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Prevalence of vitamin D deficiency in the hypertensive south Indian population

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ABSTRACT

Aim. *The leading cause of early cardiovascular death worldwide is systemic hypertension (HTN). It is accountable for 57% of stroke and 24% of coronary heart disease deaths in India. Vitamin D indirectly regulates blood pressure through regulating the RAAS across clinical, pathophysiological, and molecular domains. This study examines Vitamin D deficiency in South Indian hypertensives.*

Materials and Methods. *In this cross-sectional observational study, 500 routine health checkup patients at our clinic were assessed and enrolled. Demographics, symptoms, and lifestyle were collected using a standard questionnaire. Patients with chronic and newly diagnosed hypertension were included in the study. Blood was drawn to test Vitamin D (25-OH) levels. The data was evaluated to compare hypertensives who were already on medication and those who were newly diagnosed.*

Results. *The population showed hypovitaminosis D, with an average Vitamin D level of 20.2 ± 10.3 ng/mL. A considerable number of newly diagnosed hypertensives had Vitamin D deficiency, with an average value of 17.7 ± 8.7 ng/mL. The observed value was significantly lower than the chronic hypertensive group (17.7 ± 8.7 ng/mL vs. 21.4 ±10.9, $p < 0.001$). LDL, HDL, cholesterol, creatinine, and HbA1C levels were not significantly different across groups. Vitamin D levels were similar for outdoor and indoor workers ($p = 0.727$).*

Conclusion. *Our study demonstrates there is a high prevalence of vitamin D insufficiency in the hypertensive South Indian population. There were substantially lower levels of Vitamin D identified in those who were newly diagnosed hypertensives compared to chronic hypertensives on treatment.*

Keywords: vitamin D deficiency, systemic hypertension, India, blood pressure

Abbreviations:

HTN – Hypertension
BP – Blood pressure
CHD – Coronary Heart Disease
RAAS – Renin Angiotension Aldosterone System
ACC – American College of Cardiology
AHA – American Heart Association
SBP – Systolic Blood Pressure
DBP – Diastolic Blood Pressure
LDL – Low Density Lipoprotein
HDL – High Density Lipoprotein
BMI – Body Mass Index
VDR – Vitamin D receptor

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INTRODUCTION

Systemic hypertension (HTN), commonly known as high blood pressure (BP), is a prevalent chronic condition. It represents the primary underlying factor contributing to premature cardiovascular morbidity and mortality on a global scale. In India, 24% of deaths are directly caused by this factor and 57% of stroke-related fatalities caused by coronary heart disease (CHD) [1]. According to projections, the prevalence of hypertension (HTN) is predicted to rise to 23.6% in Indian women and 22.9% in Indian men by the year 2025. This rise in prevalence is anticipated to be more pronounced in urban areas [2]. According to published literature, it has been found that South India exhibits a higher mortality rate due to coronary heart disease (CHD), while Eastern India experiences greater rates of stroke [3].

The photochemical conversion of 7-dehydrocholesterol induced by ultraviolet B radiation accounts for around 80% of the endogenous Vitamin D that is generated in the epidermis. Meanwhile, the remaining 20% of the total dietary intake is derived from various food sources, such as egg yolks, oily fish, cereal, juice, fortified milk, yoghurt, and dietary supplements [4]. The significance of vitamin D in maintaining bone and calcium homeostasis is widely acknowledged. There exists a link between vitamin D insufficiency and the occurrence of metabolic syndrome, type 2 diabetes, renal disease, coronary heart disease, and all-cause mortality [5]. Unexpectedly, vitamin D deficiency is common in India, a tropical nation with plenty of sun exposure. Approximately 80-90% of the Indian population exhibits a deficiency in Vitamin D. This is due to factors such as the adoption of modern lifestyles characterized by prolonged indoor working hours, adherence to traditional clothing practices, the presence of darker pigmentation, increased levels of atmospheric pollution, the consumption of high-fiber diets including phytates, inadequate intake of dietary calcium, and the occurrence of closely spaced pregnancies [6]. According to research, vitamin D is impeding the growth of vascular smooth muscle cells and the process of vascular calcification. Additionally, it has a role in regulating blood pressure through its influence on the RAAS [7].

AIM

The intention of this research is to ascertain the incidence of Vitamin D deficiency within the hypertensive population residing in South India.

MATERIALS AND METHODS

This observational cross-sectional research included individuals who were offered to Sri Ramachandra Medical Centre Chennai, for a master health checkup over a span of 24 months, specifically from December 2018 to December 2020. The researchers provided a detailed explanation of the study's nature and goal to the Institutional Ethical Committee at Sri Ramachandra Institute of Higher Education and Research (SRIHER). Subsequently, ethical authorization was obtained to proceed with the study (Ref No: IEC-NI/21/OCT/80/138). The research study only accepted participants between the ages of 20 and 70. The study included individuals who were identified as having de novo hypertension (blood pressure exceeding 130/80 mmHg) as well as those who had previously received a diagnosis of hypertension and were actively managing their condition with anti-hypertensive drugs (chronic hypertension). Exclusion criteria encompassed adults with secondary hypertension, individuals who had received Vitamin D supplementation within the preceding 3 months, individuals with chronic illnesses including diabetes mellitus, chronic kidney disease, gastrointestinal or skeletal problems, and pregnant individuals. Following the process of selection, a cohort including a total of 500 patients was successfully recruited for the research. A standardized questionnaire was utilized to gather information on demographics, symptoms, and lifestyle features such as occupation, smoking habits, and alcohol consumption. Occupations were categorized into two distinct groups, namely outdoor and indoor jobs, based on the nature of the activity. The diagnosis of essential hypertension was established through the analysis of office blood pressure measurements. Specifically, the criteria used were the presence of two or more readings of either a systolic blood pressure of at least 130 mmHg or a diastolic blood pressure of at least 80 mmHg, as outlined in the ACC/AHA 2017 Hypertension Guidelines. Alternatively, individuals who were already taking antihypertensive drugs were also considered for diagnosis. Blood pressure (BP) was assessed by qualified medical professionals on a minimum of two occasions, following a 5-minute period of rest. An Aneroid sphygmomanometer was used to take the readings in the right arm while the subject was seated. Prior to the measurement, it was verified that the participant refrained from consuming any tea or coffee for a duration of 30 minutes.

Collections of blood samples

The samples of blood were taken between 08:00 am to 10:00 am. Peripheral venous blood samples were taken from each person to assess the levels of vitamin D. Centrifugation was used to separate the serum for 15 minutes at a speed of 3,500 revolutions per minute (rpm). The measurement of 25-OH Vitamin D was conducted using the COBAS 602 automated platform, which utilizes a Chemiluminescent Immunoassay

(CMIA) technique. The data obtained from the questionnaire, as well as the values of the patient's creatinine, LDL, HDL, cholesterol, and HbA1c, were collected and combined with the recorded vitamin D levels. Depending on their vitamin D levels, the individuals were divided into three groups: insufficient (20-30 ng/ml), sufficient (>30 ng/ml), and deficient (<20 ng/ml).

Data analysis

IBM SPSS version 20 was used to conduct the statistical analysis. Descriptive statistics encompassed the utilisation of ratio, proportion, or percentage to represent categorical data, while standard deviation and mean were employed to characterize discrete quantitative data. To analyze categorical data, the Chi-square test will be employed. In order to evaluate continuous data, the paired t-test was used. The analysis of variance (ANOVA) was employed to evaluate the presence of statistically significant differences between two distinct groups. Statistical significance was defined as a p-value less than 0.05.

RESULTS

The study population had a mean age of 51 years, with a higher proportion of males (54%). The mean diastolic and systolic blood pressures among individuals with chronic hypertension were recorded as 128mmHg and 78mmHg, respectively. In contrast, those with newly developed hypertension had average blood pressures of 136mmHg and 79mmHg for systolic and diastolic measurements, respectively. Between the two groups, the difference in systolic blood pressure was statistically significant (p 0.001), whereas diastolic blood pressures showed no such difference. The de novo hypertension group and the control group had significantly different mean Body Mass Indexes (p = 0.033, 30 kg/m^2 vs 27 kg/m^2), according to the study. The study population exhibited insufficient levels of vitamin D, with an average concentration of 20.2 ± 10.3 ng/mL falling within the permissible range of 20-30 ng/mL. A disparity in vitamin D levels was noted between the de novo hypertension group and the chronic hypertensives (p <0.001, 17.7 ng/mL vs 21.4 ng/mL). There is no statistically significant variations in the levels of creatinine, cholesterol, HDL, LDL, and HbA1c between the two groups, as indicated in Table 1.

In the population of individuals with newly developed hypertension, no significant disparity in Vitamin D levels was seen depending on gender, as indicated in Table 2.

TABLE 2. *Gender based difference in Vitamin D level in de Novo hypertensives*

De Novo HTN	Total n=161	Vitamin D (25-OH) (ng/mL)
Male	87	17.8 ± 8.7
Female	74	17.4 ± 8.6

p value = 0.775

During the process of categorizing Vitamin D levels into three groups, namely deficient (<20 ng/mL), sufficient (>30 ng/mL) and insufficient (20-30 ng/mL). The difference was statistically significant in the Vitamin D deficient groups when comparing de novo hypertension individuals with chronic hypertensive individuals. The next table, labelled as Table 3, displays the relevant data for analysis.

The majority of the study participants were seen to be engaged in indoor occupations, comprising 94% of the population. It is worth noting that those who were jobless or retired were also encompassed under this occupational category. Table 4 indicates that there was no

TABLE 1. *Baseline characteristics of the study population*

Variable	Total (n=500)	De Novo HTN (n=161)	Chronic HTN (n=339)	p Value
Age (years)	51 ± 11	50 ± 11	51 ± 11	0.553
Gender				
Male	268 (54%)	88 (55%)	180 (53%)	
Female	232 (46%)	73 (45%)	159 (47%)	
Blood Pressure				
SBP (mmHg)		136 ± 11	128 ± 18	**<0.001**
DBP (mmHg)		79 ± 13	78 ± 9	0.306
BMI (kg/m2)	28.3 ± 16	30 ± 27	27 ± 5	**0.033**
Vitamin D (25-OH) (ng/mL)	20.2 ± 10.3	17.7 ± 8.7	21.4 ± 10.9	**<0.001**
Creatinine (mg/dL)	0.9 ± 0.2	0.9 ± 0.2	0.9 ± 0.2	0.929
Cholesterol (mg/dL)	213.7 ± 32.3	209.7 ± 47.4	207.9 ± 44.1	0.664
LDL (mg/dL)	136 ± 33.7	159 ± 36.5	154.9 ± 36	0.087
HDL (mg/dL)	41.1 ± 5.5	41.3 ± 4.4	41 ± 6	0.558
HbA1C (%)	6.4 ± 1	6.3 ± 0.5	6.5 ± 1.1	0.159

TABLE 3. Data based on Vitamin D level subgroups – Deficient, Insufficient, Sufficient

Vitamin D level (ng/mL)	De Novo HTN		Chronic HTN		p value
	Number	Mean	Number	Mean	
<20 (Deficient)	100	12.3 ± 4.3	173	13.9 ± 3.7	0.001
20-30 (Insufficient)	46	23.4 ± 2.8	120	24.4 ± 3.1	0.052
>30 (Sufficient)	15	35.5 ± 7.5	46	41.2 ± 13.2	0.117

TABLE 4. Occupation based difference in Vitamin D levels

Occupation	Total n=500	Vitamin D (25-OH) (ng/mL)
Indoor Job	472	20.2 ± 10.4
Outdoor Job	28	19.5 ± 9.8

p value = 0.727

significant statistical disparity observed in the levels of vitamin D among individuals engaged in indoor and outdoor occupations.

A significant association was seen across alcohol intake and decreased vitamin D levels, as compared to individuals who smoked or had neither alcohol consumption nor smoking habit (p = 0.008) (Table 5).

TABLE 5. Vitamin D levels based on risk factors of smoking and alcohol consumption

Risk Factors	Total n=500	Vitamin D (25-OH) (ng/mL)
Smoking	50	22.1 ± 9.4
None	390	20.5 ± 10.7
Both	33	17.7 ± 7.6
Alcohol consumption	27	14.7 ± 6.7

p value = 0.008

Furthermore, the analysis revealed that the link between BMI and Vitamin D level was insignificant statistically (correlation coefficient -0.007, p = 0.8636). The symptoms exhibited by the research population are presented in Figure 1.

DISCUSSION

In the human body, vitamin D from dietary and sunlight exposure is converted to 25-hydroxyvitamin D (25-OH Vitamin D) in the liver through a series of metabolic processes. This particular metabolite serves as the primary circulating form of Vitamin D. The utilization of this particular metabolite is prevalent in assessing the Vitamin D levels of an individual. A level of serum vitamin D between 20 and 30 ng/mL is considered insufficient, whereas one below 20 ng/mL is regarded as deficient. Sufficiency, on the other hand, is characterized by a serum vitamin D level beyond 30 ng/mL [8]. The metabolic conversion of 25-OH Vitamin D to its biologically active form, 1,25-dihydroxyvitamin D [1,25(OH)2 Vitamin D], is facilitated by the kidney-located enzyme known as 25-hydroxyvitamin D-1-hydroxylase. The binding of 1,25(OH)2 Vitamin D to the VDR initiates a cascade of events that result in enhanced absorption of phosphorus and calcium in the intestines. This process is crucial for maintaining proper bone metabolism and mineralization. Furthermore, it has been demonstrated through study that vitamin D plays a significant role in inhibiting the production of renin, thereby effectively modulating the RAAS [9,10].

Research carried out on mice that lack the VDR have revealed an upregulated synthesis of angiotensin II and renin, resulting in the development of cardiac hypertrophy, hypertension, and heightened water consumption. It is noteworthy that the inhibitory impact of vitamin D on renin expression is unaffected by factors like

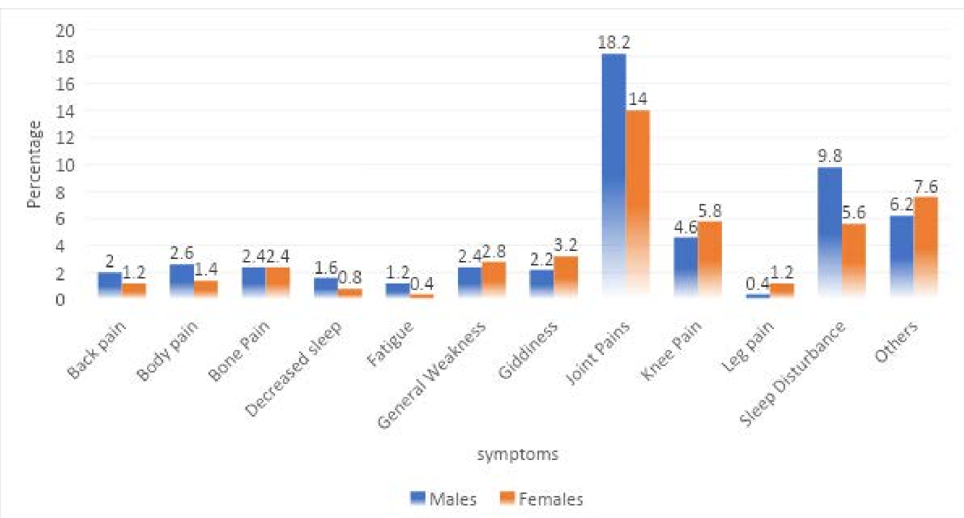

FIGURE 1. Various symptoms reported by the study population

salt-sensing mechanisms and volume, calcium metabolism, or angiotensin II feedback regulation. In mice possessing normal VDR, the absence of vitamin D prompts an increase in renin expression, whereas the introduction of 1,25(OH)2 Vitamin D diminishes the synthesis of renin. Previous investigations in cell cultures have revealed that the transcription of the renin gene is directly inhibited by 1,25(OH)2 Vitamin D through a mechanism that is dependent on the VDR. Consequently, it is plausible that a shortage in vitamin D may elevate the likelihood of developing hypertension, thereby implying that the administration of vitamin D supplements could potentially confer advantages to the cardiovascular system. Vitamin D exerts a crucial influence on blood pressure and cardiovascular well-being by modulating the RAAS and controlling the expression of renin [9].

The main objective of this study is to evaluate the incidence of insufficient vitamin D within the hypertensive population residing in South India. The high incidence of deficient Vitamin D in the Indian population has been well-documented, with studies consistently reporting rates ranging from 80% to 90% [6]. This prevalence of vitamin D deficiency is despite India's ample sunlight availability. In our study, it was observed that 54% of the population exhibited a deficiency in Vitamin D, whilst 87% of the participants displayed Vitamin D levels below the threshold of 30ng/mL. The de novo hypertension group exhibited a notable deficiency in Vitamin D levels in comparison to the chronic hypertension group. This observation could imply a potential association between the utilization of antihypertensive drugs and Vitamin D levels. Pfeifer et al. revealed a decrease in blood pressure following the administration of Vitamin D supplementation [11].

Sowah et al [12] evaluated the relationship between vitamin D levels and occupation type, hypothesising that varied exposure to sunshine throughout work hours would influence these levels. A noteworthy observation was made regarding those with indoor occupations, as they exhibited markedly decreased vitamin D levels. Nevertheless, the findings of our study indicate an absence of correlation between vitamin D levels and occupational type.

In our proposed work, we observed that there was no statistically significant association between the levels of Vitamin D and the body mass index (BMI) within the studied group. Nevertheless, a notable disparity in BMI was noted between the newly diagnosed hypertension group and the chronic hypertension group, with the former exhibiting a higher BMI. Additionally, the vitamin D levels in these groups were inversely related. This observation perhaps indicates an inverse correlation between the two variables. A negative relationship between BMI and levels of 25-OH and 1,2(OH)2 Vitamin D has been established by Lagunova et al [13] in their study.

Research has indicated a higher incidence of deficiency in vitamin D among people who engage in alcohol drinking and smoking, in comparison to those who do not partake in these behaviors [14,15]. In the present study, the population was categorized into distinct groups based on their alcohol consumption and smoking. The study revealed that individuals who engaged in alcohol drinking, as well as those who engaged in both alcohol consumption and smoking, exhibited signs of vitamin D insufficiency more frequently. The population that only engaged in smoking and the population that abstained from both alcohol use and smoking did not exhibit Vitamin D deficiency.

STUDY LIMITATIONS

While our study did not find any significant variation in Vitamin D levels among individuals with outdoor and indoor occupations, it is likely that factors such as the duration of sunlight exposure and the time of day during which solar exposure occurs may have a significant impact. The development of hypertension is believed to be caused by an increase in activity of the RAAS due to a lack in Vitamin D. The specifics of treatment within the chronic hypertension group were not included in our investigation, hence the relationship between therapeutic RAAS inhibition and Vitamin D levels remains unknown.

CONCLUSIONS

The results of our investigation indicate that there is a prevalent occurrence of vitamin D deficiency among individuals with hypertension in the South Indian population, despite the region's ample sunlight exposure. The study observed a notable decrease in Vitamin D levels among those who were recently diagnosed with hypertension, in comparison to those who had been already diagnosed with hypertension and were receiving therapy. Previous research has established a link among Vitamin D insufficiency and the stimulation of the RAAS, this elevates the threat of hypertension developing. However, it remains unclear if treating hypertension with RAAS inhibition has a reciprocal effect on Vitamin D metabolism.

Author contributions:

Conceptualization: J.V.B., J.S.M., A.T.D.; Methodology: J.V.B., T.R.M., A.T.D.; Formal analysis: A.T.D., P.K.; Investigation: J.N.A., A.T.D., J.V.B; Data curation: J.N.A, A.T.D., P.K.; Writing – Original draft preparation: J.N.A., A.T.D.; Writing Review & Editing: J.V.B, T.R.M; Supervision: J.S.M.

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