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STUDY OF VITAMIN-D STATUS IN PATIENTS WITH ESSENTIAL HYPERTENSION

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ABSTRACT

Vitamin D, a fat-soluble vitamin is produced when ultraviolet rays from sunlight strike the skin. Vitamin D deficiency has been found to contribute to various cardiovascular and cerebrovascular diseases in many ways such as hypertension, coronary artery disease, stroke and atherosclerosis. There is a interrelation between low serum vitamin D levels and pathogenesis of cardiovascular diseases and arterial hypertension. Studies have shown that lower circulating 25(OH)D levels were associated with higher blood pressures. Hypertension is one of the most important risk factors for cardiovascular disease, which is the major cause of morbidity and mortality worldwide. Hypertension is classified as either primary (essential) or secondary hypertension. About 90– 95% of cases are categorized as primary hypertension, defined as high blood pressure with no obvious underlying cause.
Aim of the study is to know the correlation between serum vitamin D3 levels and blood pressure in patients with essential hypertension and normotensive individuals.

Material and methods: The study was conducted on 50 individuals. Individuals are divided in to two groups. Group 1: comprising 50 patients with essential hypertension and Group 2: comprising of 25 healthy age and sex matched **normotensive** individuals.

RESULTS: We evaluated the Blood Pressure in Vitamin-D deficient subjects (Case and Control Group), in Cases group SBP was mean 158.54 ±12.58 and in Control Group Systolic Blood Pressure (SBP) was mean 128.53 ±6.52, P-Value is 0.0001.Individuals in cases group had high SBP recording than control group and also in cases group mean Diastolic Blood Pressure (DBP) was96.35 ±08.13 and in Control Group mean DBP was 86.38 ±4.13, P-Value is 0.0001, indicating case group had high mean DBP than control group. We also found Mean SBP and DBP was found to be high in patients with Vitamin D insufficient group than controls.

CONCLUSION: In present study involving total 50 Hypertensive patients and 25 normotensive Healthy volunteers of same age, were enrolled as a control group. In Case group, in vitamin-D sufficient level patients have good controlled SBP then compare other patients. In vitamin-D deficient patients and insufficient patients had high mean SBP and DBP P-Value was 0.004 statistically significant.

Keywords: Vitamin-D, Essential hypertension.

INTRODUCTION

Vitamin D is a fatsoluble vitamin produced endogenously when ultraviolet rays from the sunlight strike the skin and trigger Vitamin D synthesis**.** Vitamin D, has various physiological functions. The central function of Vitamin D is elevation of plasma calcium and phosphate levels for bone health[1]**.** There has been rising interest in the evaluation of role of vitamin D in extra-skeletal diseases. Vitamin D deficiency has been found to have vital association with cardiovascular and cerebrovascular conditions, such as hypertension, coronary artery disease, stroke and atherosclerosis. Vitamin D play a role in regulating blood pressure through several mechanisms, two main aspects are, Renin-Angiotensin-Aldosterone System (RAAS): Vitamin D can inhibit renin transcription, which is a part of the RAAS system that plays a central role in blood pressure regulation and vascular Function: Vitamin D has a role in vasodilatation and reduce sympathetic system activity, both of which can influence blood pressure**.** Vitamin D influences the concentration of calcium in vascular smooth muscle cells and thus plays a role in regulating vascular tone.

Unopposed activation of the Renin angiotensin aldosterone system (RAAS) and generation of angiotensin promote arterial stiffening and endothelial dysfunction that precede and contribute to the development of hypertension and are also predictors of Cardiovascular disease (CVD) risk.

Vitamin D has been implicated in the regulation of the renin-angiotensin system (RAAS) and in interacts with the RAAS to determine the intracellular calcium milieu in vascular smooth muscle[2]. Dietary sodium and increased activity of the RAAS are main factors contribute to the control of hypertension. Inappropriate activation of renin-angiotensin-aldosterone system (RAAS) has been widely known to be the important factor contributing to the development of hypertension[3]. In view of this mechanism of RAAS, drugs that inhibits the RAAS, such as renin inhibitors, angiotensin-converting enzyme inhibitors, angiotensin II type 1 receptor antagonists, and mineralocorticoid receptor antagonist are very important drugs in the treatment of hypertension. Vitamin D influence blood pressure through acting as an endogenous inhibitor of the RAAS, interacting with salt and the RAAS to modulate vascular smooth muscle tone, and indirectly affecting the vascular endothelium. Vitamin D act as a vascular protective agent, it reduces the deleterious effect of advanced glycation end products on the endothelium, improves activity of the NO system, and reduces inflammatory and atherosclerotic parameters[4].

This study was conducted to evaluate vitamin D levels in patients with primary essential Hypertension and impact of deficiency on blood pressure.

MATERIAL AND METHODS

This was a cross sectional Case Control observational Study conducted on patients admitted, diagnosed with Essential Hypertension for more than 3 months duration, irrespective of treatment. The study was conducted in the General Medicine department of Rajarajeshwari Medical College and Hospital. Ethical Committee clearance was obtained before initiation of the study.

Patients were included in the study based on the inclusion and the exclusion criteria as mentioned below.

Inclusion Criteria

1. Age group between 20-60 years of either sex.
2. All patients with diagnosis of essential hypertension for more than 3 months irrespective of treatment.

Exclusion criteria

1. Patients with diagnosis of secondary hypertension
2. Patients with chronic kidney disease, h/o ischemic heart disease, diabetes mellitus,
3. Age above 70 years
4. Patients on vitamin D supplementation in last 3 months
5. Patients with thyroid disorders, malabsorption syndrome.

Study Design:

It was a cross sectional case control study. The study subjects are divided in to two groups.

Group 1: Comprising 50 patients with essential hypertension

Group 2: Comprising of 25 healthy age and sex matched normotensive individuals.

All individuals who met with inclusion criteria are subjected for detail history and physical examination. BP was measured after 5 minutes of rest in right arm supine position with a mercury manometer.

The following investigations were done in selected patients:

Vitamin D levels will be done in fasting venous sample by chemiluminescence Immunosorbant assay, Blood urea and serum creatinine, Fasting and Postprandial blood sugar, Renal function tests, thyroid function tests, Electrocardiogram. 2D Echo, Other special investigations done whenever necessary.

Vitamin D levels are interpreted as

Deficient < 20 ng/ml

Insufficient 21 -29 ng/ml

Sufficient > 30 ng/ml

Sampling Method: Simple random sampling

Method of Collection of Data: Group1 involving 50 Cases diagnosed with hypertension. After taking obtaining consent, patients were analyzed clinically. Group2, included 25 healthy volunteers. All the patients selected for the study were examined in detail according to protocol. Clinical and laboratory investigations were carried.

Statistical Analysis

The collected data was entered into Microsoft Excel Worksheet-2010 and data was taken into IBM SPSS Statistic for windows, version 24(IBM Corp., Armonk, N.Y., USA) software for calculation of frequency, percentage, mean, standard deviation and Probability value.

Results and Observations:

During present study total 82 Essential hypertensive, Patients were reviewed in OPD, among 50 (60.97%) patients were enrolled into the study according present study inclusion criteria and 32 (39.02%) patients were excluded according exclusion criteria. And 25 Healthy volunteers of same age group subjects were enrolled as a control group, they were normotensive.

In our study the patients are categorized into four age groups and more patients are found in the age group of 41-50 years, 24 (48%) followed by 13 (26%) in the 51-60 age group, 11 (22%) in the 31-40 age group and 4 (8%) in the 20-30 years age group. In control group also same group population were enrolled. Among 50 case group, 32 (64%) were male and followed by 18 (36%) were female and in control group 17 (68%) were male and followed by 8 (32%) were female.

Vitamin-D levels were estimated and subjects were distributed disaccording Vitamin –D levels in table 1.

Table1: Vitamin-D Levels among cases and Controls.

Vitamin-D Levels	Case Group N (%)	Control Group N (%)
Deficient (< 20 ng/ml)	17 (34%)	8 (32%)
Insufficient (21 -29 ng/ml)	22 (44%)	7 (28%)
Sufficient (> 30 ng/ml)	11 (22%)	10 (40%)
Total	**50**	**25**

In case group among 50 patients, 22(44%) patients had insufficient vitamin-D levels followed by 17 (34%) patients have deficient vitamin-D levels and 11(22%) patients have sufficient vitamin-D levels. In control group among 25 patients, 10 (40%) patients have sufficient vitamin-D levels followed by 8 (32%) patients have deficient vitamin-D levels and 7(28%) patients have insufficient vitamin-D levels.

In 50 patients were monitored for blood pressure readings and compare the Systolic blood pressure (SBP) and diastolic blood pressure (DBP) based in vitamin-D levels (Table 2).

In vitamin-D deficient patients SBP was 158.54 ±12.58, vitamin-D insufficient patients SBP was 137.32 ±11.67 and vitamin-D sufficient patients SBP is 124.78 ±07.34 which was statistically significant (P-Value is 0.001), it's indicated vitamin-D sufficient level patients had good controlled SBP then compare other patients.

In vitamin-D deficient patients DBP is 96.35 ±08.13, vitamin-D insufficient patients SBP was 88.41 ±07.51 and vitamin-D sufficient patients DBP was 84.13 ±05.11 showed P-Value of 0.004 statistically (table 2) significant. patients with sufficient vitamin D levels had normal DBP.

Table 2: Blood pressure Compare Based on Vitamin-D Levels in Case Group

Vitamin-D Levels	SBP mmHg Mean ± Sd	P-Value	DBP mmHg Mean ± Sd	P-Value
Deficient (< 20 ng/ml)	158.54 ±12.58	0.001	96.35 ±08.13	0.004
Insufficient (21 -29 ng/ml)	137.32 ±11.67		88.41 ±07.51	
Sufficient (> 30 ng/ml)	124.78 ±07.34		84.13 ±05.11	

Control group

In vitamin-D deficient subjects SBP was 128.53 ±6.52, vitamin-D insufficient subjects SBP was 117.32 ±7.13 and vitamin-D sufficient subjects SBP is 122.87 ±5.14. P-Value is 0.19 statistically not significant, it's indicates that vitamin-D sufficient, insufficient and deficient level subjects have normal SBP.

In vitamin-D deficient subjects DBP is 86.38 ±4.13, vitamin-D insufficient subjects SBP was 83.75 ±5.23 and vitamin-D sufficient subjects SBP was 82.26 ±3.19. P-Value is 0.21 statistically not significant, it's indicated that vitamin-D sufficient, insufficient and deficient level subjects have normal DBP (Table 3). We found both SBP and DBP was normal in normotensive control group.

Table 3: Blood pressure Compare Based on Vitamin-D Levels in Control Group

Vitamin-D Levels	SBP mmHg Mean ± Sd	P-Value	DBP mmHg Mean ± Sd	P-Value
Deficient (< 20 ng/ml)	128.53 ±6.52	0.19	86.38 ±4.13	0.21
Insufficient (21 -29 ng/ml)	117.32 ±7.13		83.75 ±5.23	
Sufficient (> 30 ng/ml)	122.87 ±5.14		82.26 ±3.19	

Upon Comparing the blood pressure in Vitamin-D deficient subjects (Case and Control Group), in Case group SBP was 158.54 ±12.58 and in Control Group SBP was 128.53 ±6.52, P-Value is 0.0001, its indicate case group have high SBP than control group and in Case group DBP was 96.35 ±08.13 and in Control Group DBP was 86.38 ±4.13, P-Value is 0.0001, its indicate case group have high DBP then control group.

We compared the blood pressure in Vitamin-D Insufficient subjects (Case and Control Group), in Case group SBP was 137.32 ±11.67 and in Control Group SBP was 117.32 ±7.13, P-Value is 0.0001, its indicate case group have high SBP then control group and in Case group DBP was 88.41 ±07.51 and in Control Group DBP was 83.75 ±5.23, P-Value is 0.006, its indicate case group have high DBP then control group.

Compare the blood pressure in Vitamin-D sufficient subjects (Case and Control Group), in Case group SBP was 124.78 ±07.34 and in Control Group SBP was 122.87 ±5.14, P-Value is 0.24, its indicate both group are SBP were equal and in Case group DBP was 84.13 ± 05.11 and in Control Group DBP was 82.26 ±3.19, P-Value was 0.09, , its indicates both group are DBP were equal (Table 4).

Compare of Blood pressure Based in Vitamin-D sufficient subjects (Case and Control Group) Table 4.

Blood Pressure	Case Group Mean ± Sd	Control Group Mean ± Sd	P-Value
SBP	124.78 ±07.34	122.87 ±5.14	**0.24**
DBP	84.13 ±05.11	82.26 ±3.19	**0.09**

DISCUSSION:

In present study total 50 Essential hypertensive patients and 25 healthy populations same age group subjects were enrolled as a control group. We observed significant inverse association of baseline circulating levels of vitamin D with risk of incident hypertension in apparently healthy populations. Blood pressure, Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP) were significantly higher among individuals with lower vitamin D levels. We found in present study, among 50 patients, 44% patients have insufficient vitamin-D levels, 34% patients have deficient vitamin-D levels and 22% patients have sufficient vitamin-D levels.

In vitamin-D deficient patients SBP is 158.54 ±12.58, vitamin-D insufficient patients SBP is 137.32 ±11.67 and vitamin-D sufficient patients SBP is 124.78 ±07.34. P-Value is 0.001 statistically significant, it's indicated vitamin-D sufficient level patients have good controlled SBP then compare other patients. We found both SBP and DBP was found to be normal in vitamin D sufficient group, this observation was found in both cases and control groups. Forouhi et al., observed that SBP and DBP were inversely correlated with vitamin D[5].

Youssef Khalel Ahmad[6], in his study on 80 individuals involving two groups: Group 1: comprising 60 patients with essential hypertension. Group 2: comprising 20 healthy individuals**,** found in group 1 patients had low vitamin D levels compared to group 2. They found there was statistically significant increase (p value <0.001) in intimal thickness and left ventricular mass in patients with low vitamin D level in comparison to patients with normal vitamin D level. Mean SBP was 171mmhg and DBP was 110 mm hg in the group 1 compared to group 2 with normal blood pressure.

Divya V. Patil, Tarun Kumar Dutta et al., an observational study was conducted on 60 individuals dividing in to two groups as cases and controls, found among the hypertensive individuals, 90% were Vitamin D deficient and 10% had insufficiency. The mean Serum Vitamin D level in patients with essential hypertension was 14.6±4.401 (p value <0.001) and they found mean SBP in patients with Vitamin D deficiency was 146 mm hg compared to normal group[7].

Tianlong Wu[8]et al., Correlation between vitamin D levels and blood pressure in elderly hypertensive patients with osteoporosis, there is a negative correlation between 25-(OH) D3 and 24 h mean systolic blood pressure. Priya S et al., One hundred and two Vitamin D naive essential hypertensive participants were enrolled from the outpatient department. Ninety-nine healthy age- and sex-matched non hypertensive controls were taken for comparison. Serum Vitamin D level estimation was done in both groups through immunosorbent assay and deficiency defined as values <20 ng/ml. In their study they found Vitamin D deficiency was more prevalent among cases than controls (80.4% vs. 67.7%, $P = 0.01$). The mean 25-hydroxyvitamin D levels among cases were 15.15 ± 12.51 ng/ml versus a value of 33.59 ± 16.69 ng/ml among controls ($P = 0.0001$). We also observed trends towards an inverse association between Vitamin D levels and systolic blood pressure (BP) ($P = 0.02$). They concluded Vitamin D deficiency is more prevalent with HTN, and low levels tend to correlate with elevated systolic BP.

Conclusion:

In our study, we found patients with essential hypertension who had low vitamin D levels had higher SBP and DBP compared to control group. Based on this results, we concluded that there is a significant negative correlation between the serum vitamin D levels and systolic blood pressure. The lower the serum vitamin D levels, more is the severity of hypertension. It was also observed that systolic blood pressure independently affected the serum Vitamin D levels among the hypertensive individuals. However well designed randomised clinical trials to investigate the necessary vitamin D doses and appropriate target groups for the prevention or treatment of hypertension. How ever, larger studies are needed to confirm this association.

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