Research Article

Vitamin D is a suggested target in hypertensive Iraqi patients management

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ABSTRACT

Aim: Hypertension (HTN) is the leading attributable risk for cardiovascular disease. In the Middle East, the disease continues to be a worrying public health issue with modest blood pressure control rates. Vitamin D possesses antihypertensive acts through its negative regulation of renin-angiotensin aldosterone system, antioxidant, and anti-angiogenic effects. **Materials and Method:** In this cross-sectional study, a total of 68 Vitamin D naive HTN Iraqi patients with a mean age (54.8 ± 13.2) were investigated in comparison to matched 31 normotensive apparently healthy individuals. Serum Vitamin D level estimation was done in both groups by immunofluorescence assay, and the dependency sufficiency (normal) values were those ≥30 ng/ml. **Result and Discussion:** Vitamin D sufficiency was less prevalent among the patients group versus controls (4.41% vs. 54.83%). The mean of Vitamin D serum levels among patients "unexpectedly" was 13.13 ± 8.86 ng/ml which were significantly ($P = 0.000$) lower than that of controls 36.44 ± 16.66 ng/ml. We also observed a significant ($P = 0.007$) inverse correlation between Vitamin D levels and the obesity index; waist to height ratio in HTN patients. **Conclusion:** It can be concluded that a deficient level of Vitamin D is highly prevalent in Iraqi HTN patients, and low levels tend to correlate with obesity.

KEY WORDS: Hypertension, Obesity, Vitamin D, Waist-to-height ratio

INTRODUCTION

Worldwide, hypertension (HTN) is significantly associated with diseases of the cardiovascular system and has become the leading risk factor (RF) for premature death,[1] and the raising prevalence and burden of HTN is an important public health problem of the 21st century.[2] Its prevalence together with an awareness of insufficient management, has directed towered creative strategies to reduce the worsen outcomes of such health-threatening problem, since cardiovascular disease (CVD) is prevented through reducing blood pressure (BP).[3,4] Worldwide the number of people having HTN in is more than 1.4 billion.[5]

Vitamin D deficiency (VDD) has been correlated to illnesses in various organ systems including cardiovascular system.[6] Potential interaction has demonstrated to occur between VDD contributes to complications associated with HTN.[7] Vitamin D is one of the steroid receptor super-family (fat-soluble steroid hormone) with both endocrine and autocrine bio-function.[8] As a micronutrient the major endocrine role of Vitamin D is the preservation of skeletal homeostasis related calcium (Ca^{+2}) and bone metabolism which is proficient through mediating digestive and renal Ca^{+2} metabolism[9] and reabsorption from the skeleton.[10] The Vitamin D autocrine role depends on unique cellular genomic-expression of Vitamin D receptor. One of such autocrine effect is the modulation of inflammatory pathways which play a role in CVD.[11,12]

Inconsistent results have been recorded through several cross-sectional (CS) studies that explored the correlation between serum Vitamin D and HTN were reviewed by Pilz *et al*.[13] It was shown that insufficient levels of Vitamin D have been accompanied with the increased aggravation of raised BP.[14,15]

While other CS studies failed to find significant result as in Li *et al*.[16] Snijder *et al*. and Jorde *et al*., 2010, found an inverse correlation between Vitamin D and HTN.[17,18] While, Reis *et al*. results revealed an insignificant correlation between serum Vitamin D levels and HTN.[19]

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Other studies suggested that Vitamin D may play a protective role against HTN.[20,21] The mechanism by which Vitamin D influencing BP is not definitely recognized.[22] With several pathways being proposed, *via* Ras[23]suppressing parathyroid hormone,[24,25] and affecting ECs (epithelial cancers) functions.[26,27]

MATERIALS AND METHODS

The present study was conducted in a private clinic for CVDs. It was a cross-sectional case–control study for 6-month duration. The study was approved by the Institutional Scientific Committee. An ethical consent form was obtained from the Office of the Researchers belonging to the Ministry of Health and applied to the participants of this study.

Study Design

The design of this work is CS case–control study. Members of two groups were subjected to the questionnaire form to collect the data related age, sex, detailed medical history, clinical examinations, and relevant investigations, in addition to anthropometric measurements including weight, height, and waist circumference, which were included as a part of the methodology.

Patient and Controls

Our study comprised 68 participants of essential HTN and 31 age-matched controls. Participants aged 53.7 ± 13.3 (mean ± standard deviation [SD]) years who were diagnosed with essential HTN and were naive for any form of Vitamin D supplementation were enrolled after informed and written consent to participate.

Patients who referred to the General Hospital were not recruited in this study because the referrals were in the critical and emergency situations.

The criteria for inclusion were known cases of HTN on treatment with different types of antihypertensive agents. A systolic (Sys) BP of ≥140 mm Hg and a diastolic (Dia) of BP ≥90 mm Hg were considered as a cutoff level of high BPs on diagnosis.

The following groups of patients were excluded from the study:

- Patients with diabetes mellitus (DM), renal disorders, liver diseases, pregnancy, and proved secondary HTN.
- Counterparts were apparently healthy controls (AHC), without any major illness and not on any medications.

Anthropometric Measurements

Body mass index (BMI) was calculated by dividing weight (kg)/height (m)^2, and Waist-to-height ratio (WcHtR) was also calculated (waist circumference cm/height cm) as indicators for central obesity.

Collection of Samples

The samples were taken between 09:00 am and 10:00 am after a 12–14 h fasting. About 5 ml of venous blood was drown from subjects under a sterile condition, using a disposable syringe and collected in plane tubes. The serum was separated within 15–60 min of collection by centrifugation at 3000 rpm, and the aliquots were subjected to the analyzer.

Estimation of Vitamin D

The test uses a competitive immune-detection method. In this method, the target material in the sample binds to the fluorescence (FL)-labeled detection antibody in the detection buffer, to form the complex as sample mixture. This complex is loaded to migrate onto the nitrocellulose matrix, where the covalent couple of 25(OH) D3 and bovine serum albumin is immobilized on a test strip and interferes with the binding of the target material and FL-labeled antibody. If the more target material exists in blood, the less detection antibody is accumulated, resulting in the less FL signal.

Statistical Analysis

The results were presented as number, percent, and whenever possible as mean ± SD. The data were analyzed using two-tailed, unpaired difference between two means Student's *t*-test, unpaired samples Wilcoxon's test. The statistical analysis was carried on by using Excel 2007 and SPSS Version 17 programs taking a probability $P \leq 0.05$ as the lowest limit of significance.

RESULTS

The mean serum concentration (ng/ml) of Vitamin D was significantly lower in HTN patients, represented as Group I (13.13 ± 8.86), compared to Group II AHC which was (36.44 ± 16.66), ($P = 0.000$) Table 1.

We further stratified patients according to their levels of Vitamin D. Among patients, 88.23% were Vitamin D deficient, and 7.35% had insufficient levels of Vitamin D [Table 2]. Among controls, 19.35% had VDD and (25.70%) had insufficiency [Table 3].

Table 3 showed the correlations between Vitamin D concentration and metabolic indices, in addition to *r* values for Vitamin D versus HTN. This illustrated that the correlation between Vitamin D and BP Sys and Dia was negatively correlated even though not significantly, while it reached significant values (negatively correlates) with the obesity index WcHtR, but it was not with BMI.

Table 1: Baseline characteristic in study groups

Variable	Controls (Group I)	Patients (Group II)	*P* value
Age	45.8±9.5	53.7±13.3	
Sex F/M	21:10	68:23	
BP Diastolic	124.6±12.6	146.1±24.6	*P<0.001
Systolic BP	75.7±9.4	86.9±13.1	*P<0.001
WcHtR	0.543±0.08	0.685±0.095	*P<0.001
Vitamin Dng/ml	36.44±16.66	13.13±8.86	*P=0.000

Unpaired *t*-test, *Significant. BP: Blood pressure

Table 2: Distribution of VDD

VDD	Controls (%)	Patients (%)
Sufficiency≥30 ng/ml (*n* %)	(17) 54.83	(3) 4.41
Insufficiency 20–30 ng/ml (n %)	(8) 25.80	(5) 7.35
Deficiency<20 ng/ml (*n* %)	(6) 19.35	(60) 88.23

VDD: Vitamin D deficiency

Table 3: Correlations of Vitamin D

Parameter	BP-systolic	BP-diastolic	BMI	WcHtR
Vitamin D				
Patients	−0.179	−0.185	−0.17	−0.325**
Df	66	66	66	66
P	0.144	0.131	0.165	0.007
Control	*r*=−0.170	*r*=−0.237	*r*=−0.480**	*r*=−0.410*
Df	29	29	29	29
P	0.361	0.2	0.006	0.02

**The correlation is significant with 0.01 levels (two-tailed). BP: Blood pressure, BMI: Body mass index

DISCUSSION

Vitamin D plays a modificatory role in the pathophysiology of HTN through its effects on renin-angiotensin-aldosterone system.[28] This vitamin is widely varies across all ages, races, socioeconomic state, and geographical regions. It plays a key role in various body's physiological functions.[29]

The unmistakable significantly decreased Vitamin D levels in sera of Iraqi HTN patients compared with AHC Group, is comparable with the findings of Padalkar *et al*. in India,[30] and with that of Salari *et al*. in Iran.[31]

This result is also conforming the observation of meta-analysis studies, which stated that VDD is correlated with HTN.[32,33] The effect of low Vitamin D on RFs of HTN may be more potent in individuals who have VDD compared to those with normal (sufficient) concentration.[34]

Nonsufficient Vitamin D is believed to affect CVDs, by affecting the traditional RFs such as HTN, DM, and inflammation.[35]

VDD is also associated with inflammation,[36] and enhances inflammatory reactions in the vasculatures.[15] This effects may be furtherly complicated under the additive effects of metabolic derangement components particularly obesity, and elevated WcHtR, as they are prevalent in our patients group as a representative sample for Iraqi population.

The insignificant inverse correlations of Vitamin D with BP (systolic and diastolic) came across that found by Padalkar *et al.*, Scragg *et al.,* Sabanayagam *et al.,* and Skaaby *et al*.[30,37-39]

On the other hand, Vitamin D is negatively (significantly) (P = 0.00) correlated with WCHtR in Group I healthy subjects, such result consolidate firmly the opinion of potential nesting between VDD and obesity indices. Vitamin D levels among normotensive controls were also affected with Ob indices. Vitamin D is significantly influenced with waist circumference (WC).[40] It was found that Vitamin D, regardless of its source, is stored in adipose tissues in the form that is not bioavailable.[41] This might clarify why obese persons are chronically suffering from VDD.

CONCLUSION

It can be concluded that Iraqi HTN patients status in part, is influenced by the abnormalities in levels of Vitamin D, among whom metabolic disorders, furtherly complicate the situation. Insufficient sunlight exposure, social wants, and kind of favorable Iraqi foods play a profound role in the triad; VDD, HTN, and obesity.

Supplementation with Vitamin D may aid in adjusting somewhat BP in those patients.

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