

Determining correlation between changes in blood pressure and vitamin D levels: Analyzing influencing factors in hypertensive adults at Family Medicine Clinics

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ABSTRACT

Background: Dietary sodium and renin-angiotensin system activity are pivotal in causing primary hypertension. Vitamin D levels inversely relate to the renin-angiotensin system. Our study investigates the association between vitamin D fluctuations and blood pressure control in hypertensive patients undergoing general health checkups. **Methodology:** A cross-sectional study enrolled participants with essential hypertension from family medicine clinics at the Aga Khan University Hospital, Karachi, coming for a general health checkup. Data including demographics, Vitamin D levels, blood pressure, factors associated with hypertension, and vitamin D deficiency were noted and analyzed using SPSS 20. Post-stratification chi-square test was applied to check for the association between different categorical variables. **Results:** In a study of 203 hypertensive subjects (mean age: 58.07 ± 11 years, 56.2% male, 63.5% Urdu speaking), 41.4% were smokers, and 63.1% had other comorbidities along with hypertension. Significant vitamin D deficiency was observed in 81.8%, with 55.7% exhibiting uncontrolled blood pressure. Vitamin D levels were significantly associated with blood pressure changes, sun exposure, gender, physical activity, and salt restriction. Smoking and obesity are also correlated with blood pressure changes. **Conclusion:** Pakistan faces significant hypertension and vitamin D deficiency burdens. Our study found a potential link between varying vitamin D levels and blood pressure fluctuations in hypertensive patients, warranting further research.

Keywords: 25 (OH) D, calcifediol, cholecalciferol, high blood pressure, hypertension, vitamin D

Introduction

Essential hypertension affects 40% of the population globally, with the World Health Organization (WHO) projecting 1.56 billion cases by 2025.^[1] The National Health Survey of Pakistan estimated that hypertension affects 18% and 33% of adults below and above the age of 45 years, respectively.^[2]

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Globally, studies indicate that approximately one billion people are vitamin D deficient.^[3] In the US, 35% of adults are deficient in vitamin D. Vitamin D deficiency prevalence varies across WHO regions, being highest in the Eastern Mediterranean. In Oman, 44.3% of those aged 18–55 years had serum 25(OH)D levels below 30 nmol/L, whereas 34% of the Chilean population suffered serum 25 (OH)D deficiency.^[4] Despite abundant sunlight, Pakistan exhibits widespread vitamin D deficiency, with two studies reporting rates of 70% and 97%, whereas only 15.3% have sufficient levels globally.^[5,6]

Vitamin D supplementation may reduce blood pressure worldwide.^[7,8] Western studies link low vitamin D levels to

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increased plasma renin activity, contributing to hypertension.^[9,10] In South Asia, 57.9% of hypertensives showed low 25(OH)D levels.^[11]

By examining blood pressure levels in vitamin D-sufficient and deficient patients within our clinical setting of all hypertensive patients, we can observe the correlation between vitamin D levels and blood pressure control during checkups.

Methods

This cross-sectional study enrolled 203 participants. A sample size of 184 was calculated using Open-Epi. A population size of 6,000 over 6 months was used, based on an annual patient influx of 12,000 from family medicine clinics. The hypothesized frequency of vitamin D deficiency in the hypertensive population^[8] was $77\% \pm 6\%$, with a 95% confidence level. Individuals coming for general health checkups were selected via a non-probability convenient sampling technique, from family medicine clinics at the Aga Khan University Hospital, Karachi, Pakistan.

Inclusion criteria were patients aged 20–60 years visiting family medicine clinics for checkups, consenting to participate, and having Vitamin D levels tested. This included newly diagnosed hypertensive patients or those on antihypertensive medication. Exclusion criteria were patients outside the age range, non-cooperative individuals, those with impaired cognition and language barriers, non-hypertensive patients, and those with secondary causes of hypertension.

Before the study's initiation, ethical clearance was obtained from the Ethical Review Committee of Aga Khan University Hospital, Pakistan. Patients provided consent and were interviewed by the primary investigator regarding high blood pressure and general health. Information on vitamin D levels and other factors such as blood pressure levels at the moment, use of added extra salt on food from top, sun exposure, especially between 10:00 am and 3:00 pm of minimum 15 min that produces vitamin D in the skin,^[12] gender, tobacco smoking, physical activity up to 30 min/day for at least 5 days a week,^[13] obesity-body mass index (BMI) ($\geq 27.5 \text{ kg/m}^2$),^[14] any history of high blood pressure in first-degree family, compliance to their antihypertensive if in use were gathered, with additional details such as anthropometric measurements extracted from records. This interaction typically lasted 10 to 15 min.

The data were then added and analyzed using SPSS 20. Categorical data such as gender, ethnicity, marital status, addictions, comorbid, SES, physical activity, reported use of anti-hypertensive, family history of hypertension, salt restriction, physical activity, adequate sun exposure, BMI, level of blood pressure, and vitamin D levels are presented as frequency and percentages. Continuous variables such as age, weight, and height will be presented as mean \pm standard deviation.

The frequencies of all demographics and vitamin D deficiency and sufficiency were assessed and then all the groups including

gender, ethnicity, marital status, addictions, comorbid, SES, physical activity, adequate sun exposure, BMI, and blood pressure, were compared with vitamin D deficient and sufficient groups. The post-stratification chi-square test was applied to compare the proportion of vitamin D sufficient or deficient groups in patients with hypertension and its associated factors taking a *P* value of <0.05 as significant.

Results

A total of 203 subjects were enrolled, with a normally distributed mean age of 58.07 ± 11 years, as shown in Figure 1, a mean height of 162 ± 9.1 cm, and a mean weight of $76 \text{ kg} \pm 12.6$ kg. Out of them, as shown in Table 1, 114 (56.2%) were males, ethnically, of all coming to family medicine clinics at Aga Khan University Hospital, the majority were Urdu speaking (129, 63.5%). About 73 (36%) had no addictions such as pan, chalia, gutka, smoking, alcohol niswar or any other form of elements, whereas a majority of participants (84, 41.4%) were currently smokers. Furthermore, 75 (36.9%) in our study population were only hypertensive with no other comorbid.

Table 2 shows a comparison of factors influencing vitamin D levels. A significant association ($P < 0.05$) was observed between changes in vitamin D levels and altering blood pressures along with various factors, including variations in adequate sun exposure, gender, salt restriction, and physical activity. Out of 203 individuals, about 113 (55.7%) participants reported having uncontrolled BP, of which 86 (42.4%) patients had significant vitamin D level deficiency. Conversely, only 90 (44.3%) participants had controlled blood pressures, of which 80 (39.4%) had deficient vitamin D levels and the remaining had sufficient. As sun exposure is essential for vitamin D formation, especially between 10:00 am and 3:00 pm of a minimum of 15 min, of 105 (51.7%) participants who had no adequate exposure, 93 (45.8%) had vitamin D deficiency. Among the 203 participants, 114 (56.2%) were male, with 99 (48.8%) of them being vitamin D deficient. Additionally, 137 participants (66.5%) reported having no adequate physical activity, of which 116 (57.1%) had significant vitamin D deficiency.

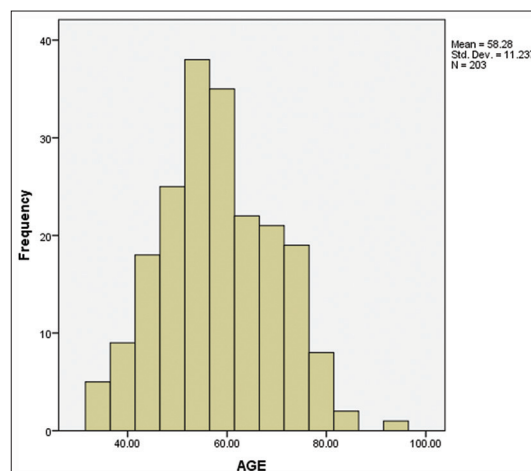


Figure 1: Age distribution and mean

Table 1: Frequency and distribution of demographics

Demographics		Frequency (n=203)	Percentage (%)
Gender	Male	114	56.2
	Female	89	43.8
Ethnicity	Sindhi	24	11.8
	Punjabi	7	3.4
	Balochi	18	8.9
	Pakhtun	10	4.9
	Urdu speaking	129	63.5
	Gilgit-Baltistan	15	7.4
Addiction	Smoking	84	41.4
	Pan, chalia, gutka	27	13.3
	Others	19	9.4
	None	73	36.0
Comorbidities	DM	64	31.5
	Dyslipidemia	13	6.4
	IHD	15	7.4
	Others or multiple comorbidities	36	17.7
	None	75	36.9
Current employment status	Unemployed	117	57.6
	Self-employed	23	11.3
	Employed	60	29.6
	Other	3	1.5
Household income (PKR)	10000–50000	18	8.9
	50001–100000	50	24.6
	100001–200000	91	44.8
	>200000	44	21.7
Prior education	No formal education	27	13.3
	Primary	24	11.8
	Secondary	36	17.7
	High school/intermediate/a levels	33	16.3
	Graduation	78	38.4
	Post-graduation	5	2.5
Vitamin D deficiency	0-20=deficiency	104	51.2
	21-30=insufficiency	62	30.5
	>30=sufficient	37	18.2
Blood pressure	<140/90 (controlled)	90	44.3
	>= 140/90 (uncontrolled)	113	55.7

Table 3 illustrates a comparison of variation in blood pressure with factors that influence it in already diagnosed hypertensive patients. Vitamin D levels, smoking, and obesity showed significant ($P < 0.05$) differences with blood pressure alterations. Overall, in 203 individuals, 113 participants (55.7%) had blood pressures above 140/90 mmHg, with 111 of these individuals (54.7%) being aged 40 years or older. Among the 114 (56.2%) males, 63 (31%) reported high blood pressure. Out of 203 participants, 116 (57.1%) were vitamin D deficient, with the majority, 85 (42.2%) participants, having blood pressure >140/90 mmHg. Among the 96 (47.3%) smokers, 61 (30%) had uncontrolled blood pressure. Most participants (180, 88.7%) were compliant with antihypertensive medication; yet, 97 (47.8%) had elevated blood pressure. More than 50% of the 203 participants added extra salt on top of their foods, with 64 (31.5%) individuals having blood pressure >140/90 mmHg. Among the 135 (66.5%) participants who had no significant physical activity, 79 (38.9%) had high blood

pressure. Additionally, 149 (73.4%) participants had a BMI over 27.5 kg/m², with 90 (44.3%) of these individuals having uncontrolled blood pressure.

Discussion

Arterial hypertension poses a significant risk for cardiovascular disease, noting the increasing prevalence of high blood pressure in South Asia and Pakistan. It emphasizes that a large hypertensive population in these regions is at risk for cardiovascular morbidity and mortality. Uncontrolled high blood pressure can result from various factors, including modifiable ones such as poor diet, lack of exercise, smoking, alcohol consumption, and certain medications, as well as non-modifiable factors such as age, genetics, and ethnicity. Additionally, the article highlights a link between vitamin D deficiency and high blood pressure, attributing the deficiency to factors such as inadequate sun exposure, dark skin, age, and medication use.^[15-17]

Table 2: Comparison of vitamin D deficiency and sufficiency in hypertensive patients with factors that impact vitamin D status

Blood pressure and Vitamin D (serum 25-OH D level)			
	Vitamin D (serum 25-OH D level)		P
	1-30 deficiency (81.8%)	> 30 sufficient (18.2%)	
Blood pressure			
<140/90 mmHg			
Controlled			
Count (total) 90	80	10	0.014
% of total 44.3%	39.4%	4.9%	
>= 140/90 mmHg			
Uncontrolled			
Count (total) 113	86	27	
% of total 55.7%	42.4%	13.3%	
Adequate sun exposure			
Yes			
Count (total) 98	73	25	0.008
% of total 48.3%	36%	12.3%	
No			
Count (total) 105	93	12	
% of total 51.7%	45.8%	5.9%	
Age category			
<40 years			
Count (total) 7	7	0	0.239
% of total 3.4%	3.4%	0%	
≥ 40 years			
Count (total) 196	159	37	
% of Total 96.6%	78.3%	18.7%	
Gender			
Male			
Count (total) 114	99	15	0.027
% of Total 56.2%	48.8%	7.4%	
Female			
Count (total) 89	67	22	
% of total 43.8%	33.0%	10.8%	
Smoking			
Yes			
Count (total) 96	80	16	0.359
% of total 47.3%	39.4%	7.9%	
No			
Count (total) 107	86	21	
% of total 52.7%	42.4%	10.3%	
Physical activity			
None			
Count (total) 135	116	19	0.026
% of total 66.5%	57.1%	9.4%	
Adequate			
Count (total) 68	50	18	
% of total 33.5%	24.6%	8.9%	
Obesity			
Yes			
Count (total) 149	125	24	0.139
% of total 73.5%	61.6%	11.8%	
No			
Count (total) 54	41	13	
% of total 26.6%	20.2%	6.4%	

Contd...

Table 2: Contd...

Blood pressure and Vitamin D (serum 25-OH D level)			
	Vitamin D (serum 25-OH D level)		P
	1-30 deficiency (81.8%)	> 30 sufficient (18.2%)	
Salt restriction			
Yes			
Count (total) 95	68	27	0.00
% of total 46.8%	33.5%	13.3%	
No			
Count (total) 108	98	10	
% of total 53.2%	48.3%	4.9%	

The precise mechanisms linking vitamin D deficiency to hypertension remain unclear; however, potential pathways include dysregulation of the renin–angiotensin–aldosterone system (RAAS), inflammation, insulin resistance, calcium regulation, and sympathetic nervous system activity. Elucidating these relationships is essential for the effective management and prevention of hypertension-related complications.^[18]

In our study, we observed that the prevalence of vitamin D deficiency (defined as vitamin D levels <30 ng/dL) among individuals with hypertension was 81.8%. Only 18.2% of hypertensive individuals exhibited sufficient vitamin D levels. These findings underscore the importance of understanding the potential mechanisms connecting vitamin D deficiency to hypertension, as such knowledge is crucial for addressing the high prevalence of vitamin D deficiency in hypertensive populations and mitigating related health risks.

As discussed, insufficient vitamin D levels may trigger RAAS over-activity, causing blood vessel constriction and increased blood pressure. Additionally, vitamin D might inhibit endothelin production, a molecule that constricts blood vessels, further influencing blood pressure.

In our study, 55.7% of the population had uncontrolled blood pressure (BP >140/90 mmHg), of which 42.4% had 25(OH) D deficiency. Meanwhile, 39.4% of the participants had systolic blood pressure (SBP) less than 140 mmHg and diastolic blood pressure (DBP) less than 90 mmHg. Duprez *et al.*^[19] conducted a study on 25 hypertensive patients and found that vitamin D levels were inversely associated with systolic blood pressure. Additionally, research by Tomaschitz *et al.*^[20] demonstrated that both 25(OH)D and 1,25(OH)D levels were inversely associated with plasma renin and angiotensin II concentrations. In one prospective study, 1,448 women demonstrated a 2.21-fold increase in blood pressures in people with vitamin D deficiency versus control group.^[9]

In primary care, managing hypertension is standard, with lifestyle adjustments such as diet, exercise, and sodium restriction recommended by the American Heart Association.^[21] Family physicians in the US and Canada increasingly explore

Table 3: Comparison of factors influencing blood pressures in all hypertensive patients

Variable		BP<140 mmHg N=90 (44.3%)	BP ≥ 140 mmHg N=113 (55.7%)	Total	P
Age category	1-39 years	5 (2.5%)	2 (1%)	7 (3.5%)	0.14
	Above 40 years	85 (41.9%)	111 (54.7%)	196 (96.5%)	
Gender	Male	51 (25.1%)	63 (31%)	114 (56.2%)	0.5
	Female	39 (19.2%)	50 (24.6%)	89 (43.8%)	
Smoking	Yes	35 (17.2%)	61 (30%)	96 (47.3%)	0.02
	No	55 (27.1%)	52 (25.6%)	107 (52.7%)	
Compliant to antihypertensive	Yes	83 (40.9%)	97 (47.8%)	180 (88.7%)	0.114
	No	7 (3.4%)	16 (7.9%)	23 (11.3%)	
Salt restriction	Yes	46 (22.7%)	49 (24.1%)	95 (46.8%)	0.16
	No	44 (21.7%)	64 (31.5%)	108 (53.2%)	
Physical activity	None	55 (27.6%)	79 (38.9%)	135 (66.5%)	0.158
	Yes	34 (16.7%)	34 (16.7%)	68 (33.5%)	
Family history of hypertension, first degree	Yes	56 (27.6%)	73 (36.0%)	129 (63.5%)	0.419
	No	34 (16.7%)	40 (19.7%)	74 (36.5%)	
Adequate sun exposure	Yes	44 (21.7%)	54 (26.6%)	98 (48.3%)	0.49
	No	46 (2.7%)	59 (29.1%)	105 (51.7%)	
Obesity	Yes	59 (29.1%)	90 (44.3%)	149 (73.4%)	0.018
	No	31 (15.3%)	23 (11.3%)	54 (26.6%)	
Vitamin D levels	<30 ng/mL	80 (39.4%)	86 (42.4%)	116 (81.8%)	0.014
	≥ 30 ng/mL	10 (4.9%)	27 (13.3%)	37 (18.2%)	

complementary and alternative medicine (CAM),^[22] including vitamin D supplementation, which shows potential in addressing cardiovascular, skin, respiratory, and musculoskeletal issues.^[23,24]

Previous research in Pakistan explored vitamin D deficiency (VDD) prevalence across regions, with limited data on its link to hypertension. A recent study established a significant correlation between serum 25(OH)D levels and various factors, suggesting VDD as a potential fifth contributor to hypertension alongside salt intake, smoking, obesity, and heredity.^[25]

Other factors that influence the hemostasis of vitamin D levels and its impact on blood pressure are also essential. Poor diet often correlates with low socioeconomic status, which includes excessive sodium intake, high intake of saturated fats, and insufficient fruits and vegetables in diet contributing to high blood pressure.^[26] In our study, 46.8% of individuals practiced salt restriction to manage blood pressure, of which 24.1% exhibited high blood pressure and a significant 33.5% showed serum vitamin D deficiency, underscoring the importance of dietary factors in hypertension management.

In our study, 38.9% of individuals reported a lack of any physical activity along with uncontrolled blood pressure. A sedentary lifestyle can lead to weight gain, which in turn increases the risk of hypertension. Some studies suggest a link between obesity and insulin resistance as well.^[27] However, other research contradicts this. In our study, we also observed a significant inverse relationship between BMI and vitamin D levels, that is, 73.5% were obese with vitamin D deficiency and 44.3% had significant HBP.

In our study, 64% of participants were addicted to some substances of abuse, including smoking (41.4%). Chemicals in tobacco smoke harm artery walls, elevating blood pressure also reduces active vitamin D (1,25-dihydroxyvitamin D) in lung cells; however, higher serum levels of its precursor (25-hydroxyvitamin D) may mitigate this.^[28] Although in many studies, including one in Saudi Arabia,^[29] no direct association could be found for smoking causing vitamin D deficiency and in turn resulting in hypertension. In our study, out of 47.3% of smokers, 39.4% had vitamin D deficiency and significantly showed uncontrolled blood pressure in 30% of individuals.

Residents of tropical regions generally receive more sunlight exposure than those in subtropical areas.^[30] Vitamin D synthesis occurs naturally in the body when sunlight triggers the process in the skin. However, melanin, responsible for skin pigmentation, reduces this synthesis, requiring darker-skinned individuals to spend more time in the sun for adequate vitamin D production. Pakistan, with its ample sunlight, supports vitamin D synthesis. Skin color and location are key factors influencing serum 25(OH) D levels.^[31] Our research highlighted disparities: 36% with substantial sun exposure were vitamin D deficient, compared to 12.3% with sufficient levels. Conversely, 45.8% lacking exposure were deficient, with 5.9% sufficient. Of the total, 48.3% of individuals had adequate sun exposure, and 26.6% had uncontrolled BP.

According to the National Nutritional Survey of Pakistan 2011, the prevalence of VDD among females is remarkably high in Pakistan (66.8% for non-pregnant females versus 68.9% for pregnant).^[32] Although we initially hypothesized that females might be more susceptible to vitamin D deficiency due to

cultural aspects, our study revealed a higher prevalence among males. Among 203 participants, 48.8% of males had vitamin D deficiency compared to 33% of females ($P = 0.03$). This discrepancy may stem from socioeconomic disparities limiting women's healthcare access and factors such as indoor work, dietary habits, and cultural practices impacting sun exposure and skin pigmentation in males.^[33]

Conclusion

This study demonstrates a noteworthy link between fluctuations in vitamin D levels and blood pressure regulation among hypertensive patients undergoing routine health assessments at the primary care level. The findings emphasize the importance of monitoring and addressing vitamin D status in this population, suggesting potential benefits for blood pressure management through interventions targeting vitamin D levels.

Limitation

Our study, conducted in a single hospital, is limited by its cross-sectional design, non-consideration of management, and homogeneous patient sample. Measurement errors and incomplete patient characterization, particularly regarding medication usage, are unavoidable. Further research in diverse hospital settings is warranted to comprehensively understand the relationship between vitamin D deficiency and the control of blood pressure in hypertensive patients.

Recommendations

Despite Pakistan's tropical climate, vitamin D deficiency is widespread among hypertensive individuals, mirroring trends observed in South India.^[34] Early vitamin D supplementation is pivotal for primary prevention to mitigate cardiovascular morbidity, particularly in high-hypertension prevalence regions such as Pakistan. Prompt identification and treatment of vitamin D deficiency are imperative for improving health outcomes in such contexts.

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List of abbreviation

25(OH)D	Vitamin D
EHTN	Essential hypertension
HTN	Hypertension
WHO	World Health Organization
UV	Ultraviolet

25-OH D	25-Hydroxyl vitamin D
CVD	Cardiovascular disease
BP	Blood pressure
SBP	Systolic blood pressure
DBP	Diastolic blood pressure
NHSP	National Health Survey of Pakistan
DASH	Dietary approaches to stop hypertension
ACE	Angiotensin-converting enzyme
RAS	Renin angiotensin system

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Conflicts of interest

There are no conflicts of interest.

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