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Original Research Article

Study of Vitamin D Levels in Patients with Essential Hypertension

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Abstract:

Introduction: The 7th report by the Joint National Committee on Prevention, Detection, Evaluation and Management of High Blood Pressure (BP) defines hypertension (HTN) as having systolic blood pressure of at least 140 mmHg and diastolic blood pressure of at least 90 mmHg. Of these hypertensive individuals, 95% have essential hypertension (EH), unfortunately little is known about the precise etiology and pathophysiology of EH. Stress, a high-salt diet, obesity and a lack of vitamin D have all been identified as environmental risk factors. We conducted the current study at Adesh Medical College in Shahbad to measure the levels of vitamin D in cases of essential hypertension due to the dearth of information on the causative relationship between hypo-vitaminosis D and patients with essential hypertension.

Aim: To determine the levels of Vitamin D in cases of essential hypertension**.**

Objectives: 1: To measure Vitamin D levels in stage 1 and stage 2 cases of essential hypertension.2: To compare severe deficiency (<10ng/ml) of Vitamin D in stage 1 and stage 2 cases of essential hypertension.

Methodology:150 cases of newly diagnosed hypertension attending OPD/IPD of Adesh Hospital were included in the study.

Results: Total cases of vitamin D deficiency was 70.7% (106) cases out of total cases of essential hypertension**.** Of the vitamin D deficient subjects 26.4%(28) were in stage 1 and 73.6%(78) were in stage 2 hypertension. Total cases of severe vitamin D deficiency were 23.3% (35),out of which 28.6%(10) were in stage 1 and 71.4%(25) were in stage 2 hypertension.

Conclusion: The findings of our investigation point to a high frequency of hypo-vitaminosis D in hypertension patients. There is a tendency for low vitamin D levels to be correlated with elevated systolic blood pressure.

Keywords: Hypertension, essential hypertension, vitamin D, vitamin D deficiency.

Introduction

The 7th report by the Joint National Committee on Prevention, Detection, Evaluation and Management of High Blood Pressure (BP) defines hypertension (HTN) as having systolic blood pressure of at least 140 mmHg and diastolic blood pressure of at least 90 mmHg. Worldwide, hypertension affects one billion individuals (HTN). About 25% of rural and 33% of urban Indians suffer from hypertension. Out of these, 42% in urban areas and 25% in rural areas are aware that they have hypertension1. Of these individuals, 95% have essential hypertension (EH), a kind of hypertension whose cause was unknown and which prevents them from maintaining normal blood pressure (BP) without regular medication. Unfortunately, little was known about the precise etiology and pathophysiology of EH, which makes treatment less targeted and less successful. [2] Nevertheless, less than 1% of EH are caused by recognized gene mutations that cause monogenic HTN, despite great efforts. [3] Stress, a high-salt diet, obesity and a lack of vitamin D have all been identified as environmental risk factors that contribute to the other 50% of EH cases. Dietary sources of vitamin D include egg yolks, fatty salmon, fortified milk, cereal, juice and yogurt which account for about 20% of the vitamin. The liver converts vitamin D from the skin, food, or oral supplements - including vitamins-D2 and D3 into 25-hydroxyvitamin D (25(OH)D). The most reliable marker for assessing vitamin D status was 25(OH)D, the primary circulating metabolite of vitamin D. It was primarily bound to vitamin D binding protein in serum and was measured in ng/ml (or 75 nmol/l) when vitamin D was sufficient, 20–30 ng/ml (or 50–75 nmol/l) when vitamin D was insufficient, and <20 ng/ml (or <50 nmol/l) when vitamin D deficient. At the moment, the most widely utilized cut-off points for vitamin

D levels are these ones [4]. Renal or extra-renal 1-hydroxylase transforms circulating 25(OH)D into 1,25 dihydroxy vitamin D3 (VD3), the physiologically active agonist for the vitamin D receptor (VDR), although it circulates at serum concentrations approximately 1000 times lower than 25(OH)D. Renal VD3 production, which was strongly correlated with calcium homeostasis and parathyroid hormone (PTH) levels, was primarily responsible for determining serum levels of VD3. The renal conversion of 25(OH)D to VD3 was suppressed by fibroblast growth factor-23, which limit 1-hydroxylase expression [5].

Conversely, lower calcium and high PTH levels will enhance VD3 synthesis by increasing 1-hydroxylase activity. In fact, 1-hydroxylase was expressed by a wide variety of other cell types, such as those found in the heart and vascular wall, which converts 25(OH)D into locally produced VD3, which has biological effects only locally in an autocrine or paracrine manner. It was unknown if PTH and serum calcium levels control the expression of local 1-hydroxylase. Apart from the principal organs that respond to vitamin D, which are the kidneys, parathyroid glands, and small intestine, vitamin D also affects other tissues and organs, such as the immune system, skeletal muscle, and cardiovascular system [6].

We conducted the current study at Adesh Medical College in Shahbad to measure the levels of vitamin D in cases of essential hypertension due to the dearth of information on the causative relationship between hypo-vitaminosis D and patients with essential hypertension.

Aim and Objectives

Aim: To determine the levels of Vitamin D in cases of essential hypertension

Objectives:

1. To measure Vitamin D levels in stage 1 and stage 2 cases of essential hypertension.
2. To compare severe deficiency (<10ng/ml) of Vitamin D in stage 1 and stage 2 cases of essential hypertension.

Study Population: All cases of essential hypertension fulfilling inclusion and exclusion criteria.

Inclusion Criteria:-

- 18 - 59 years of age population.
- Both sexes.
- Cases with essential hypertension (Defined as when 2 BP readings measured on right arm in sitting position after 5 minutes of rest by a trained physician. Essential hypertension was when the systolic blood pressure readings ≥140 mm Hg and/or the diastolic blood pressure readings ≥90 mm Hg)

Exclusion Criteria

- <18years and >59 years of age.
- Cases of secondary HTN
- People with chronic renal, hepatic, cardiac, gastrointestinal, skeletal, endocrine diseases, diabetes, acute critical illness and pregnancy.
- Participant who had taken Vitamin D supplementation or any other Vitamin D metabolite in the last 3 months.
- Patients who had not given consent.

Methodology

150 cases of newly diagnosed hypertension attending OPD/IPD of Adesh Hospital were included in the study. All the patients were subjected to complete physical as well as systemic examination. Routine investigations such as – Complete blood count, Liver function test, Kidney Function Test, Blood Sugar (Random) and Serum Vitamin D_3 levels was done. Any other specific investigations were done as and when required.

Method of Blood pressure measurement

Diagnosis of essential HTN was based on BP recordings with 2 or more values measured by a trained physician after 5 min of rest in the right arm in sitting position with a mercury sphygmomanometer. It was ensured that the patient must not have taken either tea, coffee, smoke or exercise within a period of 30 min before measurement.

Method of estimation of serum Vitamin D_3: Vitamin D will analysed by kinetic fluorescence immunoassay method using TOSOH-AIA-360. . Participants were classified as vitamin D deficient, insufficient, and sufficient on the basis of vitamin D concentration of <20 ng/ml, 20-30 ng/ml, and >30 ng/ml, respectively.

Observations and Results

Table 1: Summary of Basic Details

Basic Details	Mean ± SD || Median (IQR) || Min-Max OR N (%)
Age (Years)	50.17 ± 9.46 || 53.00 (48.00-57.00) || 21.00 - 59.00
Age	
21-30 Years	11 (7.3%)
31-40 Years	13 (8.7%)
41-50 Years	30 (20.0%)
51-60 Years	96 (64.0%)

Gender	
Male	82 (54.7%)
Female	68 (45.3%)
Study Parameters	Mean ± SD || Median (IQR) || Min-Max OR N (%)
Vitamin D (ng/mL)	17.61 ± 10.57 || 15.05 (10.22-23.40) || 3.60 - 72.80
Vitamin D	
<20 ng/mL	106 (70.7%)
20-30 ng/mL	24 (16.0%)
≥30 ng/mL	20 (13.3%)
Vitamin D Deficiency (Yes)	106 (70.7%)
Severe Vitamin D Deficiency (Yes)	35 (23.3%)
HTN Stage	
Stage 1	38 (25.3%)
Stage 2	112 (74.7%)

Table 2: Association between 'Vitamin D' and 'HTN Stage'

HTN Stage	**Vitamin D**				**Chi-Squared Test**	
	<20 ng/mL	**20-30 ng/mL**	**≥30 ng/mL**	**Total**	**χ2**	**P Value**
Stage 1	28 (26.4%)	4 (16.7%)	6 (30.0%)	38 (25.3%)	1.249	0.536
Stage 2	78 (73.6%)	20 (83.3%)	14 (70.0%)	112 (74.7%)		

Table 3: Association between 'Vitamin D' levels with adjusted p values.

Vitamin D	**Adjusted P Values**
<20 ng/mL vs. 20-30 ng/mL	0.707
<20 ng/mL vs. ≥30 ng/mL	0.786
20-30 ng/mL vs. ≥30 ng/mL	0.707

Table 4: Association between 'Vitamin D' and 'Systolic BP (mm Hg)

Systolic BP (mm Hg)	**Vitamin D**			**Kruskal Wallis Test**	
	<20 ng/mL	**20-30 ng/mL**	**≥30 ng/mL**	**χ2**	**p value**
Mean (SD)	162.89 (14.31)	163.88 (7.80)	159.55 (10.70)	2.474	0.290
Median (IQR)	160 (154-166)	164 (159.5-168.5)	163 (156.5-166)		
Min - Max	132 - 240	150 – 185	125 - 172		

Table 5: Association between 'Vitamin D' and 'Diastolic BP (mm Hg)'

Diastolic BP (mm Hg)	**Vitamin D**			**Kruskal Wallis Test**	
	<20 ng/mL	**20-30 ng/mL**	**≥30 ng/mL**	**χ2**	**p value**
Mean (SD)	93.63 (9.17)	94.75 (6.07)	91.95 (9.89)	1.255	0.534
Median (IQR)	94 (90-100)	94 (92-100)	93 (90-96)		
Min - Max	70 - 120	80 – 110	70 – 110		

Table 6: Association between 'Severe Vitamin D Deficiency' and 'Systolic BP (mm Hg)'

Systolic BP (mm hg)	**Severe Vitamin D Deficiency**		**Wilcoxon-Mann-Whitney U Test**	
	Yes	**No**	**W**	**p value**
Mean (SD)	162.63 (12.09)	162.59 (13.36)	1967.000	0.841
Median (IQR)	160 (152-170)	160 (156-166)		
Min - Max	146 - 190	125 - 240		

Table 7: Association between 'Severe Vitamin D Deficiency' and 'Diastolic BP (mm Hg)'

Diastolic BP (mm hg)	**Severe Vitamin D Deficiency**		**Wilcoxon-Mann-Whitney U Test**	
	Yes	**No**	**W**	**p value**
Mean (SD)	94.60 (8.41)	93.28 (8.97)	2037.500	0.913
Median (IQR)	92 (90-100)	94 (90-100)		
Min - Max	72 - 120	70 - 114		

Table 8: Odds Ratios and Relative Risks.

Predictor/Risk Factor	Outcome	Odds Ratio (95% CI)	Relative Risk (95% CI)
Severe Vitamin D Deficiency: Yes	HTN Stage: Stage 1	1.24 (0.53-2.9)	1.17 (0.62-2.08)
Severe Vitamin D Deficiency: Yes	HTN Stage: Stage 2	0.8 (0.34-1.88)	0.94 (0.72-1.16)
Severe Vitamin D Deficiency: No	HTN Stage: Stage 1	0.8 (0.34-1.88)	0.85 (0.48-1.61)
Severe Vitamin D Deficiency: No	HTN Stage: Stage 2	1.24 (0.53-2.9)	1.06 (0.87-1.4)

Total cases of vitamin D deficiency was 70.7% (106) cases out of total cases of essential hypertension. Of the vitamin D deficient subjects 26.4% (28) were in stage 1 and 73.6% (78) were in stage 2 hypertension. Total cases of severe vitamin D deficiency were 23.3% (35), out of which 28.6% (10) were in stage 1 and 71.4%(25) were in stage 2 hypertension.

Discussion

There are few data on vitamin D insufficiency in the Asian Indian population with hypertension. There is mounting evidence that vitamin D deficiency contributes to the development of metabolic syndrome and cardiovascular illnesses, based on epidemiological research conducted recently. According to a number of studies, low vitamin D levels are particularly linked to a higher risk of developing a number of illnesses, including hypertension, abnormal vascular endothelial function, vascular smooth muscle proliferation, vascular calcification, and myocardial infarction. Moreover, conflicting results have been reported from randomized trials investigating the relationship between vitamin D administration and hypertension. [7]

Thus the following study was undertaken at Adesh Medical College and Hospital, Shahbad on 150 patients with the aim of determining the levels of Vitamin D in cases of essential hypertension. Regarding the primary aim of our study to determine levels of Vitamin D in cases of essential hypertension, we observed that patients with hypertension had a lower than normal level of circulating Vitamin D in their bloodstream. The objective of our study to measure Vitamin D levels in stage 1 and stage 2 cases of essential hypertension was fulfilled. It was observed that patients with Stage 2 hypertension had relatively lower levels of Vitamin D; however, the difference was not statistically significant. We also sought to compare severe deficiency (<10ng/ml) of Vitamin D in stage 1 and stage 2 cases of essential hypertension. We observed that severe deficiency of Vitamin D was more frequently encountered in patients of stage 2 hypertension. The findings of our study correlate with previous studies on the subject few of which are mentioned below.

The findings of our study were in alignment with previous studies on the topic. In a study published in 2020, Del Pinto et al. investigated the relationship between serum vitamin D levels and the European guidelines' definition of uncontrolled blood pressure in persons receiving treatment for hypertension. Compared to individuals with vitamin D levels at least 75 nmol/l, treated hypertensive adults with vitamin D insufficiency had higher mean blood pressure (+2.4/3.5 mmHg; P < 0.01) and a 25–29% higher likelihood of uncontrolled blood pressure. [8]

Additionally, Judd et al.'s analysis of the NHANES III survey data revealed a statistically significant inverse relationship between systolic blood pressure and circulating 25(OH)D concentrations. When age was taken into account in the model, however, this link was not statistically significant, nor was it significant in the black subpopulation. [9] Christian Legarth et al. (2018) reviewed the literature to determine whether vitamin D supplementation and lowering blood pressure in hypertension individuals are related. It's interesting to note that vitamin D supplementation dramatically reduces blood pressure and renin synthesis in mice, according to experimental research. Nevertheless, there hasn't been any conclusive evidence from randomized controlled studies (RCTs) linking vitamin D administration to reductions in hypertension. [10] In order to evaluate the contribution of vitamin D insufficiency to the development of essential hypertension and the exacerbation of its vascular consequences, Sameh Ahmad Abd-El Kader et al. (2018) carried out a study. Those with low vitamin D levels exhibited a highly statistically significant increase in left ventricular mass and intimal thickness when compared to those with normal vitamin D levels. [11]

According to the study's findings, most individuals with essential hypertension also have vitamin D deficiency, hence having lower serum vitamin D levels is thought to be an additional risk factor for cardiovascular morbidity and mortality. [11] In order to determine the impact of vitamin D supplementation on primary hypertension, Vida Sheikh et al. (2020) carried out a double-blind, randomized clinical trial on patients with essential hypertension who were 26–84 years of age. Patients were randomized to either a placebo or vitamin D supplements. The trial's findings point to possible advantages of vitamin D supplementation for blood pressure endpoints. [12] In a North Indian population cohort, Shalini Priya et al. (2017) investigated the relationship between vitamin D and essential hypertension. From the outpatient department, 102 subjects who were essential hypertensive but lacking in Vitamin D were recruited. For comparison, 99 healthy, sex- and age-matched non hypertensive controls were included. Vitamin D deficiency was more prevalent in cases than controls. The scientists came to the conclusion that hypo vitamin D tends to be associated with higher systolic blood pressure and is more common in people with hypertension. Larger research is necessary to validate this link, though. [13] The relationship between serum Vitamin D levels in hypertensive and non-hypertensive patients, as well as in patients with isolated systolic hypertension (ISH), isolated diastolic hypertension, and systolo-diastolic hypertension, was investigated by Arnab Kar et al. (2018) through a cross-sectional study involving 154 patients. The relationship between serum vitamin D and blood pressure was inverse. The negative connection between serum Vitamin D and SBP is still statistically significant in populations with serum Vitamin D levels <30 ng/ml (deficient or inadequate). [14] Mehmet Demir et al. (2012) examined the 25-OH vitamin D levels in hypertension patients who were dippers and those who were not. The study's findings imply that there is a positive relationship between blood pressure and vitamin D insufficiency, and that non-dipper hypertension may be associated with vitamin D deficiency. [15] In patients with essential hypertension, Arash Aghajani Nargesi et al. (2016) investigated the relationship between vitamin D insufficiency and the risk of coronary heart disease. The greatest number of hard CHD events were observed in patients in the lowest quartile of 25-hydroxyvitamin D. [16] Yusuf Karadeniz et al. (2021) looked at an 8-year follow-up and the association between blood pressure and vitamin D levels in healthy persons. . The study found a substantial correlation between low levels of vitamin D and HNBP (high normal blood pressure) and (normal blood pressure) NBP. In an 8-year follow-up, low vitamin D levels were also linked to the onset of hypertension. [17]

Conclusion and Summary

Despite plenty of sunshine, vitamin D insufficiency is a rising risk factor for several comorbidities globally. Numerous research had been conducted too far to demonstrate a link between vitamin D deficiency and hypertension. Although the connection has previously been proven in the population of the West, further evidence is required in the Indian context. The findings of our investigation point to a high frequency of hypo-vitaminosis D in hypertension patients. There is a tendency for low vitamin D levels to be correlated with elevated systolic blood pressure. Larger randomized trials are yet required to validate these possible results. Consequently, since vitamin D supplementation is safe, well-tolerated by patients, and can significantly lower both systolic and diastolic blood pressure while assisting patients in returning to normal serum vitamin D levels, it may be considered in the treatment of essential hypertension in patients with vitamin D deficiency.

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