the evaluations performed at the baseline moment. The following participants were considered eligible: adults (>18 years old), individuals who had home-cooked meals frequently (more than 4 days a week and at least 3 Sundays per month) and who reported motivation to control dietary salt consumption. Participants who were pregnant; hypotensive; had an active infection that impacts renal function, kidney disease, urinary incontinence, acute coronary syndrome, severe liver disease or heart failure; were members of the faculty that promoted the study (i.e., Faculty of Nutrition and Food Sciences); did not used salt for cooking, and/or whose 24h urine collection was considered invalid (considering the previously defined criteria described below) were excluded.

Sociodemographic, Lifestyle and Clinical Data

To collect sociodemographic and clinical data, a structured face-to-face questionnaire, based on the WHO STEPS questionnaire⁽¹⁴⁾, was applied to the participants, by trained interviewers. It consisted of sociodemographic questions, namely sex, age, education level and marital

status; medication and supplements taken on the previous 15 days; and lifestyle related questions, namely on tobacco use, alcohol and salt consumption. The data collection also included a physical evaluation, where anthropometric and blood pressure measures were registered. Height, using a stadiometer (SEA 213 portable stadiometer, Hamburg, Germany) and waist circumference, using the SECA 201 tape, were assessed according to the international standard procedures⁽¹⁵⁾; weight was measured using the Tanita MC180MA body composition analyser (Tanita, IL, USA). Body mass index (BMI) was calculated. Measurements were taken with participants wearing light clothing and without shoes. Hypertension diagnosis was made by the occupational medicine doctor responsible for the recruitment.

The level of physical activity was also assessed, using the International Physical Activity Questionnaire-Short Form⁽¹⁶⁾, validated and adapted for the Portuguese population.

Food intake was assessed using a 24h dietary recall, where participants were asked to recall all foods and beverages consumed the day before (time of urine collection) and to estimate the consumed portion size, with the support of a picture book. Energy and nutritional intake were estimated using the Food Processor Plus nutritional analysis software (version 11.9, ESHA Research, Salem, OR, USA).

Urinary Biomarkers and Hydration Status

For the 24h urine collection, as a proxy of salt intake, every participant was given one standard sterilized coded container, as well as

an illustrative leaflet explaining the collection procedure. From the 24h urine sample, urinary volume, sodium and potassium urinary excretion (by indirect potentiometry), urinary creatinine (by photometry), and urinary osmolality, were assessed. The validity of 24h urine collection was assessed by the relationship between urinary creatinine (mg/day) and body weight (kg). Samples were excluded when creatinine (mg/day/kg) was <10.8 and >25.2 in women and <14.4 and >33.6 in men⁽¹³⁾. The conversion of mmol to mg was performed by multiplying sodium (mmol) and potassium (mmol) respectively by 23 or 39 (mmol = mg/atomic weight) and the Na/K ratio was determined by dividing sodium (mmol) by potassium (mmol). The 24h urine analysis was performed by laboratory technicians who were unaware of the origin of the samples for analysis.

Inadequate hydration status was considered when the Free Water Reserve (FWR) was negative, representing a risk of hypohydration/hypohydration⁽¹⁷⁾. FWR (mL/24 h) was calculated using the formula:

$$FWR = 24 \text{ h urine volume} - \text{obligatory urine volume}$$

The obligatory urine volume is the ideal urine volume required to excrete the actual 24h urine solutes and is calculated using the formula⁽¹⁸⁾:

$$\text{Obligatory urine volume} = 24\text{h urine solutes (mOsm/d)} (830 - 3.4 \times (\text{age} - 20))$$

Data Analysis

Quantitative data, namely the age, height, waist circumference, daily potassium and sodium excretion, Na/K ratio, energy intake, average weekly consumption of alcoholic beverages and moderate and/or vigorous

physical activity variables data, was transformed into categorical through the median of the sample, for each sex, and frequencies were reported. Through a Pearson chi-squared test for categorical variables, participants were compared according to blood pressure (hypertensive versus non-hypertensive) and hydration status (euhydration versus hypohydration), for sociodemographic and lifestyle characteristics, and clinical measures.

To estimate the association between hydration status and hypertension, a multivariable binary logistic regression model was used, and odds ratios (OR) and respective 95% confidence intervals (95% CI) were calculated. The results were adjusted for the confounders, namely BMI, use of antihypertensives, Na/K ratio and, only for men, physical activity.

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS Version 27). Two-sided significance levels were set at 0.05, with 95% confidence intervals.

Results

From the initial sample of 114 participants, 107 (51.4 % women) were included in the analysis, as 7 did not meet the urine validity criteria. The participants were aged between 24-69, with a mean age of 48.0 years (sd=10.5). Hypohydration was found in 30.9% of women and 25.0% of men, whereas 29.1% of women and 50.0% of men were reported as hypertensive. Socio-demographic and lifestyle characteristics, clinical data and urinary biomarkers, according to blood pressure and hydration status, are shown in Table 1.

TABLE 1 Socio-demographic and lifestyle characteristics, clinical measures and urinary biomarkers in 107 Portuguese adults, according to blood pressure and hydration status.

		Women (n=55)							Men (n=52)						
		Hypertension			Hydration status				Hypertension			Hydration status			
		No (n=39)	Yes (n=16)		EH (n=38)	HH (n=17)			No (n=26)	Yes (n=26)		EH (n=39)	HH (n=13)		
		n (%)	n (%)	p	n (%)	n (%)	p		n (%)	n (%)	p	n (%)	n (%)	p	
Age (years)	≤46	20 (51.3)	8 (50.0)	0.931	20 (52.6)	8 (47.1)	0.702	≤48.5	17 (65.4)	9 (34.6)	0.270	20 (51.3)	6 (46.2)	0.749	
	>46	19 (48.7)	8 (50.0)		18 (47.4)	9 (52.9)		> 48.5	9 (34.6)	17 (65.4)		19 (48.7)	7 (53.8)		
Height (cm)	≤ 161.0	18 (46.2)	10 (62.5)	0.271	21 (53.3)	7 (41.2)	0.334	≤ 172.5	14 (53.8)	14 (53.8)	1.000	22 (56.4)	6 (46.2)	0.521	
	> 161.0	21 (53.8)	6 (37.5)		17 (44.7)	10 (58.8)		> 172.5	12 (46.2)	12 (46.2)		17 (43.6)	7 (53.8)		
BMI (kg/m ²)	Underweight + Normal	27 (69.2)	5 (31.3)	0.017	24 (63.2)	8 (47.1)	0.502	Underweight + Normal	9 (34.6)	2 (7.7)	0.042	8 (20.5)	3 (23.1)	0.916	
	Pre-obese	10 (25.6)	7 (43.8)		10 (26.3)	7 (41.2)		Pre-obese	14 (53.8)	17 (65.4)		23 (59.0)	8 (61.5)		
	Obese	2 (5.1)	4 (25.0)		4 (10.5)	2 (11.8)		Obese	3 (11.5)	7 (26.9)		8 (20.5)	2 (15.4)		
Waist circumference (cm)	≤ 77.0	24 (61.5)	5 (31.3)	0.041	22 (57.9)	7 (41.2)	0.251	≤93.9	17 (65.4)	9 (34.6)	0.027	19 (48.7)	7 (53.8)	0.749	
	>77.0	15 (38.5)	11 (68.8)		16 (42.1)	10 (58.8)		>93.9	9 (34.6)	17 (65.4)		20 (51.3)	6 (46.2)		
Education level	no higher education	5 (12.8)	4(25.0)	0.267	6 (15.8)	3 (17.6)	0.863	no higher education	1 (3.8)	4 (15.4)	0.158	5 (12.8)	0 (0.0)	0.174	
	higher education	34 (87.2)	12 (75.0)		32 (84.2)	14 (82.4)		higher education	25 (96.2)	22 (84.6)		34 (87.2)	13(100.0)		
Marital status	single	17 (43.6)	3 (18.8)	0.082	13 (34.2)	7 (41.2)	0.62	single	6 (23.1)	8 (30.8)	0.532	12 (30.8)	2 (15.4)	0.279	
	married	22 (56.4)	13 (81.3)		25 (65.8)	10 (58.8)		married	20 (76.9)	18 (69.2)		27 (69.2)	11 (84.6)		
Daily potassium excretion (mg/day)	≤2418	18 (46.2)	10 (62.5)	0.271	18 (47.4)	10 (58.8)	0.432	≤ 2827.5	12 (46.2)	14 (53.8)	0.579	19 (48.7)	7 (53.8)	0.749	
	>2418	21 (53.8)	6 (37.5)		20 (52.6)	7 (42.2)		>2827.5	14 (53.8)	12 (46.2)		20 (51.3)	6 (46.2)		
Daily sodium excretion (mg/day)	≤2461	23 (59.0)	5 (31.3)	0.062	17 (44.7)	11 (64.7)	0.171	≤3933	17 (65.4)	9 (34.6)	0.027	18 (46.2)	8 (61.5)	0.337	
	>2461	16 (41.0)	11 (68.8)		21 (55.3)	6 (35.3)		>3933	9 (34.6)	17 (65.4)		21 (53.8)	5 (38.5)		

Quantitative variables were transformed into categorical ones through each sex median.

Bold p values are <0,05 and considered statistically significant.

Abbreviations: IMC, body mass index; EH, euhydrated; HH, hypohydrated.

TABLE 1 (continuation)

	Women (n=55)							Men (n=52)						
	Hypertension			Hydration status				Hypertension			Hydration status			
	No (n=39)	Yes (n=16)	p	EH (n=38)	HH (n=17)	p	No (n=26)	Yes (n=26)	p	EH (n=39)	HH (n=13)	p		
	n (%)	n (%)		n (%)	n (%)		n (%)	n (%)		n (%)	n (%)			
Na/K ratio	≤1.8	23 (59.0)	5 (31.3)	0.062	19 (50.0)	9 (52.9)	0.84	≤2.1	17 (65.4)	9 (34.6)	0.027	16 (41.0)	10 (76.9)	0.025
	>1.8	16 (41.0)	11 (68.8)		19 (50.0)	8 (47.1)		>2.1	9 (34.6)	17 (65.4)		23 (59.0)	3 (23.1)	
Energy intake (kcal)	≤1881	19 (48.7)	9 (53.6)	0.612	18 (47.4)	10 (58.8)	0.432	≤ 2305	12 (46.2)	14 (53.8)	0.579	18 (46.2)	8 (61.5)	0.337
	>1881	20 (51.3)	7 (43.8)		20 (52.6)	7 (41.2)		>2305	14 (53.8)	12 (46.2)		21 (53.8)	5 (38.5)	
Average weekly consumption of alcoholic beverages (drinks/week) ^a	≤0.14	17 (63.0)	6 (60.0)	0.869	17 (68.0)	6 (50.0)	0.291	≤0.57	13 (54.2)	10 (41.7)	0.386	16 (45.7)	7 (53.8)	0.616
	>0.14	10 (37.0)	4 (40.0)		8 (32.0)	6 (50.0)		>0.57	11 (45.8)	14 (58.3)		19 (54.3)	6 (46.2)	
Smoking tobacco	yes	4 (10.3)	1 (6.3)	0.639	3 (60.0)	2 (40.0)	0.645	yes	3 (11.5)	4 (15.4)	0.685	6 (85.7)	1 (14.3)	0.482
	no	35 (89.7)	15 (93.8)		35 (70.0)	17 (30.9)		no	23 (88.5)	22 (84.6)		33 (73.3)	12 (26.7)	
Moderate and/or vigorous physical activity (min/week)	≤ 60.0	18 (46.2)	11 (68.8)	0.127	18 (47.4)	11 (64.7)	0.234	≤ 60.0	7 (26.9)	20 (76.9)	<0.001	23 (59.0)	4 (30.8)	0.078
	>60.0	21 (53.8)	5 (31.3)		20 (52.6)	6 (35.3)		>60.0	19 (73.1)	6 (23.1)		16 (41.0)	9 (69.2)	

Quantitative variables were transformed into categorical ones through each sex median.

Bold *p* values are <0,05 and considered statistically significant.

Abbreviations: IMC, body mass index; EH, euhydrated; HH, hypohydrated.

^aThere are missing values for the Average weekly consumption of alcoholic beverages.

The prevalence of hypertension was higher among participants living with excessive weight (65.8% vs 31.3%; $p=0.017$, for women and 92.3% vs 7.7%, $p=0.042$ for men) and with a waist circumference above the median (68.8% vs 31.3%; $p=0.041$, for women and 65.4% vs 34.6%, $p=0.027$ for men). The prevalence of hypertension in men was higher among those with proportions of daily sodium excretion and a Na/K ratio above the median (64.5% vs 34.6%; $p=0.027$ and 65.4% vs 34.6, respectively) and among those who practiced less moderate and/or vigorous physical activity than the median (76.9% vs 23.1%; $p<0.001$). Hypohydration was more prevalent among men with a lower Na/k ratio than the median (76.9% vs 23.1%; $p=0.025$).

The OR and respective 95% CI for the association between hydrations status and hypertension are presented in Table 2. After adjustment for confounders, hypohydration was associated with a 5-fold increased risk of hypertension, in women (OR=5.423; 95% CI: [1.217-24.176]). No such significant association was observed among men (OR=1.167; 95% CI: 1.167 [0.152-8.956]).

TABLE 2 Odds ratio for the association between hydration status and hypertension in 107 Portuguese adults

	Hydration status	Crude OR [95% CI]	p-value	Adjusted OR ^a [95% CI]	p-value
Woman (n=55)	Euhydrated	1	0.012	1	0.027
	Hypohydrated	4.982 [1.418-17.509]		5.423 [1.217-24.176]	
Men (n=52)	Euhydrated	1	0.033	1	0.882
	Hypohydrated	0.209 [0.049-0.880]		1.167 [0.152-8.956]	

Abbreviations: CI, confidence interval; OR, odds ratio.

^a Model adjusted for body mass index, use of antihypertensives and Na/k ratio (women) and, body mass index, use of antihypertensives and Na/k ratio and (men)

Discussion

In this sample of occupational health service users, hypohydrated women showed a 5-fold increased risk of hypertension.

Although being widely acknowledged that the body can minimize water losses and adapt to mild dehydration to maintain osmotic balance, long-term activation of biological mechanisms to preserve it can have negative effects on one's health⁽¹⁹⁾. Chronical triggering of these systems, such as the renin-angiotensin-aldosterone and the vasopressin may increase the risk of chronic non-communicable diseases' early development⁽¹⁹⁾.

The precise mechanism behind these findings is still not fully understood, although some possible explanations can be considered.

When a decrease in plasma volume and increase in plasma osmolality is experienced, due to hypohydration, the renin-angiotensin-aldosterone system is activated, leading to an increase in thirst sensation, and AVP is released. A cascade is initiated culminating in an increase in sodium and water retention⁽⁷⁾. In turn, when a low extracellular fluid volume is detected in the afferent arterioles' walls, near the glomeruli, it leads to the release of renin by the juxtaglomerular cells. This initiates a cascade ultimately resulting in elevated levels of angiotensin II and aldosterone and, consequently, also in increased sodium and water retention⁽⁷⁾. On the other hand, V2 AVP receptors, sensible to plasma osmolality variations⁽²⁰⁾ and mainly expressed in kidney collecting ducts, regulate water excretion, as well as modulate sodium absorption in the thick-ascending limb and distal tubules⁽²¹⁾. Through translocation of aquaporin-2 to the cellular membrane, AVP enables water reabsorption, simultaneously retaining sodium and urea, to

strengthen the intramedullary hypertonicity⁽³⁾. This leads to an excretion of a smaller volume of more concentrated urine, to maintain body water balance and plasma osmolality⁽²⁰⁾.

Although this mechanism might align well with the limited availability of water and salt in ancestral diets, nowadays salt has become easily accessible and inexpensive⁽²¹⁾. Our daily salt intake has significantly increased from 1-3g, in the past⁽²¹⁾, to a range of 5.4-18.5 g for men and 4.3-16.1 g for women, in the WHO European Region⁽⁹⁾. In fact, 78.5% of our sample showed a sodium excretion above the World Health Organization recommendations (<2000 mg/day). To compensate for insufficient water consumption even more sodium is consequently being retained, so kidneys are being challenged to retain water at the same time as they eliminate sodium⁽²¹⁾. Therefore, and as increased salt consumption is a significant contributor to high blood pressure⁽⁹⁾, it is suggested that the combined effects of high sodium intake and low water consumption have a significant impact on non-communicable chronic disease development, namely hypertension⁽²¹⁾.

On the other hand, as a response to hypohydration, high plasma levels of angiotensin II result in small arterioles vasoconstriction, causing an increase in total peripheral resistance, which contributes to endothelial dysfunction⁽⁷⁾ and, consequently, to hypertension⁽²²⁾. Additionally, chronic AVP secretion leads to elevated levels of copeptin, a stable vasopressin analogue that has been strongly linked to an increased risk of cardiovascular disease⁽¹⁹⁾.

Although a different method was used to assess the hydration status, an association between hypertension and hypohydration was found, in a sample of adults, from Saudi Arabia⁽²³⁾. In the later, in which bioelectrical impedance was

used, total body water and intercellular water percentages were found to be inversely related to hypertension status, but no association was found when the absolute values of water were used⁽²³⁾. Differences between men and women were not analysed. Also, a study among American adults, after a six-year follow-up, found a 4.21-fold higher risk of death from chronic diseases when individuals were underhydrated⁽¹⁹⁾. Conversely, in a prospective interventional study in Turkey, an association between negative hydration and lower blood pressure was found⁽²⁴⁾. However, it is noteworthy that, in the later study, the sample analysed was restricted to hypertensive participants and hypohydration was induced and kept using diuretics⁽²⁴⁾.

Regarding the found difference between men and women, mechanisms responsible for sex disparities in blood pressure control have not been elucidated yet⁽²⁵⁾. Literature shows that, in general, men have higher blood pressure and cardiovascular disease risk than age-matched, premenopausal women⁽²⁶⁾. After menopause, this tendency seems to reverse, but blood pressure can take an average of 5 to 20 years to increase, not increasing during the transition phase⁽²⁵⁾. Taking this into consideration, the lack of significant association between age and hypertension in the above results and the median age of our women sample, it is suggested that menopause impact might not be a plausible explanation for the found disparities. Nevertheless, available evidence strongly supports those androgens⁽²⁵⁾, such as testosterone, have a significant impact on sex differences in blood pressure regulation⁽²⁶⁾. Some literature suggests that androgens, acting through angiotensin II⁽²⁵⁾, may stimulate sodium reabsorption in the proximal tubule⁽²⁶⁾ and trigger oxidative stress to enhance renal vasoconstriction, increasing

blood pressure⁽²⁵⁾. Also, copeptin levels, above mentioned to increase the propensity to cardiovascular risk, tend to be higher in men, when compared to women⁽²⁰⁾. As a hypothesis, it can be suggested that the greater men's natural predisposition for high blood pressure might be diminishing hydration status impact on this group's blood pressure.

Moreover, it is well known that comorbid conditions such as type II diabetes can aggravate hypertension mechanisms, increasing blood pressure⁽²⁵⁾. This chronic disease can also be interfering with the results, as data on its diagnosis was not collected⁽²⁵⁾. Also, insufficient water intake and sugar-sweetened beverages consumption in combination, activate not only the vasopressin pathway but also the aldose reductase-fructokinase one, which can synergize together and aggravate the target organ's damage⁽¹⁹⁾.

Regarding the hypohydration prevalence, in our sample, 30.9% of women and 25.0% of men were found to be hypohydrated. The NHANES III survey data indicated that dehydration affected approximately 16-28% of adults⁽¹⁹⁾, and a study conducted in 13 countries across three continents revealed that only 40% of males and 60% of females met the recommended water intake guidelines set by the European Food Safety Authority (EFSA)⁽²⁷⁾. These numbers are very worrying when, in humans, the primary method to restore lost water is through the oral intake of liquids and food⁽¹⁹⁾, and we notice that hypohydration impacts negatively people's health.

It is worth mentioning that daily Total Water Intakes and Adequate Intakes were already described⁽²⁾. EFSA recommends a 2500 ml/day water intake, for both men and women adults, whereas the National Academy of Medicine stands for

3700 ml/day for men and 2700 ml/day for women⁽²⁾. However, there is no unanimous agreement on the water requirements for various demographic groups, due to the intricate and ever-changing nature of the human water regulatory system and the significant differences among individuals, depending on physical activity levels, climate conditions, and dietary composition, among other factors⁽²⁾. Nevertheless, among literature, it is suggested that optimal hydration should go beyond replacing daily fluid losses, but it should also maintain a sufficient urine volume to prevent urine concentration and supersaturation and reduce the excessive secretion of AVP⁽³⁾. As such, it is suggested that intermediate consumption between the two proposed Adequate Intakes is reasonable⁽³⁾.

Despite more research is necessary to study and better understand the mechanisms behind our results, we believe that hydration should be considered for health maintenance and disease prevention.

Our findings should be interpreted considering the study's strengths and limitations. In terms of limitations, the fact that participants were from a convenience sample of occupational health service users from the University of Porto and not randomly selected from the general population, prevents the generalizability of the findings. Moreover, since only one urine specimen per participant was collected, it is not possible to conclude long-term hydration status. However, it is worth noting that this method is commonly used to assess hydration status as water balance is typically regulated over 24-hour periods⁽²⁸⁾ and as FWR, the method used, takes both the maximal kidney concentration capacity and a safety margin to ensure adequate water intake in the general population into account⁽²⁹⁾. Nevertheless, our study has important strengths worth

to be mentioned such as the high quality of urine data collection, specifically the use of 24h urine excretion to assess sodium and potassium excretion, as it is considered the golden standard method, and the use of FWR to assess the 24h hydration status⁽²⁸⁾ that, accounting for the considerations made above, is considered suitable. Also, the study design adherence to recommended guidelines and best practices for clinical trials is an important strength.

Conclusion

Hypohydration was associated with a 5-fold increased risk of hypertension in women from an occupational University of Porto health service users' sample. Further research is needed to better understand the mechanisms behind these findings and how to put them into practice to protect people's health. Regarding the latter, educational campaigns to sensitize communities to the importance of hydration at all ages is recommended.

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