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A Study of Association of Serum Vitamin D Level with Hypertension in GNRC Hospital, Dispur, ASSAM

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Abstract: ***Background**: Evidence suggests that low levels of Vitamin D may adversely affect the cardiovascular (CV) system. Several studies have been done regarding the relation and possible causative role of Vitamin D in CV disorders and its well-known risk factors; The aims were as follows: (1) To study the relation between serum Vitamin D level between nonhypertensive and hypertensive patients. (2) To study the relation of serum Vitamin D levels in patients with isolated systolic hypertension (ISH), isolated diastolic hypertension, systolo-diastolic hypertension, and their comparison with nonhypertensives. **Materials and Methods**: A cross-sectional study was conducted with 154 patients attending cardiology OPD of GNRC Hospital of Dispur, ASSAM from June 2016 to June 2019. The Vitamin D was measured by direct ELISA method. Blood pressure (BP) measurements were done. Statistical analysis was done by using SPSS 16.0 for Windows. Results: The Vitamin D level in the hypertensive group was 22.36 ± 12.64; ISH Group was 22.04 ± 14.26; the isolated diastolic hypertension (IDH) Group was 18.82 ± 0.00; Then, the mean value of Vitamin D in nonhypertensive Group (27.47 ± 13.43) was significantly (P < 0.05) higher than IDH, SDH, and the hypertensive as a whole groups. The relation with ISH Group also reached near significance (P = 0.074). There was a negative correlation with BP and serum Vitamin D. This remained statistically significant (P = 0.044) for systolic BP (SBP) and near significant (P = 0.075) for mean arterial pressure. In population having serum Vitamin D <30 ng/ml (deficient or insufficient), the negative correlation relationship between SBP and serum Vitamin D remains statistically significant (P = 0.010). **Conclusion**: Among the hypertensives, SDH shows significantly lower levels of serum Vitamin D. The patients with ISH show a trend, though not statistically significant, toward a lower level of Vitamin D compared to the non-hypertensive population.*

Keywords: Hypertension, isolated diastolic hypertension, isolated systolic hypertension, mean arterial pressure, Vitamin D

1. Introduction

Vitamin D is an essential component of our body. A growing body of evidence suggests that low levels of Vitamin D may adversely affect the cardiovascular (CV) system.[1] Low levels of 25-hydroxyvitamin D (25[OH]D) are associated with many markers of CV disease; for example, hypertension, increased vascular resistance, and increased left ventricular mass index.[2-4] In addition, 25(OH)D levels correlate inversely with coronary calcification, an indicator of atherosclerosis, and a precursor, of CV events.[5] Deficient or insufficient serum 25(OH)D levels have been documented in patients with myocardial infarction, heart failure, stroke, diabetic CV disease, and peripheral arterial disease.[6-10] Till date, several studies have been done regarding the relation and possible causative role of Vitamin D in CV disorders and its well-known risk factors; however, Hypertension itself is an independent risk factor for many CV and neurological disorders. In this study, we will find out the relationship between the 25(OH)D level and hypertension in persons attending the Cardiology outpatient department (OPD) of GNRC Dispur, ASSAM.

2. Materials and Methods

This cross-sectional study was conducted at the cardiology OPD of a GNRC, Dispur of Guwahati, ASSAM from June 2016 to June 2019. The patients aged >40 years with any grade of hypertension and normotension without any clinically apparent cardiac, hepatic, neurologic, or renal disorder were included in the study. Simple active infections were corrected before inclusion. The patients having diabetes mellitus, abnormal renal function, (estimated glomerular filtration rate <60 ml/min/1.73 m^2 by Modification of Diet in Renal Disease formula,[11] clinical or laboratory evidence of secondary hypertension, already on Vitamin D supplement and/or steroid therapy, chronic inflammatory conditions, abnormal resting electrocardiography (ECG), abnormal liver function tests (LFTs), abnormal thyroid function, and patients not giving consent for the study were excluded from the study.

A total of 154 patients were selected for the study. Assuming the prevalence of Vitamin D deficiency 50% (P) in *n* population, the sample size was calculated by applying the formula

$$n = Z^2 \times P \times (1 - P)/L^2$$

$n = 150$

where $Z = 1.96$. $P = 50\%$. L = Absolute allowable error (8%).

Considering a 20% attrition rate initially a total of 180 patients were selected by systematic random sampling. Among those attending medicine OPD, every 10th patient was selected as a sample in a specified weekday, every week. Data collection was done from July 2016 to May 2019. Among those selected, 21 were excluded from the study due to calculated GFR <60; three having hypothyroidism, and two did not give consent. Hence, the final number of the sample was 154.

History taking

- Age, sex, and religion (Hindu, Muslim, and Others) of the participants were noted as per voter ID card
- Dietary pattern was classified as non-vegetarian and vegetarian
- Sunlight exposure was quantified as average hours of direct sunlight per day based on direct questioning
- Smoking status was defined as smokers and nonsmokers. Smokers Group included current smoker (having regular smoking in the preceding year - any number of bidi, cigarette) and former smoker (quit smoking 1 year back)[12]
- Alcohol addiction was defined as patients taking at least one or two standard drink per day. Nondrinker was defined to those having never taken a drink or social drinker with lesser frequency than the previously mentioned values
- Diabetes was defined as per the American Diabetes Association Guidelines 2011.

Measurements

Blood pressure

Blood pressure (BP) was measured in the sitting position using a mercury sphygmomanometer. Patients were kept seated quietly for at least 5 min in a chair with feet on the floor and arm supported at heart level. Caffeine, exercise, and smoking were avoided for at least 30 min before measurement. An appropriately sized cuff (cuff bladder encircling at least 80 percent of the arm) was used to ensure accuracy. At least, two measurements were taken, and the average was recorded. For manual determinations, palpated radial pulse obliteration pressure was used to estimate systolic BP (SBP)– the cuff was inflated 20–30 mmHg above this level for the auscultatory determinations; the cuff deflation rate for auscultatory readings was 2 mmHg per second. SBP is the point at which the first of two or more Korotkoff sounds was heard (onset of phase 1), and the disappearance of Korotkoff sound (onset of phase 5) was used to define diastolic BP (DBP).

The hypertension categories were defined[14,15] as follows:

Hypertension (overall): SBP of ≥140 mmHg and/or DBP of ≥90 mmHg, or use of antihypertensive drugs, including diuretics.

- Isolated systolic hypertension (ISH): When SBP ≥140, DBP <90 mm Hg
- Isolated diastolic hypertension (IDH): When SBP <140, DBP ≥90 mmHg
- Nonhypertensive was defined SBP <140, DBP <90 mmHg
- Mean arterial pressure (MAP) was defined as 1/3 SBP + 2/3 DBP.

Height, weight, body mass index, and waist circumference

Body weight (kg) was measured without upper clothes and shoes using a calibrated balance beam scale. Height (cm) was measured using a stadiometer. Body mass index (BMI) was calculated by weight divided by height squared (kg/m^2). BMI >18.5 ≤24.9 was considered as normal, BMI ≤18.5 was considered underweight, BMI ≥25 ≤29.9 overweight, BMI ≥30 obesity. Waist circumference (cm) was measured midway between the lower rib margin and the iliac crest following a normal expiration.[16]

Vitamin D

Blood samples were obtained and centrifuged immediately to separate the serum portion. Patients were allowed to have tea and toast, but no dairy products before blood sampling. These samples were analyzed either within 30 min of collection or in case of expected delay, were stored at −40°C for analyzing later on.

For measurement, a competitive ELISA technique with a selected monoclonal antibody recognizing 25(OH) D was used (immundiagnostik 25[OH]D direct ELISA). The intra- and inter-assay coefficients of variation were 10.0% and 8.0%, respectively. The analyses were carried out at Pathology department of GNRC Hospital, ASSAM.

Vitamin D status was categorized as follows [Table 1]:[17]

Deficiency (moderate, severe), insufficiency, and sufficient (normal) level.

Other investigations

Other laboratory tests and/or imaging studies were done when indicated to rule out secondary hypertension.

- Ultrasonography (USG) of the kidney, ureter, and bladder: To look for kidney size.
- USG Doppler study of renal artery (as and when necessary)
- Fasting blood sugar, postprandial blood sugar, T_3 Na+, K+, creatinine, LFT, ECG.

Statistical analysis of data

The data were entered in Microsoft Office Excel Worksheet and expressed as mean ± standard deviation for continuously distributed variables and in absolute numbers and percentages for discrete variables. Chi-square test was used for testing of significance in case of discrete variables, and independent t-test was used to test continuous variables. Tests for a linear trend were conducted by multivariate linear regression analysis. Statistical analysis was done using SPSS 16.0 for Windows Microsoft Corporation 2008. For each test, a 95% confidence interval was used. Results were considered statistically significant if $P < 0.05$.

3. Results

The present study included 154 patients. There were 98 male (63.63%) and 56 (36.37%) female patients. The mean age of the participants in this study was 53.45 (±10.661). The mean age of the male participants was 55.73 (±11.156) while that of the female participants was 49.45 (±8.427) [Table 2].

In our study, the prevalence of hypertension was 53.24% in total. For male and female population, the figure was 53.06% and 53.57%, respectively [Table 3].

Correlation analysis [Table 4] between systolic, diastolic, and MAP with serum Vitamin D level shows that there was a negative correlation with BP and Serum Vitamin D though the relation remained statistically significant (*P* = 0.044) for systolic BP and near significant (*P* = 0.05–0.09) for MAP.

As other covariates such as age, sunlight exposure, and waist circumference were also having a significant correlation with SBP and MAP [Table 4], Multivariate linear regression analysis was performed after adjusting for those variables.

In population having serum Vitamin D < 30 ng/ml (deficient or insufficient), the negative correlation relationship between SBP and serum Vitamin D remains statistically significant (P = 0.010), i.e., Vitamin D had an independent negative impact on SBP [Table 5 and Model 1]. There was no independent impact of Vitamin D on SBP after adjusting for age, sunlight exposure and waist circumference in Vitamin D sufficient population [Table 5 and Model 2].

Similarly, the near significant correlation between Vitamin D and MAP became insignificant after adjusting for age, sunlight exposure, waist circumference, and BMI [Table 6].

In this study, 53.24% population was hypertensives. Among them, 35.36% having ISH, 2.44% having IDH, and 62.20%. having SDH [Table 7 and Figure 1]. The Vitamin D level in as a whole hypertensive Group was 22.36 ± 12.64; ISH Group was 22.04 ± 14.26; the IDH Group was 18.82 ± 0.00; Comparing the serum Vitamin D level of these individual Groups with that of the nonhypertensive Group (27.47 ± 13.43), it showed that the mean value of Vitamin D in nonhypertensive Group (27.47 ± 13.43) was significantly (*P* < 0.05) higher than IDH, SDH, and the hypertensive as whole groups. The relation with ISH Group also reached near significance (*P* = 0.074).

Table 1: Vitamin D status definitions [17]

Definition	Serum 25-hydroxyvitamin D (ng/ml)
Deficiency	
Severe deficiency	≤10
Moderate deficiency	10-20
Insufficient	≥20-30
Sufficiency	≥30

1 ng/ml=2.5 nmol/l, 1 nmol/l=0.4 ng/ml

Table 2: Mean age and standard deviation of the study population

	Gender	n	Mean±SD	SEM
Age	Male	98	55.73±11.156	1.127
	Female	56	49.45±8.427	1.126
	Total	154	53.45±10.661	0.859

SD: Standard deviation; SEM: Standard error of mean

Table 3: Distribution of hypertension in the study population according to gender

Variables	Sub-group	Male (*n*=98), *n* (%)	Female (*n*=98), *n* (%)	Total (*n*=154), *n* (%)
Hypertension	Hypertensive	52 (53.06)	30 (53.57)	82 (53.24)
	Nonhypertensive	46 (46.97)	26 (46.42)	72 (46.75)

Table 4: Correlation analysis of blood pressure with other variables

Variables	SBP		DBP		MAP	
	Pearsons correlation	*P*	Pearsons correlation	*P*	Pearsons correlation	*P*
Age	0.416	<0.0001	−0.012	0.880	0.225	0.005
Sunlight	−0.217	0.007	−0.197	0.014	−0.231	0.004
Height	−0.039	0.632	−0.136	0.093	−0.094	0.247
Weight	0.040	0.621	0.118	0.144	0.087	0.284
BMI	0.067	0.411	0.198	0.014	0.143	0.076
Waist	0.156	0.054	0.225	0.005	0.204	0.011
Vitamin D	−0.162	0.044	−0.150	0.196	−0.144	0.075

BMI: Body mass index; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; MAP: Mean arterial pressure

Table 5: Multivariate linear regression analysis of systolic blood pressure with Vitamin D and other co-variates

Model 1 (cases with Vitamin D <30 ng/ml): Coefficients

Model 1	Unstandardized coefficients		Standardized coefficients	*t*	*P*
	B	SE	Beta		
Constant	76.468	18.795		4.068	<0.0001
Age	1.231	0.180	0.527	6.858	0.000
Sunlight	−1.428	1.409	−0.080	−1.013	0.313
Waist	0.257	0.157	0.126	1.641	0.104
Vitamin D	−0.872	0.332	−0.208	−2.632	0.010

*Adjusted R^2=0.324, SE of the estimate=21.652, df=4, significance=0.00

Model 2 (cases with Vitamin D ≥30 ng/ml): Coefficients

Model 1	Unstandardized coefficients		Standardized coefficients	t	Significant
	B	SE	Beta		
Constant	70.471	58.92		1.196	0.24
Age	−0.189	0.815	−0.043	−0.232	0.818
Sunlight	−14.306	4.988	−0.487	−2.868	0.007
Waist	1.347	0.501	0.419	2.686	0.011
Vitamin D	0.422	0.564	0.129	0.748	0.46

*Adjusted R^2=0.217, SE of the estimate=33.63, df=4, significance=0.018
SE: Standard error

Table 6: Multivariate linear regression analysis of mean arterial pressure with Vitamin D and other covariates

Model 1 (cases with Vitamin D <30 ng/ml) coefficients

Model 1	Unstandardized coefficients		Standardized coefficients	*t*	*P*
	B	SE	Beta		
Constant	75.126	13.369		5.619	<0.0001
Age	0.432	0.134	0.313	3.234	0.002
BMI	0.655	0.594	0.177	1.103	0.272
Sunlight	-1.236	.9677	-0.117	-1.278	0.204
Waist	-0.003	0.184	-0.003	-0.017	0.987
Vitamin D	−0.317	0.229	-0.128	-1.384	0.169

*Adjusted R^2=0.092, SE of the estimate=14.826, df=5, significance=0.007

Model 2 (cases with Vitamin D ≥30 ng/ml) coefficients

Model 1	Unstandardized coefficients		Standardized coefficients	*t*	Significant
	B	SE	Beta		
Constant	58.869	35.153		1.675	0.104
Age	-0.294	0.502	-0.107	-0.586	0.562
BMI	1.264	1.215	.279	1.041	0.306
Sunlight	-11.463	3.472	-0.629	-3.302	0.002
Waist	0.691	0.440	0.346	1.572	0.126
Vitamin D	0.345	0.371	0.171	0.929	0.360

*Adjusted R^2=0.327, SE of the estimate=19.349, df=5, significance=0.003

Table 7: Comparison of Vitamin D level between nonhypertensive and isolated systolic, isolated diastolic hypertensive groups

Variables	Total, *n* (%)	Serum Vitamin D (mean±SD)	*P*
ISH	29 (35.36)	22.04±14.26	0.074
IDH	2 (2.44)	18.82±0.00	<0.0001
Hypertensive as a whole	82 (100)	22.36±12.64	0.018
Nonhypertensive	72	27.47±13.43	Reference*

*Test applied: Independent t-test. ISH: Isolated systolic hypertension; IDH: Isolated diastolic hypertension; SD: Standard deviation

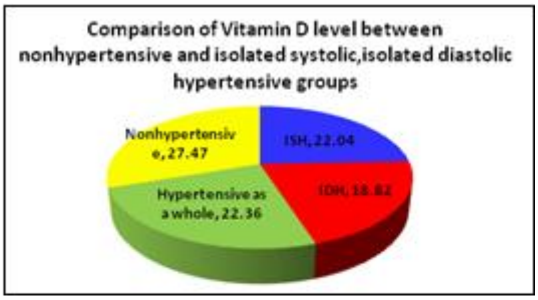

Figure 1: Comparison of Vitamin D level between nonhypertensive and isolated systolic, and isolated diastolic hypertensive groups

4. Conclusion

In this study, Vitamin D deficiency is significantly prevalent in otherwise healthy middle-aged and elderly population with significant relation with female gender (irrespective of the religion status), vegetarian diet, higher waist circumference, and patients with higher BMI. The association of diabetes with hypertension is significantly related with lower blood level of Vitamin D compared to nondiabetic, normotensive healthy population. Among the hypertensives, ISH shows significantly lower levels of serum Vitamin D. compared to the nonhypertensive population. The relationship of Vitamin D status with IDH was not much conclusive, in our study, due to a very low patient number.

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