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Research Article

ASSOCIATION BETWEEN VITAMIN D LEVEL AND ESSENTIAL HYPERTENSION

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ABSTRACT

Objective: There is relationship between vitamin D deficiency and hypertension (HTN). The mechanism causing the development of HTN, the Renin Aldosterone Angiotensin System, was discovered to be strongly inhibited by vitamin D. This study was piloted to assess the role of vitamin D deficiency in the development of essential hypertension (EH).

Methods: A total of 50 patients with EH and 50 healthy participants participated in this study. Every participant was subjected to clinical history, physical examination, and other necessary blood testing, electrocardiography, and echocardiography.

Results: There was a significant decrease in vitamin D in hypertensive group (20.25±3.28 ng/mL) than normotensive group (38.33±6.89 ng/mL). Vitamin D level was moderately negative correlated with systolic blood pressure (BP) (r – 0.43, p – 0.001), strong negative correlation with diastolic BP (r – 0.76, p<0.001), strong negative correlation with intimal thickness (r – 0.67, p<0.001), and moderate negative correlation with ventricular mass (r – 0.48, p<0.001). Intimal thickness and ventricular mass were significantly higher in patients with EH with low vitamin D than those with normal vitamin D levels.

Conclusion: There is a strong inverse relationship between serum vitamin D and HTN. Vitamin D deficiency levels are considered an additional risk factor for cardiovascular morbidity and mortality.

Keywords: Blood pressure, Essential hypertension, Intimal thickness, Vitamin D, Ventricular mass.

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INTRODUCTION

Hypertension (HTN) affects one billion people worldwide [1]. About 95% of these patients had essential hypertension (EH), with no recognized cause [2]. Higher latitudes with less intense ultraviolet B (UVB) radiation, colder climates with less skin exposure, and darker skin with less UVB penetration are all directly linked to the occurrence of hypovitaminosis D [3]. Higher incidence of EH also occurs in the winter, in persons who live in higher latitudes, and in those with deep skin pigmentation who live distant from the equator. Therefore, it is fair to assume that vitamin D insufficiency may contribute to an increased prevalence of EH [4]. Vitamin D deficiency is associated with an increased risk of cancer, Alzheimer's disease, HTN, and cardiovascular disease [5-7].

The unstable balance between vasoconstriction and vasodilation caused by vitamin D deficiency significantly shifts in favor of vasoconstriction, resulting in HTN in susceptible middle-aged individuals. Therefore, in hypertensive individuals with vitamin D insufficiency, a suitable high dose of vitamin D treatment that regularizes blood 25(OH)D levels should lower blood pressure (BP) [8]. There have been a number of published meta-analyses of observational studies and randomized controlled trial (RCTs), although the conclusions vary [9-12]. Golzarand *et al.* [9] evaluated 30 RCTs with 4,744 subjects and concluded that vitamin D has a positive effect in subgroups with daily doses >800 IU/d, a duration <6 months, or elderly subjects. In participants with pre-existing cardiometabolic disorders, Kunutsor *et al.* [11] reported that supplementation with vitamin D significantly reduced diastolic BP (DBP) by 1.31 mmHg. However, another meta-analysis concluded that taking vitamin D supplements does not lower BP. This study was carried out to evaluate role of vitamin D in EH.

METHODS

This observational study was conducted among patients visiting outdoor patient department and admitted in the department of general medicine in collaboration with the Department of Pathology and the Department Community Medicine of tertiary care hospital in Gujarat. After getting approval from the institutional ethics committee, the subjects were categorized into two groups: Group 1 (hypertensive group): 50 patients having EH and Group 2 (normotensive group): 50 apparently healthy, with matched age and gender. Exclusion standards are individuals with chronic liver disorders, renal impairment, secondary HTN, and diabetes, pregnancy, patients receiving calcium or vitamin D treatments.

All individuals underwent a complete medical history, thorough physical examination, electrocardiography and echocardiography, and all relevant blood tests, including CBC, liver enzymes, renal function tests, fasting and postprandial blood glucose, lipid profiles, and serum vitamin D (25 hydroxycholecalciferol), which was determined using radioimmunoassays. Vitamin D level was <20 ng/mL considered as deficiency, 20–30 ng/mL as insufficiency, 31–100 ng/mL as normal, and >100 ng/mL as toxicity [13].

Statistical analysis

Data were entered in Microsoft Excel version 2016. Quantitative data were expressed as mean±standard deviation and qualitative data as frequency and percentage. Differences between groups were tested with tailed student's *t*-test for unpaired data for quantitative data and Chi-square test for qualitative data. Pearson's correlation coefficient (r) was calculated for correlation. p<0.05 were considered as statistically significant.

RESULTS

A total of 50 hypertensive patients and 50 normotensive subjects were included in the study. Age and gender-matched normotensive patients were selected as control. The mean age was 20.25±3.28 years for hypertensive subjects and 38.33±6.89 years for normotensive subjects. There were 62% and 68% males in the hypertensive and normotensive group, respectively. There was no significant difference in age and gender between two groups (p – 0.334 for age and 0.529 for gender). Height, weight, and body mass index (BMI) were also comparable between the two groups. Systolic BP (SBP) and DBP were significantly higher in the hypertensive group than normotensive group (Table 1).

Left axis deviation (LAD) and Left ventricular hypertrophy (LVH) were significantly higher in hypertensive group than normotensive group. (Hypertensive group: LAD-62.0%, LVH-50.0%; Normotensive group: LAD-12.0%, LVH-4.0%; p<0.001) (Table 2).

Intimal thickness was higher in the hypertensive group (0.78±0.07 mL) than normotensive group (0.45±0.09 mL, p<0.001). Ventricular mass (g) was also more in the hypertensive group (126.34±14.32 g) than in the normotensive group (72.34±8.76 g, p<0.001) (Table 3).

A total of 23 (46.0%) and 17 (34.0%) hypertensive subjects had vitamin D deficiency and insufficiency, respectively. However, 5 (10.0%) and 16 (32.0%) normotensive subjects had vitamin D deficiency and insufficiency, respectively. This difference was statistically significant (p<0.001) (Table 4).

Vitamin D level had a moderately negative correlation with SBP (r–0.43, p–0.001), a strong negative correlation with DBP (r–0.76, p<0.001), a strong negative correlation with intimal thickness (r–0.67, p<0.001), and a moderate negative correlation with ventricular mass (r–0.48, p<0.001) (Table 5).

Intimal thickness was higher in patients with vitamin D level <30 ng/mL (0.84±0.09 mL) and patients with vitamin D level >30 ng/mL (0.64±0.04 mL, p–0.001). Ventricular mass (g) was also higher in patients with vitamin D level <30 ng/mL (132.56±12.38 g) and patients with vitamin D level >30 ng/mL (100.12±7.98, p–0.001) (Table 6).

DISCUSSION

HTN is one of the most prevalent disorders that contributing significantly to morbidity and mortality [14]. Approximately 1 billion people globally suffer from vitamin D deficiency [15].

Several mechanisms can elucidate the relationship of vitamin D deficiency with HTN. Recent study demonstrated that 1,25(OH)2-D directly modulates the renin–angiotensin system. Vitamin D deficiency leads to secondary which have unfavorable cardiovascular effects, promoting arterial HTN, LVH, and cardiac fibrosis. Other potential mechanisms could be the actions of vitamin D on the arterial wall cells which express the vitamin D receptor (VDR) and 1-hydroxylase. Therefore, it is believed that a normal level of BP depends on the optimal level of circulating 1, 25(OH)D, which is controlled by 25(OH) D concentrations [16].

In the present study, age, gender, height, weight, and BMI were comparable between the two groups. Therefore, there were no any confounding factors in the study. Serum vitamin D was significantly lower in the hypertensive patients group (20.25±3.28 ng/mL) than in the normotensive group (38.33±6.89 ng/mL, p<0.001). About 46.0% and 34.0% of hypertensive subjects had vitamin D deficiency and insufficiency, respectively. However, 10.0% and 32.0% of normotensive subjects had vitamin D deficiency and insufficiency, respectively (p<0.001). In addition, negative correlation of vitamin D level was observed with SBP (r–0.43, p–0.001) and DBP (r–0.76, p<0.001).

Table 1: Comparison of baseline characteristics between two groups

Age group (years)	Hypertensive (%)	Normotensive (%)	p-value
<40	3 (6)	2 (4)	0.334
41–50	5 (10)	8 (16)	
51–60	19 (38)	17 (34)	
61–70	17 (34)	19 (38)	
>70	6 (12)	4 (8)	
Mean±SD	20.25±3.28	38.33±6.89	
Gender			
Male	31 (62)	34 (68)	0.529
Female	19 (38)	16 (32)	
Height	1.62±0.12	1.66±0.15	0.88
Weight	71.23±8.54	66.54±5.34	0.34
BMI	27.23±3.45	26.34±4.78	0.22
SBP	166.32±19.8	116±14.45	<0.001
DBP	96.61±9.32	75.65±8.32	<0.001

SD: Standard deviation, BMI: Body mass index, SBP: Systolic blood pressure, DBP: Diastolic blood pressure

Table 2: Comparison of ECG findings between two groups

ECG findings	Hypertensive (%)	Normotensive (%)	p-value
LAD	31 (62)	6 (12)	<0.0001
LVH	25 (50)	2 (4)	
WNL	19 (38)	44 (88)	

ECG: Electrocardiography

Table 3: Comparison of ECHO findings between two groups

ECHO findings	Hypertensive	Normotensive	p-value
Intimal thickness (mL)	0.78±0.07	0.45±0.09	<0.001
Ventricular mass (g)	126.34±14.32	72.34±8.76	<0.001

ECHO: Echocardiography

Table 4: Comparison of vitamin D level between two groups

Vitamin D level (ng/mL)	Hypertensive (%)	Normotensive (%)	p-value
Deficiency (<20)	23 (46)	5 (10)	<0.001
Insufficiency (20–30)	17 (34)	16 (32)	
Normal (31–100)	10 (20)	29 (58)	
Toxicity (>100)	0 (0)	0 (0)	
Mean±SD	20.25±3.28	38.33±6.89	

Table 5: Correlation of vitamin D level with other parameters

Parameter	Correlation coefficient (r)	p-value
SBP	−0.43	0.001
DBP	−0.76	<0.001
Intimal thickness (mL)	−0.67	<0.001
Ventricular mass (g)	−0.48	<0.001

SBP: Systolic blood pressure, DBP: Diastolic blood pressure

In the study of Ahmad *et al.* [17], 60 hypertensive and 20 normotensive subjects were included. In comparison of normotensive subjects (9.8±11.1 ng/mL), hypertensive subjects had low serum vitamin D level (24.1±16.3 ng/mL, p<0.05). Vitamin D was negatively correlated with SBP (r–0.3, p–0.006) and DBP (r–0.7, p<0.001). About 10% were suffering from vitamin D deficiency while 50% were suffered from vitamin D insufficiency while 35% show normal levels of vitamin D. Purari *et al.* [16] also reported lower vitamin D level in the hypertensive group (45.71 nmol/L) than normotensive group (62.3 nmol/L). Another study observed that patients with vitamin D levels below 37.5 nmol/L

Table 6: Comparison of ECHO findings according to vitamin D level in hypertensive subjects

ECHO findings	Patients with vitamin D level <30 ng/mL (n-40)	Patients with vitamin D level >30 ng/mL (n-10)	p-value
Intimal thickness (mL)	0.84±0.09	0.64±0.04	0.001
Ventricular mass (g)	132.56±12.38	100.12±7.98	0.001

ECHO: Echocardiography

are three times more likely to develop HTN than those with normal level (>75 nmol/L) [18].

The results of this study were matched with the study of Alpsoy *et al*. [19] which included 53 normotensives, 42 white coat HTN, and 59 sustained HTN patients recruited for this study. The participants were matched for age and gender. Plasma vitamin D levels were significantly lower in the sustained HTN group than in the white coat HTN group and normotensive group (26.4±4.9, 34.3±3.6, and 36±5 ng/mL, respectively).

Another study reported that plasma renin activity (PRA) and 1,25- dihydroxyvitamin D were inversely correlated (r–0.65) and that low 25(OH)-D levels were independently related with a 6.6 mmHg increase in SBP (95% confidence interval (CI): 1.5–11.6) after controlling other variables [20]. SBP, DBP, and MAP were considerably higher in people with lower 25(OH)D levels [17]. On the other hand, it was noted that there is no connection between BP and 25-hydroxyvitamin D levels [21-23]. Furthermore, it was stated that there is no difference between the levels of 25-hydroxyvitamin D in HTN patients and controls [23].

In the present study, LAD and LVH were significantly higher in the hypertensive group as compared to the normotensive group. A similar finding was observed in the study of Purari *et al*. Treatment with activated vitamin D may result in the regression of LVH, according to two small clinical studies of hemodialysis patients, suggesting a cardioprotective effect [24]. The hearts of vitamin D-deficient mice exhibit cardiac hypertrophy [19]. In cultured cardiomyocytes, activated vitamin D has been demonstrated to suppress proliferation and hypertrophy [25].

In the present study, a negative correlation of vitamin D level was observed with intimal thickness (r–0.67, p<0.001) and with ventricular mass (r–0.48, p<0.001). Interestingly, intimal thickness and ventricular mass were significantly higher in patients of EHT with low vitamin D (0.84±0.09 mL, 0.64±0.04 mL, respectively) than the patients of EHT with normal vitamin D levels (132.56±12.38 g, 100.12±7.98 g, respectively).

In the study of Ahmad *et al*. [17], intimal thickness and ventricular mass were significantly higher in patients with EH with low vitamin D than those with normal vitamin D levels (p<0.01). A negative correlation of vitamin D level was also observed with intimal thickness (r–0.5, p<0.001) and with ventricular mass (r–0.4, p<0.001).

In another investigation, it was discovered that the relationship between vitamin D level and IMT was inverted in HTN participants. Vitamin D's small but substantial impact on SBP was mediated by endothelial dysfunction and increased intima-media thickness (20). Another study found that participants with inadequate vitamin D level (<20 ng/mL) were 6.5 times more likely to develop CHD than subjects with appropriate vitamin D status. Several others have seen comparable outcomes. Angina and MI were more common in persons with vitamin D insufficiency in the US than in participants with appropriate levels of vitamin D, according to an NHANES study (odds ratio: 1.20 (95% CI: 1.01–1.36) [24]. A study in an Indian community found that people with low levels of vitamin D (<10 ng/mL) had a 4.5 times increased risk of MI [25]. More recently, research in the Gulf nation of Qatar found that men with insufficient vitamin D levels had a three times higher risk of MI than men with adequate vitamin D levels [26].

CONCLUSION

HTN is one of the most crucial chronic diseases, which can cause many other cardiovascular disorders and eventually may lead to death. There is a strong inverse of serum vitamin D with HTN. Vitamin D deficiency levels are considered an additional risk factor for cardiovascular morbidity and mortality. Physicians should keep a check on the vitamin D levels of their patients to curb the ever-increasing incidence of HTN.

CONFLICTS OF INTEREST

The authors declare that there were no conflicts of interest in this research.

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