Original Article

Are Vitamin D Levels Related to Serum Renin Levels in Hypertensive Patients?

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ABSTRACT

Objective: To correlate vitamin D levels with serum renin levels in hypertensive male subjects.
Study Design: Analytical case control study
Place and Duration of Study: This study was conducted at the Lahore General Hospital, Lahore from January to June 2015.
Materials and Methods: The participants in this study were 75 male individuals were separated into stage I and stage II hypertension groups, with healthy attendants serving as controls. Subjects' blood pressure was recorded with a mercury sphygmomanometer, and blood samples were obtained for examination of vitamin D and renin levels.
Results: Subjects included had a mean age of 39.97 ± 8.24 years. Mean vitamin D levels (ng/mL) were 35.99 ± 8.08, 28.71 ± 10.85 and 28.12 ± 9.94 in controls, stage I hypertension and stage II hypertension groups respectively. The association between serum vitamin D and renin levels among the three groups was statistically significant with an 'r' value of -0.275 and p value of 0.017 as indicated in Table.1 and Fig.1.
Conclusion: Our findings in hypertensive patients showed an inverse relationship between blood pressure and vitamin D with an increase in levels of systolic BP, diastolic BP and plasma renin.
Key Words: Renin, Vitamin D, Hypertension

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INTRODUCTION

Stage I hypertension is defined as having a diastolic blood pressure of 90 to 99 mm Hg or a systolic blood pressure of 140 to 159 mm Hg. Stage II hypertension is defined as a systolic pressure of less than 160 mm Hg and/or a diastolic pressure of less than 100 mm Hg, according to James et al. (2014)[1]. The pathogenesis of hypertension is widely speculative. Essential hypertension is defined as having no underlying determinable cause and a tiny percentage of patients with an underlying renal or adrenal abnormality.

For the purposes of homeostasis, the RAAS is the prime director of body fluid volume, blood pressure, and salt equilibrium. Renin, an aspartyl protease, is the first component of RAAS,and it is produced by the juxtaglomerular (JG) cells of the renal glomerular afferent and partly efferent arterioles. By cleaving the N-terminal region of angiotensinogen, the enzyme renin works on the 2-globulin angiotensinogen generated in the liver and drives the synthesis of angiotensin I, a 10 amino acid peptide. The key step that controls the RAAS system is the production of physiologically inactive angiotensin I. Angiotensin converting enzyme (ACE), which is found in the epithelial lining of capillaries speeds up the hydrolytic removal of the C-terminal dipeptide from angiotensin I creating angiotensin II[2]. The physiologically active 8-amino-acid peptide hormone, Angiotensin II, affects tiny renal and systemic arteries to contract, raising total peripheral resistance and henceforth blood pressure. Angiotensin II transmits messages to the heart via brain sympathetic stimulation, resulting in increased cardiac output and, in combination with increased total peripheral resistance, higher blood pressure.

Mounting verification suggests vitamin D insufficiency plays a key task in the occurrence of cardiac risk elements and blood pressure-linked CVD. Four decades after being identified as a steroid hormone, vitamin D is still being studied today, and new chapters in its history are being revealed[3]. The biological reactions to 1, 25-(OH)2 D3 are mediated by the vitamin D receptor (VDR), which is found in the nucleus of a cell, according to Bikle[4]. VDR is a member of the retinoic acid, steroid, and thyroid hormone superfamily. Active vitamin D3 improves VDR's interaction with RXR

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(retinoic acid X receptor) in the cell nucleus. They interact to form a heterodimer called VDR/RXR. This complex binds to vitamin D response elements (VDREs), which are short DNA sequences, when 1, 25-dihydroxy vitamin D is present. Vitamin D's non-calcitropic actions are mediated by receptors of vitamin D and 1-hydroxylase, which are found in a wide range of human tissues. It influences insulin release, renin secretion from the RAAS, vascular genesis, programmed cell death, cell proliferation and differentiation, and immunological responses by controlling roughly 200 genes[5].

1, 25dihydroxy D3 acts as a negative endocrine controller of the RAAS as seen in adult male Wistar rats[6]. Vitamin D's significance in regulating renin gene expression and, eventually, blood pressure can be used to lower blood pressure. In the long run, these with fewer side effects may be able to take the position of angiotensin II receptor blockers and ACE inhibitors[7].

Vitamin D deficiency is thought to cause vascular smooth muscle and ventricular muscle hypertrophy as well as over activation of the renin-angiotensin-aldosterone pathway. The US government's recommendation to update the recommended vitamin D intake amounts for daily consumption and sun exposure is stressed[8].

With nearly one billion individuals suffering from insufficiency or deficiency, vitamin D deficiency has become a global epidemic[9, 10]. Vitamin D deficiency was once thought to be a rare occurrence in South Asia, but that has altered in recent years[11]. In a study conducted in Pakistan, deficient serum vitamin D levels was found in 163.4% patients, 14.9% patients showed insufficiency while only 21.8% had normal levels (>30 ng/ml)[12]. Vitamin D deficiency was shown to be prevalent in a sample of patients studied by Haque et al. in Lahore, with a frequency of 66% out of which 33% were hypertensive[13].

Studies further suggest that active vitamin D has a short-term BP lowering impact that is not seen with cholecalciferol administration, bolstering the theory of vitamin D's negative renin endocrine control. After a biweekly dosage of calcitriol it was found that blood pressure reduces from a starting value of 145/96 mm Hg to a concluding value of 128/85 mm Hg[14].

Vitamin D supplementation taken in conjunction with antihypertensive medicines for three months was likewise shown to dramatically lower systolic blood pressure. A putative participation of the RAAS system and calcium-regulating hormones has been proposed in this regard, according to several practical and logical explanations[15].

The enigma of the sunshine vitamin remains a source of debate in the Western realm, and the goal of our research was to learn more about the linkage between hypertension and vitamin D insufficiency in the Lahore populace. Once established, this would aid in the progress of our population by minimising the load of some threat variables such as hypertension and CVD through low-cost screening and vitamin D supplementation. This might have significant implications and consequences for patient management and health-care policy development.

MATERIALS AND METHODS

Seventy-five male individuals were recruited using non-probability convenience sampling from the outdoor department of Lahore General Hospital in Lahore, Pakistan, between September and December 2016. The cohort comprised of three groups of Controls: stage I, stage II hypertension, and stage III hypertension, each with 25 patients. Newly diagnosed hypertensive male patients aged 30-55 years were enrolled in the study and were divided into two groups: stage I and stage II patients, with healthy attendants serving as controls. Patients with secondary hypertension, poor vitamin D levels, or known renal, liver, thyroid, parathyroid, or cardiac disorders were not included in the study. Patients' medical histories, examinations, and laboratory tests were recorded on a questionnaire pro forma. An enzyme linked immunosorbent assay (ELISA) kit and an automated analyzer were used to perform the vitamin D test. Data was analyzed by SPSS 20.0. Vitamin D, SBP and DBP were described as mean and standard deviation (mean± SD).

Serum Renin was measured using a Human Renin ELISA kit and a conventional immunoassay (Creative Diagnostics, New York, USA). The wells of the microtiter plates are coated with an antibody that is specific for human renin. When pipetted into the wells, samples and standards bind to the coated antibody (Susan, 2010). This assay used an automated analyzer to quantify serum renin (STAT-FAX, model 303, USA).

Statistical Analysis: SPSS (Statistical Package for Social Sciences) version 20.0 was used to enter and analyse the data. The mean and standard deviation (mean SD) of vitamin D and renin levels were calculated. A one-way ANOVA (analysis of variance) was used to compare both variables between the three groups.

By comparing all feasible pairings of means, the post hoc Tukey test was used to determine whether means were substantially different from one another. To determine the relationship between dependent and independent variables, Pearson's co-efficient of correlation 'r' was used. An 'r' coefficient approaching 1 indicated a strong linear relationship between the two measured variables, whereas an 'r' value of 0 indicated no correlation between the two variables. A perfect positive relationship was represented by +1, whereas a perfect negative relationship was represented by -1. Statistical significance was defined as a p-value of less than 0.05.

RESULTS

The current study included 75 male volunteers aged 30-55 years old. They were separated into three groups, each with 25 participants.

Analyzing and comparing the mean SD renin (ng/mL) values in controls (3.51±3.57), stage I (4.81±3.98), and stage II hypertension groups (8.6 ±6.98) revealed that the difference between the control and stage I hypertension groups was non-significant (p=0.64), as shown in Table.1. When the control group was related to the stage II hypertension group, both were different statistically (p=0.002) (Table.1), and the variance in mean SD renin (ng/mL) between the stage I and stage II hypertension groups was significant statistically (p=0.02) (Table.1).

The Pearson's coefficient of correlation, or "r," was calculated to examine the link between the dependent variables (renin, aldosterone, systolic blood pressure, and diastolic blood pressure) and the independent factors (vitamin D) in the control, stage I, and stage II hypertension groups.

Table.1 and Fig.1 show that there was a statistically significant relationship between serum vitamin D and renin levels in the three groups, with an 'r' value of -0.275 and a p value of 0.017.

Table No.1: Comparison of vitamin D, Serum renin, Systolic and Diastolic BP in Control, Stage I Hypertension and Stage II Hypertension Groups

	Control (n=25)	Stage I Hypertension (n=25)	Mean difference	p-value
Vitamin D (ng/mL)	35.99±8.082	28.71±10.85	7.29	0.026*
Serum Renin (ng/mL)	3.51±3.57	4.81±3.98	-1.29	0.642†
Systolic BP (mm Hg)	110.72±5.59	131.20±8.83	-20.48	0.000***
Diastolic BP (mm Hg)	73.24±3.35	91.80±5.86	-18.56	0.000***
	Control (n=25)	Stage II Hypertension (n=25)	Mean difference	p-value
Vitamin D (ng/mL)	35.99±8.082	28.12±9.94	7.88	0.015*
Serum Renin (ng/mL)	3.51±3.57	8.66±6.98	-5.14	0.002**
Systolic BP (mm Hg)	110.72±5.59	144.28±19.28	-33.56	0.000***
Diastolic BP (mm Hg)	73.24±3.35	103.40±12.05	-30.16	0.000***
	Stage I Hypertension (n=25)	Stage II Hypertension (n=25)	Mean difference	p-value
Vitamin D (ng/mL)	28.71±10.85	28.12±9.94	0.59	0.975††
Serum Renin (ng/mL)	4.81±3.98	8.66±6.98	-3.85	0.024*
Systolic BP (mm Hg)	131.20±8.83	144.28±19.28	-13.08	0.001**
Diastolic BP (mm Hg)	91.80±5.86	103.40±12.05	-11.60	0.000***

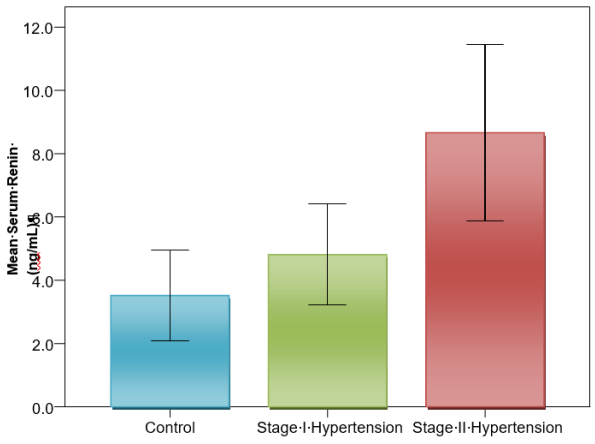
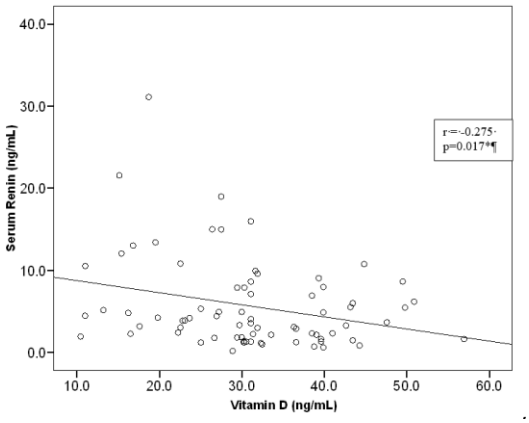


Figure No. 1: Mean Values of Serum Renin (ng/mL) levels in various groups



*= statistically significant

Figure No. 2: Correlation between vitamin D (ng/mL) and serum renin (ng/mL) in study population

DISCUSSION

High blood pressure is known for its high mortality rate[16], with an estimated 8 million fatalities each year[17]. With a prevalence rate of about 24% in adults over the age of 15, and every third person over the age of 45 suffering from high blood pressure, hypertension has invaded South Asian nations, including Pakistan.[18].

There has been much discussion about and agreement on the part of RAAS in the pathophysiology of hypertension[19] and the vitamin D-RAAS link has been studied by some researchers functioning on animals, but human evidence is scarce. We don't have any solid data, either animal or human, in this regard in Pakistan. In our research, we discovered that low vitamin D levels are linked to a high BMI, high serum renin, and high blood pressure.

The goal of our research was to see if there was a link between hypertension and low vitamin D levels, with a focus on the RAAS gene. We examined the levels of vitamin D, renin, and aldosterone in the serum of hypertensive male patients to a sample of healthy adult males.

Observational studies consistently show that serum vitamin D levels and high blood pressure have an inverse relationship. Vitamin D insufficiency was identified as an independent risk factor for the development of a cardiovascular event in the study. In 4 years of follow-up, they found that people with 25(OH) D levels less than 15ng/mL had a threefold increased chance of having high blood pressure compared to those with levels of 30 ng/mL or above[20].

In our investigation, serum renin levels were higher in participants with high blood pressure and low 25 (OH) D compared to controls with normal blood pressure and adequate vitamin D levels. Mice with the VDR gene knocked out had high plasma renin activity and high blood pressure, which could be reversed with the use of ACE inhibitors and activated 25 (OH) D3[21]. A study conducted recently showed that Vitamin D deficiency can cause over-activation of the pulmonary renin-angiotensin system (RAS) leading to the respiratory syndrome [22].

We concluded from our small study that there is a possible relationship between vitamin D deficiency and hypertension.

CONCLUSION

In hypertensive individuals, our data revealed an inverse connection between blood pressure and vitamin D, with an increase in systolic, diastolic, and plasma renin levels. Because screening for vitamin D deficiency and subsequent vitamin D supplementation is not a difficult task, it seems reasonable to test vitamin D status in regular patients in general and cardiovascular disease patients in particular.

Author's Contribution:

Concept & Design of Study:	Saima Mukhtar
Drafting:	Sara Naeem, Mah-E-Jabeen Sear
Data Analysis:	Iram Qamar, Shaista Hussain, Humaira Hashmat
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Final Approval of version:	Saima Mukhtar

Conflict of Interest: The study has no conflict of interest to declare by any author.

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