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Correlation between serum vitamin-d and essential hypertension

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Abstract
Background: Inadequate vitamin D affects about 50% of the world's population. Hypovitaminosis D pandemic may largely be attributed to lifestyles and environmental conditions which limit exposure to sun. Adequate exposure to sunlight is necessary for synthesis of ultraviolet-B (UVB) - induced vitamin-D in the skin.
Objective: To study the correlation between the level of vitamin- D and the presence of essential hypertension in patients presenting to a hospital.
Methods: The subjects were segregated into two groups: Group 1 (case group) - 50 patients with essential hypertension, Group 2 (control group) - 50 ostensibly healthy individuals. Each subject was interviewed and a standardized questionnaire was answered and completed, which included demographics, anthropometric profile, individual characteristics associated with major risk factors for cardiovascular disease, past medical history, sun exposure details (type of job and average time spent in the sun per day), and biochemical parameters. Hypertension was documented based on disclosure of known hypertensive patients self-reporting on out-patient visit or newly diagnosed hypertensives based on physician measurements. Vitamin D levels were measured from a venous sample taken at the time of hospital visit.
Results: The control group comprised 50 patients, 34 of whom were male and 16 of whom were female, and 50 hypertensive patients, 36 of whom were male and 14 of whom were female. There was no significant difference in the gender distribution of the study and control groups (P=0.8272). The hypertensive group had an age of 58.7±9.3 years and the normotensive group 60.5±5.3 years. There was no statistically significant difference. The normotensive and hypertensive patients studied had no significant differences in height, weight, or BMI ($p > 0.05$). The normotensive group's systolic and diastolic blood pressures (114±5.89 and 75.0±5.0) were considerably lower than the hypertensive group's (162.10±16.5 and 95.90±9.30).
Conclusion: Vitamin D and essential hypertension have an inverse relationship. When systolic and diastolic blood pressure were considered as continuous variables, a substantial relationship of high blood pressures corelating with low vitamin-D levels was observed. In addition, left ventricular hypertrophy was also shown to be correlated to hypovitaminosis D.

Keywords: Vitamin-D, Hypertension, Calcium, Hypovitaminosis D

Introduction
The deficiency in vitamin D is quite widespread and of paramount significance, especially with regard to Indian public health. Vitamin D insufficiency is known to be related to several of the musculoskeletal disorders. Vitamin D supplementation is advised in order to avoid rickets in children and osteomalacia in adults. Vitamin D controls bone and mineral metabolism and hemostasis. It has been found that all human cells have vitamin D receptors (VDRs). Hence vitamin D insufficiency has been associated with a number of chronic extra skeletal illnesses [1].
Inadequate vitamin D levels affects about 50% of the world's population. Hypovitaminosis D pandemic may largely be attributed to lifestyles and environmental conditions which limit exposure to sun which is necessary for skin synthesis of ultraviolet-B (UVB) - induced vitamin-D [2].
Black people absorb more UVB than white people due to difference in skin's melanin and consequently need more sunlight in order to create equal quantities of vitamin D [3]. During winter months, levels of UVB radiation decrease with an increased distance from earth's equator. Similarly, in areas with increased air pollution, UV-B rays reach the earth surface inadequately.

Consequently, increases in blood pressure levels were all associated with different variables causing lower UVB-induced vitamin D production, such as high latitude, industrialization, and dark skin [4].
Deficiency of vitamin D has an additional component of elevated risk of cardiovascular events, although it remains uncertain if this combination has a direct correlation. One of the probable reasons for a correlation between vitamin D and cardiovascular diseases could be the influence of vitamin D on blood pressure [5].
In this study, we will outline the processes hypothesized to underpin the association between vitamin D and systemic arterial hypertension, as well as analyze the clinical data supporting this relationship.

Materials and methods

Study Design: It's a Cross-Sectional Study
Sample Size: 100 patients (50 Cases and 50 Controls)

Inclusion Criteria

- Patients over the age of 45 years with essential hypertension.

Exclusion Criteria: Patients with

- <45 years of age
- Calcium/Vitamin – D supplementations
- Long term diuretics
- Pregnancy
- Secondary hypertension
- Other comorbid conditions like
  - diabetes mellitus
  - hypothyroidism
  - renal failure

Controls: Age and gender matched participants above the age of 45, attending out-patient clinics of departments of Ophthalmology and Otorhinolaryngology with no history of systemic hypertension and having normal blood pressure, and who fulfilled the aforementioned exclusion criteria.
The study group determined by the aforementioned criteria (inclusion and exclusion criteria) was first briefed about the study's purpose. After obtaining written informed consent from willing participants, the subjects were enrolled. The subjects were segregated into two groups: Group 1 (patient group) - 50 patients with essential hypertension, Group 2 (control group) - 50 ostensibly healthy individuals. Each subject was interviewed and a standardized questionnaire was filled up, which included demographics, anthropometric profile, individual characteristics associated with major risk factors for cardiovascular disease, past medical history, sun exposure details (type of job and average time spent in the sun per day), and biochemical parameters. On the baseline and follow-up assessments, hypertension was detected based on self-reports or physician measurements.

Statistical Analysis: All data were statistically evaluated using the t-test and the chi-square test in SPSS Version 21, with $p<0.05$ deemed significant.

Observation and results

Table 1: Distribution based on age and gender across cases and controls

Sex	Normotensive cases		Hypertensive Cases	
	No	**%**	**No**	**%**
Male	34	68%	36	72%
Female	16	32%	14	28%
Total	50	100%	50	100%
P-Value	0.8272 Not significant			
AGE GROUP (in years)				
45-50	10	20%	18	36%
51-60	18	36%	12	24%
61-70	21	42%	16	32%
> 70	1	2%	4	8%
Total	50	100%	50	100%
Mean ± S.D	60.5±5.3		58.7±9.3	
P-Value	0.131			
Variables	**Mean**	**SD**	**Mean**	**SD**
Height (in cms)	166.5	6.0	163.5	6.5
P-Value	0.1110			
Weight (in kgs)	70.5	7.5	66.1	8.5
P-Value	0.1049			
BMI	25.41	2.79	25.5	3.05
P-Value	0.669			
SBP	114	5.89	162.10	16.5
P-Value	0.0001			
DBP	75.0	5.0	95.90	9.30
P-Value	0.0001			

The control group comprised 50 patients, 34 of whom were male and 16 of whom were female, and 50 hypertensive patients, 36 of whom were male and 14 of whom were female. There was no significant difference in the gender distribution of the study and control groups (P=0.8272).

The hypertensive group had an age of 58.7±9.3 years and the normotensive group 60.5±5.3 years. There was no statistically significant difference.
The normotensive and hypertensive patients studied had no significant differences in height, weight, or BMI ($p > 0.05$).

The normotensive group's systolic and diastolic blood pressures (114±5.89 and 75.0±5.0) were considerably lower than the hypertensive group's (162.10±16.5 and 95.90±9.30).

Table 2: Distribution based on Vitamin-D level across Cases and controls

Vitamin D level	Normotensive Cases		Hypertensive Cases	
	No	%	No	%
Level – I - (< 37.5 nmol L^{-1})	3	6.0%	29	58.0%
Level II - (<37.5 – 49.9 nmol L^{-1})	10	20.0%	4	8.0%
Level III - (50 – 74.9 nmol L^{-1})	27	54.0%	10	20.0%
Level IV- (75 – 100 nmol L^{-1})	10	20.0%	7	14.0%
Vit D (in nmol L^{-1}) Range	24.9-90		20.8-88.9	
Mean±S.D	62.4±18.5		46.5±20.5	
P-Value	0.0071 Significant			

The normotensive patients had a Vitamin D level of 62.4 nmol/L on an average. This was substantially greater than the mean values observed in hypertensive patients (46.5 nmol L-1). This was a statistically significant.

Table 3: Distribution based on Vitamin – D levels and other parameters

Variable	Value (Mean ±SD) for cases with Vit. D level				'p'
	I	II	III	IV	
Urea	27.7±7.3	23.3±1.6	28.3±7.5	29±6.9	0.6670 Not significant
Corr. Calcium	7.65±0.41	7.58±0.45	8.02±0.30	8.5±0.50	0.0059 Significant
Phosphate	3.97±0.69	3.8±1.30	3.86±0.79	3.52±0.49	0.5439 Not significant
Albumin	3.51±0.45	3.73±0.23	3.55±0.29	3.4±0.20	0.4623 Not significant
Sr. Creatinine	1.2±0.25	1.07±0.19	1.16±0.15	1.13±0.15	0.7159 Not significant

In hypertensives, there was a positive correlation between calcium and vitamin D levels.

Table 4: Vitamin-D levels and ECG Changes

Risk factors - ECG	No. of cases with Vit D level								P-Value
	I		II		III		IV		
	No	%	No	%	No	%	No	%	
LAD, LVH (36)	30	83.3	1	2.7	3	8.3	2	5.5	0.0001
WNL (14)	2	14.2	3	21.4	5	35.7	4	28.5	Significant

In instances where vitamin D levels were low, the percentage of ECG abnormalities was substantially greater (level I)

Table 5: Vitamin-D and concentric LVH

Risk factors - Echo	No. of cases with Vit D level								P-Value
	I		II		III		IV		
	No	%	No	%	No	%	No	%	
Normal (32)	7	21.8	5	15.6	11	34.3	9	28.1	0.0001
Abnormal (18)	16	88.8	2	11.1	-	-		-	Significant

The percentage of aberrant echocardiographs was substantially greater in cases when vitamin D levels were low (level I)

Table 6: Vitamin D levels and BP

Vit D level	SBP		DBP	
	Mean	SD	Mean	SD
I	175.23	9.8	101.3	8.3
II	154.23	3.6	96.3	5.3
III	146	3.9	88.65	4.2
IV	141	2.7	84.38	4.5
P-Value	(0.0001) significant			

There was a significant relationship between blood pressure values and vitamin D levels in hypertension patients (p 0.05).

Discussion

Hypertension in both developed and developing nations is a significant cause of mortality and morbidity, which is

generally diagnosed by health care workers during regular checks.

The correlation between vitamin D deficiency and high blood pressure can be attributed to a number of mechanisms. Even though the link between circulating vitamin D levels and renin activity has previously been highlighted in important clinical hypertension research, 1.25(OH)2-D has only recently been shown to directly influence the renin–angiotensin system.

Other possible pathways include vitamin D's effects on vessel wall, cells such as endothelial cells, vascular smooth muscle cells, and macrophages, which all express the vitamin D receptor (VDR) and 1α-hydroxylase. As a result, a normal level of BP is considered to need an optimum amount of circulating 1,25(OH)D, which is regulated by 25(OH)D concentrations.

Our findings corroborate these processes, and Burgaz *et al.* found that males with vitamin D levels of <37.5 nmol/L had a three-fold higher risk of hypertension compared to those with normal levels (>75 nmol/L) [6, 7].

In this study age, gender, and physical characteristics such as BMI were all adjusted between the normotensive and hypertension groups. The ‘p' value indicated that there was no confounding factor. Random blood sugar (RBS) and renal functions also were matched for both groups. Conversely, as compared to normotensive individuals, serum uric acid was found to be higher in the hypertension group. However, relation of increased uric acid levels and vitamin D levels has to be determined. Cannon *et al*. did a study that showed similar results of increased uric acid levels in hypertensive individuals [8].

In contrast to the normotensive group, hypertensive patients had retinopathy, left ventricular hypertrophy on echocardiography, and electrocardiographic abnormalities suggesting left axis deviation and left ventricular hypertrophy. The mean vitamin-D level in male hypertension patients was lower than that in females, although the difference was not statistically significant. This is in accordance to research by Bansal *et al* and his colleagues [9].

When compared to hypertensive patients, the serum vitamin-D level was substantially lower in normotensive patients. Hintzpeter B *et al*., found a substantial negative relationship between plasma 25(OH)D levels and blood pressure and hypertension in his observational research [10].

Although numerous research by Burgaz *et al*., and other authors have shown an inverse relationship between vitamin-D and hypertension, few studies, such as the one by Formann *et al*., have shown no significant relationship between vitamin-D level and hypertension [11]. Given the uncertainties, it is recommended that prospective studies be conducted among vitamin-D deficient individuals and followed up on to determine the rate of incident hypertension.

Conclusion

Vitamin D and essential hypertension have an inverse relationship. Left ventricular hypertrophy was shown to be correlated to hypovitaminosis D. When systolic and diastolic blood pressure were considered as continuous variables, a substantial relationship with low vitamin-D levels was observed. Hence regular measurement and subsequent replacement of vitamin D must be recommended as a regular practice.

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