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Impact evidence of the vitamin D status in hypertensive patients in Morocco

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ABSTRACT

Vitamin D deficiency is a hot topic as it affects about 50% of the world's population. Beyond its extra-osseous effects, notably on the cardiovascular system. In recent years many epidemiological studies have looked at the role of vitamin D status in modulating blood pressure. It appears that there is an inverse association between serum vitamin D levels and blood pressure. It is in this context that our prospective study on the Moroccan population allows having global knowledge of the association between vitamin D and arterial hypertension. This is a descriptive study of vitamin D status in Moroccan hypertensive patients in whom blood samples were taken for serum 25(OH)D determination. The data collected were anonymised and entered into SPSS software. X2 and ANOVA tests were used to investigate the existence of correlations between vitamin D status and age, age at menopause, body mass index, sex and hypertension. 1015 hypertensive patients were included in this study with a female predominance of 84.2%, mainly over 50 years old in 80.8%, of whom 31.5% were overweight or obese, 13.2% had a hypertensive parent and 70.8% had vitamin D deficiency. Vitamin D regulates at least 3% of the human genome with receptors throughout the body, including vascular smooth muscle cells, vascular endothelium and cardiomyocytes, where it acts by vasodilation and by blocking the renin-angiotensin-aldosterone system (RAAS) to lower blood pressure. There is a relationship between low serum vitamin D levels and high blood pressure. Our study concluded that there is an association between hypovitaminosis D and the pathology of hypertension. However, further randomised studies are needed and in the meantime, clinicians could propose it in the therapeutic arsenal of Moroccan hypertensive patients.

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Introduction

According to the World Health Organization, hypertension is defined by a systolic blood pressure ≥ 140 mmHg and/or a diastolic blood pressure ≥ 90 mmHg (1). More than a billion people are affected in the world; which makes it a real public health problem (2). Hypertension is a primary risk factor in the occurrence of ischemic cardiomyopathy, stroke and chronic kidney disease (3). It is also one of the leading causes of mortality and morbidity in the world (4, 5). To this end, the World Health Organization aims to reduce, globally, the prevalence of hypertension by 25% by 2025 (6,7). A partnership between the body of health and the policies of the economy of health made it possible to put in active measures to fight against the risk factors associated with arterial hypertension: programs to fight against tobacco consumption, reduction of the use of salt, fight against obesity, and valorization of the physical activity. As well as these cardiovascular risk factors, the hypothetical role of vitamin D in the homeostasis of arterial pressure is the object of a current scientific debate (8). It is for this reason that we are interested in studying the possible association between vitamin D and arterial hypertension in the Moroccan population, which may lead to the establishment of a therapeutic strategy to reduce arterial hypertension in Morocco.

Materials and Methods

Study population

This is a descriptive epidemiological study conducted prospectively and includes a total of 1015 hypertensive patients under antihypertensive treatment and 789 controls. Patients were recruited from two private medical practices in Casablanca (Morocco), from October 2020 to October 2021.

The patients included in this study were over 25 years of age, known to be hypertensive and on antihypertensive treatment for at least 6 months. Patients with associated cardiovascular disease, inflammatory rheumatic disease, cancer, pregnancy, breastfeeding, corticosteroids and vitamin D supplementation were excluded from this study.

Clinical endpoints

A face-to-face interview was conducted with each enrolled hypertensive patient to collect data regarding the sex, age, age at menopause for women, weight, size, skin color, number of children, profession and physical activity.

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Blood pressure measurements

Initial blood pressure measurements were taken, one on arrival and one after 15 minutes of rest in the supine position; the average of these two measurements was taken.

Thereafter, blood pressure was taken twice a week at home by the patient, once in the morning and once in the evening, for the duration of the study.

Vitamin D measurements

This phase took place in the immunoserology room of a private medical analysis laboratory, carried out by a specialised technician using the VIDAS3 machine; this is an automatic assay machine based on the enzyme immunoassay technique with fluorimetric detection. Vitamin D deficiency is defined as 12 ng/nl, vitamin D insufficiency as 12 and 30 ng/nl and vitamin D sufficiency as 30 ng/nl. Vitamin D is considered toxic for a serum concentration of 150 ng/nl.

Statistical analysis

The statistical analysis was carried out using SPSS software for Windours, version 20 (SPSS Inc, Chicago). The comparison between hypovitaminosis D and the clinical and biological parameters was performed using χ^2 test, and Fisher bilateral exact test was used for the comparison of percentages. The associations are considered statistically significant when the p-value is inferior to 0.05.

Results

The demographic and clinical characteristics of recruited hypertensive patients are reported in Table 1. The sex ratio of our patients is 0,18. Hypertension was more prevalent in women (84.2%) than in men (15.8%).

The distribution of patients according to age shows a predominance of patients aged more than 50 years. The clinical data on hypertension show that 60% of the patients (609 patients) have normal blood pressure and 40% (406 patients) have high blood pressure.

Data analysis of family history shows that hypertension was reported in 13.2 % of patients (134/1015).

The results of vitamin D status show a significant difference between normal subjects and hypertensive patients (p 0.03), with a superior rate of vitamin D insufficiency (≥12-<30 ng/nl) in normal subjects, as opposed to vitamin D deficiency (<12 ng/nl) that is more pronounced in hypertensive cases (Table 2).

The distribution of vitamin D status according to socio-demographic characteristics of hypertensive patients is reported in (Table 3) which shows that hypovitaminosis D is significantly associated with gender (p= 0,02) with vitamin D insufficiency being more pronounced in females.

Table 1. Demographic and clinical characteristics of hypertensive patients.

		N	%
Sex	Male	160	15.8
	Female	855	84.2
Age	25 – 35 years old	61	6.01
	36 – 50 years old	134	13.20
	> 50 years old	820	80.78
Blood pressure	Normal	609	60
	Anormal	406	40
Family history	Hypertension	134	13.2

Table 2. Comparison of vitamin D status between normal subjects and hypertensive cases.

		Vitamin D						
		Deficiency		Insufficiency		Normal		P value
	N	N	%	N	%	N	%	
Hypertensive Patients	1015	219	21.6	719	70.8	77	7.6	0.03
Controls	789	133	17.01	596	76.21	53	6.78	

Table 3. Distribution of vitamin D status according to socio-demographic characteristics of hypertensive patients.

		Vitamin D						P value
			Deficiency		Insufficiency		Normal	
		N	N	%	N	%	N	%	
Gender	Male	160	49	30.6	99	62	12	7.3	0.02
	Female	855	182	21.3	620	72.5	53	6.2	
Age	25 – 35 years old	61	18	29.5	36	59	7	10.9	0.012
	36 – 50 years old	134	35	26	87	65	12	9	
	> 50 years old	820	152	18.6	617	75.2	51	6.2	
Physical Activity	Yes	192	35	18	115	60.2	42	21.8	< 0.001
	No	823	176	21.4	578	70.2	69	8.4	
Skin color	Matte color	609	140	23	369	60.6	100	16.4	< 0.001
	White color	254	36	14	127	50	91	36	
	Black color	152	54	35.2	98	64.8	0	0	

Similarly, in the control group, hypovitaminosis D is significantly associated with gender (p<0.0001) with vitamin D deficiency that is more pronounced in females and insufficiency more prevalent in males (Table 4).

Furthermore, hypovitaminosis D is significantly associated with age (p= 0.012), and physical activity (p= 0.00000) in the group of hypertensive patients.

In this study, known hypertensive patients were classified into two groups according to blood pressure. The distribution of vitamin D status in hypertensive patients according to blood pressure is shown in Table 5. This shows a significant association between vitamin D status and blood pressure (p= 0.0000).

After vitamin D supplementation, 25(OH)D levels normalised in all patients who were hypovitaminotic. About the impact of vitamin D supplementation in patients with high blood pressure (406/1015) 71% normalized their blood pressure.

Discussion

The analysis of the results shows that the majority of patients are women with vitamin D deficiency. In 2009, a Moroccan study reported that 91% of Moroccan women are 25(OH)D deficient. These results may be explained by the traditional Moroccan style of dress which covers the skin (9). The hypovitaminosis D observed in Moroccan women could be explained by the absence or low exposure to sunlight throughout the year and throughout the day, the diet, and the high body mass index (10).

The majority of patients are over 50 years of age and older people have a reduced ability to synthesise vitamin D from sunlight. A study published in the Lancet in 1989 showed that 25(OH)D levels were less increased after exposure to UVB in the sunbed in subjects aged 62-80 years compared to subjects aged 20-30 years. The concentration of 7-dehydrocholesterol in the deep layers of the epidermis decreases with age. A 20-year-old produces 4 times more vitamin D through the skin than a 70-year-old (11).

Furthermore, in our study, the majority of hypertensive patients were not physically active and were predominantly vitamin D deficient. Recent studies suggest that vitamin D influences skeletal muscle by activating the expression of genes that influence muscle growth and differentiation, particularly in fast-twitch fibres (12,13). Vitamin D also has non-genomic effects that include regulation of sarcoplasmic calcium supply and cell signalling (13). Biopsy studies in deficient patients show atrophy of type II skeletal muscle fibres (14).

In addition, it is noted that the black hypertensive patients in our study have the highest level of vitamin D deficiency. Indeed, skin pigmentation is a major cause of vitamin D deficiency because melanin absorbs UVB radiation. This pigmentation acts as a natural sunscreen and increased skin pigmentation may decrease skin synthesis of vitamin D under UVB (15). A study of African-Americans found that they are the most vitamin D deficient and whites the least with a prevalence of 34.9% (16). This is also the case in the 2008 study by G. Guardia which found that the proportion of people with vitamin D deficiency was significantly higher in black-skinned people than in light-skinned people (17).

Table 4. Distribution of vitamin D status according to socio-demographic characteristics of controls.

			Vitamin D						
			Deficiency		Insufficiency		Normal		P value
		N	N	%	N	%	N	%	
Gender	Male	158	5	3.16	129	81.65	26	16.46	<0.0001
	Female	631	128	20.29	467	74.01	27	4.28	
Age	<12	8	3	37.50	3	37.50	2	25.00	0.1990
	13-21	22	3	13.64	19	86.36	0	0.00	
	22-35	127	23	18.11	95	74.80	9	7.09	
	36-50	237	48	20.25	166	70.04	23	9.70	
	>50	395	72	18.23	296	74.94	27	6.84	
	<40	52	13	25.00	34	65.38	5	9.62	
	41-50	184	33	17.93	125	67.93	26	14.13	
	>50	97	17	17.53	73	75.26	7	7.22	
Physical activity	Yes	241	44	18.26	169	70.12	28	11.62	0.8235
	No	548	104	18.98	373	68.07	71	12.96	
Skin color	No	686	151	2.01	514	74.93	21	3.06	<0.0001
	Matte	473	102	21.6	284	62.2	77	16.3	
	White	197	35	17.8	113	57.4	49	24.9	
	Black	119	38	31.9	78	65.5	3	2.5	

Table 5. Distribution of vitamin D status according to hypertensive.

		Vitamin D						
		Deficiency		Insufficiency		Normal		P value
N		N	%	N	%	N	%	
Normal blood pressure	609	130	21.3	321	52.7	158	26	0.0000
High blood pressure	406	123	30.4	277	68.2	6	1.4	

Furthermore, our study reports that the majority of our hypertensive patients are over 50 years old (80.78%). Indeed, the prevalence of arterial hypertension increases with age and in particular that of systolic pressure.

Systolic hypertension is a relatively specific problem of the elderly, as the results of the Framingham Heart Study have shown. More than 70% of people over 60 years of age have high systolic blood pressure and more than 25% of people over 80 years of age have "pure" isolated systolic hypertension.

Ageing is accompanied by an increase in peripheral resistance, a decrease in compliance and an increase in arterial stiffness. This vascular remodelling is explained by important tissue modifications: thickening of the arterial walls, embrittlement and fragmentation of the elastin with rupture of the elastic fibres of the media of the elastic arteries, replacement of the elastic fibres by stiffer collagen fibres, deposition of calcium salts and increased atheroma lesions.

The arteries then lose their ability to modulate the pulsatile pressure wave from the heart, resulting in increased blood pressure (18, 19).

Risk factors for hypertension include a sedentary lifestyle and lack of physical activity; this is consistent with the results of our study which shows that 81.1% of our hypertensive patients are not physically active. 13.2% of our hypertensive patients have a family history. Heredity may indeed play a role in the occurrence of hypertension; this heredity relates to an increased sensitivity to sodium linked to a decrease in renal excretion of a sodium load. About 60% of this familial inheritance is genetically determined with 40% environmental factors (20). 70.8% of our hypertensive patients are vitamin D deficient. Indeed, blocking the renin-angiotensin system is recognised in the treatment of hypertension. Several epidemiological studies report an inverse relationship between serum 1,25(OH)2D and blood pressure as 1,25(OH)2D decreases renin expression. Low UVB exposure is associated with a higher prevalence of hypertension and conversely, UVB exposure decreases blood pressure (21, 22).

In addition, vitamin D supplementation in hypertensive patients with high blood pressure levels has been shown to normalise blood pressure in 71% of cases. In a randomised controlled trial of 148 women (mean age 74±1 year) the combination of 1600 IU/day vitamin D with 800 mg/day calcium for eight weeks significantly reduced systolic blood pressure compared with calcium alone (23).

Three large cohort studies showed no reduction in the incidence of hypertension in those consuming more than 1000 IU/d or less than 200 IU/d of vitamin D. The problems in these studies are related to the method of self-measurement of blood pressure by patients and the absence of a strict diet to control dietary vitamin D intake (24).

Conclusion

Our study agrees with the literature in affirming the association between vitamin D and hypertension. The contribution of vitamin D supplementation to the prevention of hypertension is not yet clear. Randomised trials are needed before vitamin D supplementation can be incorporated into a preventive and therapeutic strategy for hypertension.

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Credit authorship contribution statement

HA: Participated in the study design, formal analysis and investigation, and statistical analysis and drafted the manuscript. ML: Participated in data analysis and review of the final manuscript SAF: Participated in statistical analysis; ME: Participated in the study design & review of the final manuscript; MME: Participated in the design and coordination of the project and review of the final manuscript. All authors have reviewed and approved the manuscript.

Competing interests

The authors declare no competing interests.

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