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Relation between Serum 25-Hydroxy Vitamin D and Blood Pressure in Sunsari and Morang Districts of Nepal

Perspective Article

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Abstract

Background: Vitamin D has a great impact on multiple body systems including cardiovascular health and blood pressure. Objective: Our study aims to examine the relation between the circulating serum 25 (OH)D level and systolic and diastolic Blood pressure. Method: This cross-sectional study was conducted on people above the age of 18 years from the Sunsari and Morang districts of Nepal. After receiving written informed consent, a questionnaire was administered to obtain sociodemographic variables followed by examining blood pressure (BP) and anthropometric measurements. Blood samples were drawn, serum separated and 25 (OH) D level was measured by Chemiluminescence immunoassay (CLIA) technique via Maglumi 1000 analyzer (SNIBE Co, Ltd, China). Serum 25(OH)D was classified as deficient, insufficient and sufficient (<20 ng/ml, 20–29 ng/ml and 30–100 ng/ml respectively). Blood pressure was classified according to seventh Joint National Committee on the Prevention, Detection, Evaluation and Treatment of High Blood Pressure. Result: There was negative correlation between log 25(OH) D and systolic blood pressure (R=–0.3; p value: 0.001), similarly the correlation between serum 25(OH)D and diastolic blood pressure was negative one (R=–0.1; p value: 0.1). Conclusion: Correlation between log 25(OH)D and systolic BP was statistically significant, however the strength of correlation was a weak negative one similarly the correlation between serum 25(OH)D and diastolic blood pressure was weak negative one.

Keywords: Blood pressure, serum 25(OH)D, vitamin D deficiency

Introduction

In recent years, empirical studies have established a wider role of vitamin D affecting immunity, mood, cognition, reproductive health, and cardiovascular system including blood pressure [1,2,3]. Vitamin D performs this wide array of work by binding to its cytoplasmic receptor which translocates to the nucleus and regulates gene expression [4]. Vitamin D induces genes for calcium-binding protein which increases calcium absorption from the duodenum and calcium influx into vascular smooth muscles [5,6]. Since intracellular free calcium can trigger vascular smooth muscle contraction which can modulate blood pressure; this raises a question as to whether vitamin D regulates blood pressure. If so, does it regulate both systolic and diastolic blood pressure?

Many scientific studies have indeed explored the relation between Vitamin D and blood pressure giving conflicting results. A cross-sectional survey conducted in United States found a significant inverse relation between serum 25(OH)D and blood pressure; which remained the same even after adjusting for age, sex, ethnicity, and leisure–time physical activity [7]. A study conducted by Judd et al examined the relation of serum 25(OH)D with blood pressure categorized as per Joint National Committee 7 between white and black populations. They found stage 2 hypertensives had a significantly lower serum 25(OH)D compared to normotensives, amongst the white population. The same did not hold true for the black subpopulation or when age was included in the model [8].

Unlike these findings, a population-based cross-sectional study conducted on the Chinese population concluded vitamin D did not have independent association with blood pressure [9]. Similarly, another study conducted in Amsterdam amongst their aging population found no significant association between serum 25(OH)D and systolic and diastolic blood pressure [10].

Keeping these conflicting evidence in mind, we aim to examine the relationship between the circulating serum 25 (OH)D level and systolic and diastolic BP.

Methods

Participant enrollment

A cross-sectional study was conducted in people above the age of 18 years from the Sunsari and Morang districts of eastern part of Nepal for period of two months from May to July 2018. Sample size was calculated using the formula $n = Z^2 \times p \times q / d^2$

Where n: sample size, z: z score at 95% confidence interval (1.96), d: margin of error 0.05, p: estimated prevalence of hypertension among vitamin d deficient (0.93) [11].

n= 100

Participants were asked to give consent for the study and refusing to do so were excluded. Pregnant, lactating women and on anti–hypertensive medication were also excluded from the study. Ethical approval was obtained from the Biochemistry Departmental research unit of B.P Koirala Institute of Health Sciences. Questionnaire was administered to obtain sociodemographic variables followed by examining blood pressure (BP) and taking anthropometric measurements. Blood samples were drawn for measuring vitamin D.

Sociodemographic variables and anthropometric measurements

We included gender, ethnic groups (Brahman and Chhetri, Newar, Janajati, Madhesi and Dalit), age groups (≤ 60 years and >60 years), residential district (Sunsari and Morang), dietary habit (vegetarian and non–vegetarian), tobacco consumption (use tobacco: smoking, chewing tobacco and does not use tobacco), alcohol intake (takes ≥2 glasses of alcoholic beverages per week: drinks alcohol, takes<2 glasses or life time abstainers: does not drink alcohol), employment status (employed and unemployed including housewives), education status (illiterate, primary school, high school, above high school). Body weight and height were measured using standard procedures. Body mass index (BMI) was calculated as weight (kg) divided by height squared (m^2). BMI was classified as normal weight (18.5–22.9kg/m^2), overweight (≥23.0–24.99kg/m^2), and obese (≥25kg/m^2) [12].

Blood pressure measurement

Blood pressure was measured using mercury sphygmomanometer and a stethoscope. Blood pressure was measured three times and the average of the three was taken. Blood pressure was divided into four categories as per the Joint National Committee on the Prevention, Detection, Evaluation and Treatment of High Blood Pressure (JNC 7); normotensive (<120/80 mm Hg), prehypertensive (systolic blood pressure: 120–139 or diastolic blood pressure: 80–89 mm Hg), hypertensive stage 1 (systolic blood pressure: 140–159 or diastolic blood pressure: 90–99 mm Hg), hypertensive stage 2 (systolic blood pressure: ≥160 or diastolic blood pressure: ≥100 mm Hg) [13].

Blood sample collection and Vitamin D measurement

Venous blood samples (3 ml) were collected under strict aseptic manner; irrespective of last meal. Serum was separated by centrifugation and 25(OH)D was measured using Chemiluminescence technique as an index of vitamin D status. Maglumi 1000 analyzer (SNIBE Co, Ltd, China) was employed to perform the tests. Vitamin D status was categorized as deficient, insufficient and sufficient (<20 ng/ml, 20–29 ng/ml and 30–100 ng/ml respectively) based on levels of 25(OH) D [14].

Statistical analyses

The data was analyzed using Statistical Package of Social science (SPSS) version 11.5. The data was evaluated for normal distribution and descriptive statistics was used to express the demographics and anthropometric characteristics of the study sample. The mean (standard deviation) systolic blood pressure, diastolic blood pressure and the median (25^{th}, 75^{th} centile) of serum 25(OH)D were compared across the baseline characteristics. Statistical comparison was done using students T-test. test and One way Anova for parametric and Mann Whitney U test and Kruskal Wallis for non-parametric data. The different categories of blood pressure were compared across sociodemographic variables using Chi-square except for BMI Fischer's exact test was used. A probability P<0.05 was considered statistically significant. Pearson correlation was run between log-transformed serum 25(OH)D and systolic BP and diastolic BP.

Result

The mean age of the study participants was 56.9±16.2 years. The mean systolic and diastolic blood pressure were 121.6±16.7 mm Hg and 83.4±11.9 mm Hg respectively. The median (25–75^{th} centile) of serum 25(OH)D was 21.9 ng/ml (18–26.6).

Baseline data (Table 1) shows the mean ± standard deviation of systolic and diastolic blood pressure and median (25^{th} and 75^{th} centile) of serum 25(OH)D between the study variables. Out of the total participants; 63(41.7%) were male and 88(58.3%) were female. The mean systolic blood pressure was not statistically different between the two genders but the mean diastolic blood pressure was significantly higher in male (85.5±11.9 mm Hg) compared to female (81.7±11.6 mm Hg) (p=0.03). People in the age group ≤ 60 years had significantly higher systolic blood pressure (124.3±18.6 mm Hg) than those >60 years (117.7±12.6 mm Hg) (p=0.03).

Residents of Sunsari district had significantly higher systolic (126.5±18.2 mm Hg) and diastolic (86.4±12.2 mm Hg) blood pressure compared to residents of Morang 116.9±13.6 mm Hg and 80.7±11 mm Hg respectively) (p=0.001 and p=0.005). We also found people who were employed had higher diastolic blood pressure (84.7±11.8 mm Hg) than unemployed people (80.7±12 mm Hg) (p=0.03). People who consumed alcoholic beverages had higher diastolic blood pressure than those who did not consume alcohol (85.7±13.3 mm Hg and 81.6±10.5 mm Hg respectively) (p=0.04). The mean systolic and diastolic blood pressure varied significantly according to categories of serum 25(OH)D. The mean systolic blood pressure was 129.7±19.4 mm Hg among vitamin D deficient and 116.9±12.1 mm Hg among vitamin D insufficient and 115.6±13.6 mm Hg among vitamin D sufficient (p=0.001). The mean diastolic blood pressure was 87.1±13.6 mm Hg among vitamin D deficient and 81.5±9.8 mm Hg among vitamin D insufficient and 80.4±11.4 mm Hg among vitamin D sufficient (p=0.01).

The serum 25(OH)D levels were significantly different between the employed and unemployed category [22.7(18.8,27.9) ng/ml and 20.6(15.2,25.5) ng/ml respectively] (p=0.03). The median serum 25(OH)D was significantly different between those who used and did not use tobacco [22.8(19.4,27.9) and 20.4(15.7,25.5) respectively] (p=0.01).

Amongst 151 participants, most were prehypertensive 51(33.8%) while 44(29.1%) had stage 1 HTN, 19(12.6) had stage 2 HTN. We found 37(24.5%) were normotensive; amongst the normotensive participants, most were female (Chi–sq = 8.9, d.f. = 3, p < 0.03) and people residing in Morang district (Chi–sq = 8.8, d.f. = 3, p < 0.03). When examining the different categories of blood pressure amongst vitamin D status, we found a significantly higher prevalence of stage 2 HTN among vitamin D deficient individuals while people with sufficient vitamin D mostly had normal blood

Table 1: Comparison of blood pressure and serum 25(OH)D between the study variables

Variables		Total n(%)[a]	Mean systolic BP (mm Hg)[b]		Mean diastolic BP (mm Hg)[b]		Serum 25(OH)D[c] (ng/ml)	
			Mean(SD)	P *value*	Mean(SD)	P value	Median (25th,75th percentiles)	P *value*
Gender	Male	63(41.7)	121.4(16.3)	0.9	85.9(11.9)**	0.03	21.9(18.8,26.3)	0.4
	Female	88(58.3)	121.7(17.1)		81.7(11.7)		22.3(16.6,26.7)	
Age groups	≤60 years	89(58.9)	124.3(18.6)*	0.03	83.3(12)	0.7	21.3(15.8,26.2)	0.9
	> 60 years	62(41.1)	117.7 (12.6)		83.7(11.9)		23.3(19.5,26.6)	
Ethnic group	Brahman, Chhetri	29(19.2)	123.8 (13.9)	0.5	85.5(12.4)	0.8	21.5(17.4,25.2)	0.5
	Newar	7(4.6)	128.6 (16.8)		84.3 (9.8)		20.4(14.1,21.4)	
	Janajati	54(35.8)	122.6 (20.5)		82.9(13.2)		21.3(18,26.2)	
	Madhesi	39(25.8)	117.7 (13.5)		82.6 (11.6)		23.9(18.6,26.2)	
	Dalit	22(14.6)	120.9(14.4)		83.2 (9.5)		23.7(17.8,26.7)	
Residential district	Sunsari	74(49)	126.5 18.2)*	0.001	86.4(12.2)**	0.005	21.4(16.8, 26)	0.1
	Morang	77(51)	116.9(13.6)		80.7(11)		22.7(18.4, 29.7)	
Employment status	Unemployed	46(30.5)	122.8 (20.2)	0.8	80.7(12)**	0.03	20.6(15.2,25.5)***	0.03
	Employed	105(69.5)	121.1(14.9)		84.7(11.8)		22.7(18.8,27.9)	
Education status	Illiterate	42(27.8)	122.4 (20.9)	0.07	82.1(12.8)	0.4	21.2(18.8,26.7) ***	0.001
	Primary School	52(34.4)	118.3 (12.5)		83.3(10.4)		24.4(20.4,29.1)	
	High School	40(27.5)	121.3 (14.9)		83(11.8)		21.8(16.7,27)	
	Above high school	17(11.3)	130.6 (18.2)		88.2(14.2)		15.2(13.8,18.9)	
Dietary habit	Vegetarian	24(15.9)	122.1(16.7)	0.8	83.3(11.7)	0.9	20.9(17.8,24)	0.3
	Non-vegetarian	127(84.1)	121.5 (16.8)		83.5(12.1)		22.4(18.2,26.7)	
Tobacco use	Uses tobacco	77(51)	121(18.8)	0.3	84.4(13)	0.3	22.8(19.4,27.9) ***	0.01
	Does not use	74(49)	122.2(14.3)		82.4(10.7)		20.4(15.7,25.5)	
Alcohol Intake	Does not drink	84(55.6)	120(14.2)	0.4	81.6(10.5)**	0.04	21.4(18.2,26.3)	0.6
	Drinks alcohol	67(44.4)	123.6(19.3)		85.7(13.3)		22.6(17.9-26.6)	
Body Mass Index	Normal	18(11.9)	118.9 (17.8)	0.6	79.4(12.6)	0.06	22.9(17.8,29.2)	0.9
	Overweight	28(18.5)	118.9(12.9)		80 .4(9.9)		23.4(17.3,26.6)	
	Obese	105(69.5)	122.8 (17.4)		84.9 (12.1)		21.4(18.3,26.5)	
Serum 25(OH)D	Deficient	58(38.4)	129.7(19.4)*	0.001	87.1(13.6)**	0.01	16.7(14,18.5)	0.001
	Insufficient	68(45)	116.9(12.1)		81.5(9.8)		24.3(21.9,26.1)	
	Sufficient	25(16.6)	115.6(13.6)		80.4 (11.4)		32.9(31.4,40.9)	

[a]Study variables are expressed as number (percentage) [n(%)] of rows

[b]Expressed in mean (Standard deviation)

[c]Serum 25(OH)D Median (25th and 75th centile)

*The distribution of mean systolic BP was different across age group, region of residence (student T test) and vitamin D status (One way Anova).

**The distribution of mean diastolic BP was different across gender, region of residence, employment status, alcohol intake (student T test) and vitamin D status (One way Anova).

***Serum 25(OH)D was different across employment status, tobacco use (Mann Whitney) and education status (Kruskal wallis test).

pressure than other categories of blood pressure (Chi-sq = 16.7, d.f. = 6, $p < 0.01$). There was no significant difference between categories of BMI (Table 2).

Table 2: Distribution of variables according to different categories of blood pressure

Variable		n(%)[a]	Normotensive[c]	PreHTN[d]	Stage 1 HTN[e]	Stage 2 HTN[f]	P *value*
n(%)[b]		151(100)	37(24.5)	51(33.8)	44(29.1)	19(12.6)	
Gender	Male	63(41.7)	8(5.3)	26(17.2)	19(12.6)	10(6.6)	0.03
	Female	88(58.3)	29(19.2)	25(16.6)	25(16.6)	9(6)	
Age groups	≤60 years	89(58.9)	22(14.6)	31(20.5)	26(17.2)	10(6.6)	0.9
	> 60 years	62(41.1)	15(9.9)	20(13.2)	18(11.9)	9(6)	
Ethnicity	Brahman, Chhetri	29(19.2)	5(3.3)	11(7.3)	6(4)	7(4.6)	0.8[g]
	Newar	7(4.6)	1(0.7)	3(2)	2(1.3)	1(0.7)	
	Janajati	54(35.8)	15(9.9)	18(11.9)	15(9.9)	6(4)	
	Madhesi	39(25.8)	11(7.3)	12(7.9)	13(8.6)	3(2)	
	Dalit	22(14.6)	5(3.3)	7(4.6)	8(5.3)	2(1.3)	
Region of Residence	Sunsari	74(49)	12(7.9)	25(16.6)	23(15.2)	14(9.3)	0.03
	Morang	77(51)	25(16.6)	26(17.2)	21(13.9)	5(3.3)	
Employment status	Unemployed	46(30.5)	16(10.6)	16(10.6)	10(6.6)	4(2.6)	0.1
	Employed	105(69.5)	21(13.9)	35(23.2)	34(22.5)	15(9.9)	
Education status	Illiterate	42(27.8)	12(7.9)	16(10.6)	9(6)	5(3.3)	0.6[g]
	Primary	52(34.4)	12(7.9)	19(12.6)	15(9.9)	6(4)	
	High School	40(27.5)	11(7.3)	10(6.6)	15(9.9)	4(2.6)	
	Above high school	17(11.3)	2(1.3)	6(4)	5(3.3)	4(2.6)	
Dietary habit	Vegetarian	24(15.9)	6(4)	7(4.6)	8(5.3)	3(2)	0.9
	Non-vegetarian	127(84.1)	31(20.5)	44(29.1)	36(23.8)	16(10.6)	
Tobacco use	Uses tobacco	77(51)	19(12.6)	23(15.2)	22(14.6)	13(8.6)	0.3
	Does not use	74(49)	18(11.9)	28(18.5)	22(14.6)	6(4)	
Alcohol Intake	Does not drink	84(55.6)	25(16.6)	30(19.9)	20(13.2)	9(6)	0.1
	Drinks alcohol	67(44.4)	12(7.9)	21(13.9)	24(15.9)	10(6.6)	
Body Mass Index	Normal	18(11.9)	7(4.6)	6(4)	2(1.3)	3(2)	0.1g
	Overweight	28(18.5)	8(5.3)	12(7.9)	7(4.6)	1(0.7)	
	Obese	105(69.5)	22(14.6)	33(21.9)	35(23.2)	15(9.9)	
Serum 25(OH)D	Deficient	58(38.4)	10(6.6)	16(10.6)	19(12.6)	13(8.6)	0.01
	Insufficient	68(45)	17(11.3)	30(19.9)	16(10.6)	5(3.3)	
	Sufficient	25(16.6)	10(6.6)	5(3.3)	9(6)	1(0.7)	

[a]Study variables are expressed as number (percentage) [n(%)] of rows
[b]Variables are expressed as number (percentage) [n(%)] of column
[c]Normotensive: blood pressure (<120/80 mm Hg),
[d]prehypertensive (systolic blood pressure: 120-139 or diastolic blood pressure: 80-89 mm Hg),
[e]hypertensive stage 1 (systolic blood pressure: 140-159 or diastolic blood pressure: 90-99 mm Hg),
[f]hypertensive stage 2 (systolic blood pressure: ≥160 or diastolic blood pressure: ≥100 mm Hg) as per JNC 7.
P *value* are obtained from $\chi 2$ test except
[g]obtained from fischer's exact test.

Correlation between log 25(OH)D and systolic BP was statistically significant, however the strength of correlation was a weak negative one (R=–0.3; p value: 0.001), similarly the correlation between serum 25(OH)D and diastolic blood pressure was weak negative one (R=–0.1; p value: 0.1) (Figure 1 &2).

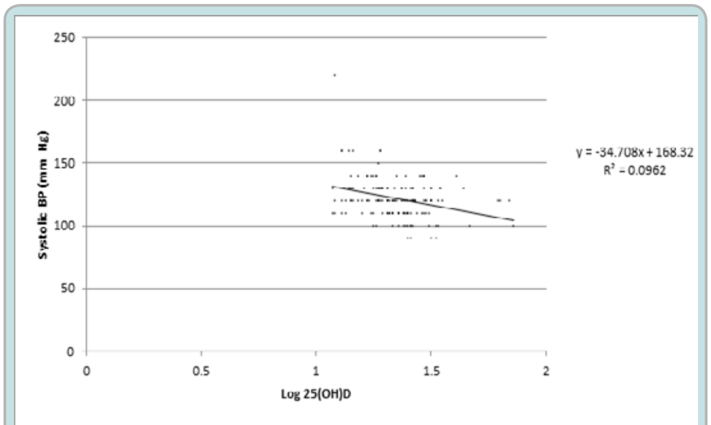

Figure 1: Correlation between log 25(OH)D and Systolic BP.

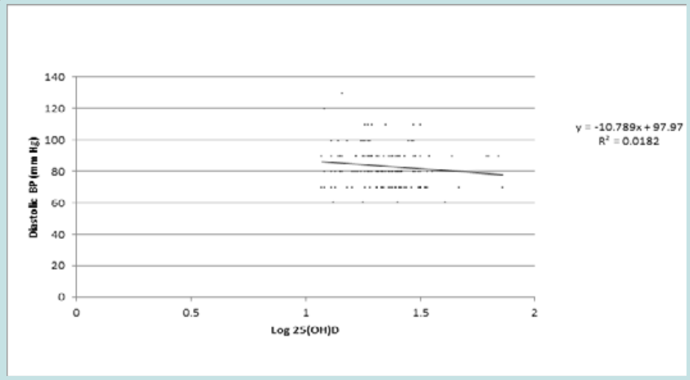

Figure 2: Correlation between log 25(OH)D and Diastolic BP.

Discussion

In our study, we found an inverse relationship between serum vitamin D and blood pressure (both systolic and diastolic). This finding was similar to the national health survey of the US where they found an inverse relationship between vitamin D with blood pressure [7]. However, another study found such inverse relationship amongst men but not in women [15].

When different categories of blood pressure were compared to vitamin D status, we found a significantly higher prevalence of stage 2 HTN amongst vitamin D deficient individuals. Similarly, a significantly higher number of vitamin D sufficient people had normotensive blood pressure than other categories. Numerous scientific evidences have emerged throughout the years stating the plausible mechanisms by which vitamin D regulates blood pressure. Both direct and indirect underlying mechanisms are held responsible; vitamin D can directly bind to its receptors in vascular smooth muscle cells and endothelial cells and promotes vascular health by upregulating endothelin, nitrous oxide and modulating inflammatory mediators [16]. Indirectly, vitamin D influences vessel tone and blood pressure by its inhibitory effect on renin–angiotensin system and its calciotropic actions regulating calcium influx into vascular smooth muscles [6,17].

In our study, females had significantly lower mean diastolic blood pressure than males. A study conducted in Cedars–Sinai Medical Center suggests; that the normal physiological range of blood pressure might be lower in women than men [18]. Similarly, while comparing the various categories of blood pressure between the two sexes, we found a significantly higher proportion of females were normotensive than younger males. This gender difference in blood pressure may be attributed to differential interplay of sex hormones [19]. This theory is further supported by the changes in blood pressure induced by higher levels of estrogen, progesterone, prolactin and relaxin during pregnancy [20].

In our study, we found significantly higher systolic and diastolic blood pressure among the residents of Sunsari district compared to people residing in Morang district. Also, a greater proportion of people residing in Sunsari were associated with stage 2 HTN. Geographical variation in blood pressure has been demonstrated in several studies. A study conducted in Chile, the longest country found the further the residence from equator the higher the blood pressure and prevalence of hypertension [21]. However, in our study we had collected samples from eastern Nepal which did not differ much in terms of distance from equator, hence other factors might be in play. We postulate the reason behind this geographical heterogeneity may be due to variability in terms of ethnicity, dietary patterns and socio-cultural factors. However, we did not find any difference in blood pressure among the ethnic groups and dietary pattern. However, we had only subdivided diet into vegetarian and non-vegetarian without a detailed dietary history.

Conclusions

We found a significant but weak inverse relation between 25(OH)D and systolic BP, similarly the relation between serum 25(OH)D and diastolic blood pressure was weak negative one. We also found a significantly higher prevalence of stage 2 HTN among vitamin D deficient individuals than those with sufficient level.

Acknowledgement

None.

Conflict of Interest

Authors declare there is no conflict of interest.

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