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Association of 25-Hydroxy Vitamin D Levels with Arterial Stiffness Index in Newly Diagnosed Untreated Hypertensive Patients in Rural Tertiary Care Centre of North India

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Abstract: 25-hydroxy vitamin D is considered to be the best indicator of vitamin D status in those with normal renal function and reflects the circulating substrate for the tightly regulated hydroxylation into the active hormonal form of vitamin D [1]. More recently, vitamin D deficiency has been implicated as a risk factor for cardiovascular disease and overall mortality in general population. It is well established that vascular endothelial dysfunction and arterial stiffness precede and contribute to the development of cardiovascular disease and both are predictors of long term morbidity and mortality. Vitamin D effects the vascular wall by regulating the renin-angiotensin-aldosterone axis and exerts anti-proliferative effects on vascular smooth muscle. Arterial stifffnes index is a novel measure of arterial stiffness that independently predicts cardiovascular mortality. Previously two cross sectional studies observed an inverse relationship between serum 25 (OH) vit. D level and arterial stiffness [12, 16]. Several other studies have presented inconsistent findings [12-15]. Also these studies had been conducted in urban centers, therefore this study was planned to find the association of 25-hydroxy vitamin D level with arterial stiffness in newly diagnosed untreated hypertensive patients. This cross sectional descriptive study was conducted among hypertensive patients of age groups 18-69 years, attending general medicine OPD in BPS GMC, Khanpur Kalan, Sonepat. A data of total 35 patients was collected over a period of 2 months. It was seen that arterial stiffness index was comparatively higher in patients with lower 25-hydroxy vitamin D levels. Our study showed a negative correlation between arterial stiffness index and 25-hydroxy vitamin D levels among the newly diagnosed untreated hypertensive patients. So, vitamin D insufficiency can increase cardiovascular risk in untreated patients with hypertension.
Keywords: 25-hydroxy vitamin D, Arterial stiffness index, Hypertension, Rural tertiary care centre.

INTRODUCTION

25-hydroxy vitamin D, 25 (OH) vit. D, is considered to be the best indicator of vitamin D status in those with normal kidney function and reflects the level of circulating substrate for the tightly regulated hydroxylation into the active, hormonal form of vitamin D [1]. In most industrialized countries, cardiovascular disease is the leading cause of morbidity and mortality and elevated brachial artery blood pressure (BP) is a major risk factor and powerful predictor of cardiovascular organ damage, morbidity and mortality [2-4]. More recently, vitamin D deficiency has been implicated as a risk factor for cardiovascular disease and overall mortality in general population [5]. Vitamin D effects the vascular wall by regulating the renin-angiotensin-aldosterone axis and exerts anti-proliferative effects on vascular smooth muscle [6]. It is well established that vascular endothelial dysfunction and arterial stiffness precede and contribute to the development of cardiovascular disease and both are predictors of long-term morbidity and mortality [7].

Arterial stiffness characterized by high intravascular distending pressure has been recognized as a marker of cardiovascular disease (CVD) and associated with long-term prognosis in several populations [8]. A recent meta-analysis including 17 longitudinal studies, demonstrated that aortic stiffness

was an independent predictor of incident CVD and all-cause mortality in the general population [9]. Therefore, evidence-based approaches for improving arterial stiffness are of clinical importance to reduce the hazards of subsequent CVD. In essential hypertension, the elastic properties of large arteries are impaired, although it is not clear whether disease itself alters the intrinsic elastic properties or this is the ultimate final effect of increase in distending pressure [10]. Thus the arterial stiffness index (ASI) is introduced as anovel measure of arterial stiffness, which independently predicts cardiovascular mortality [11].

AIMS AND OBJECTIVE

To find out the association of 25 (OH) vit. D level with arterial stiffness in newly diagnosed untreated hypertensive patients

METHODOLOGY

Study setting: Rural tertiary care centre, BPS GMC (W), Khanpur Kalan, Sonepat.

Study design: Cross-sectional descriptive study.

Inclusion criteria

Newly diagnosed untreated hypertensive patients of age group18-69 years attending genral medicine OPD.

Exclusion criteria

- Patients <18 and >69 years of age.
- Previously treated or on treatment hypertensive patients.
- Coronary artery disease; exclusion on the basis of history and ECG.
- History of peripheral arterial disease.
- History of cerbrovascular disease.
- Alcohol addiction.
- Pregnancy/lactation.
- Any chronic inflammatory condition: Hepatic, Renal, GIT, Neurological or

Hematological; excluded on the basis of history, examination and investigations.

- Diabetes mellitus.
- Thyroid disorders.

The following baseline investigations were performed and recorded on the proforma designed.

- Blood sugar, fasting and post-prandial.
- Renal function tests e.g. Blood urea, serum-creatinine and serum-electrolytes.
- Liver function tests e.g Serum bilirubin, serum transaminases (SGOT/SGPT).
- Thyroid function tests (T3, T4, and TSH).
- ECG.
- Chest x-rays.

Sample size

All the newly diagnosed untreated hypertensive patients enrolled during period of 2 months. The study was conducted in General Medicine OPD, Central laboratory and Central research laboratory of BPS, GMC (W), Khanpur Kalan, Sonepat.

Study variables

Sociodemographic profile with anthropometric measurements -

- Name, Age, Sex, Caste, Occupation, Income, Literacy status, Height (in meters), Weight (in Kg), BMI (weight in Kg/ height in sq. meters).
- 25(OH) vit.D level: About 2-3 ml of blood was withdrawn from each subject by venepuncture. And vit.D insufficiency was defined as levels less than 30 ng/ml.
- Arterial stiffness index (ASI): ASI at left brachial artery was calculated by quantifying the oscillometric envelopes derived from the oscillations in the concerned artery using periscope.
- ASI = Systolic side value of cuff pressure at 80% of maximal oscillation amplitude of cuff
- Diastolic side value of cuff presssure at 80% of maximal oscillation amplitude of cuff.
- Blood Pressure: Blood pressure of the entire subject was taken left brachial artery in supine position, keeping mercury sphygmomanometer at the level of heart. Total 3 readings were recorded at an interval of one minute and average was noted.
- Hypertension is defined by - Systolic pressure equal to or more than 135 mm of Hg or Diastolic pressure equal to or more than 85 mm of Hg.
- The study was conducted in a quiet, temperature controlled room. Patients were advised to avoid exercise, tea or coffee and tobacco before test.

Study tool

Semi-structured schedule.

25(OH)vit. D: The quantitative determination of 25(OH) vit. D in human serum was done by microplate ELISA.

Arterial stiffness index: Left brachial artery stiffness was calculated by periscopy in Central Research Laboratory.

Blood pressure: was measured by mercury sphygmomanometer.

Ethical issue

Institutional Ethical Committee BPS, GMC, Khanpur Kalan, Sonepat.

OBSERVATIONS

A total of 35 patients that fitted in our criteria were enrolled over a period of 2 months. The data was entered in MS-Excel and analysed using SPSS software.

Mean±Standard deviation (SD), Percentage and proportion was calculated. Chi- square test was used to find out the association. P Value < 0.05 was considered as statistically significant.

Table-1: Descriptive statistics

	Minimum	Maximum	Mean± Std. Deviation
Age	35	68	50.97±10.77
Height(cm)	140	178	154.34±8.94
Weight(kg)	46	85	65.63±10.73
BMI(kg/m^2)	22	39	27.57±3.76
Mean systolic BP	129	182	157.34±13.51
Mean Diastolic BP	83	112	94.44±7.47
Arterial stiffness index	14	44	27.06±6.50
25-hydroxy vitamin D level (mg/ml)	6	40	17.86±6.95
Blood sugar fasting (mg/dl)	67	96	84.26±7.75

Table-2: Correlation coefficient between the variables

	Mean systolic BP		Mean diastolic BP		Arterial stiffness index		25-hydroxy vit.D level (mg/ml)	
	Correlation coefficient r	p-value	Correlation coefficient r	p-value	Correlation coefficient r	p-value	Correlation coefficient r	p-value
Age	-0.023	0.897	0.254	0.148	-0.107	0.54	0.127	0.466
BMI(kg/m$^{2)}$	-0.193	0.266	-0.22	0.211	0.162	0.352	-0.222	0.201
Mean systolic BP	……	……	0.454	0.007	0.408	0.015	-0.324	0.057
Mean Diastolic BP	0.454	0.007	……..	…….	0.056	0.754	-0.211	0.231
Arterial stiffness index	0.408	0.015	0.056	0.754	……	…….	-0.66	0.001
25-hydroxy vit D level (mg/ml)	-0.324	0.057	-0.211	0.231	-0.66	0.001	…….	……
Blood sugar fasting (mg/dl)	-0.169	0.333	0.011	0.95	0.031	0.859	0.009	0.957

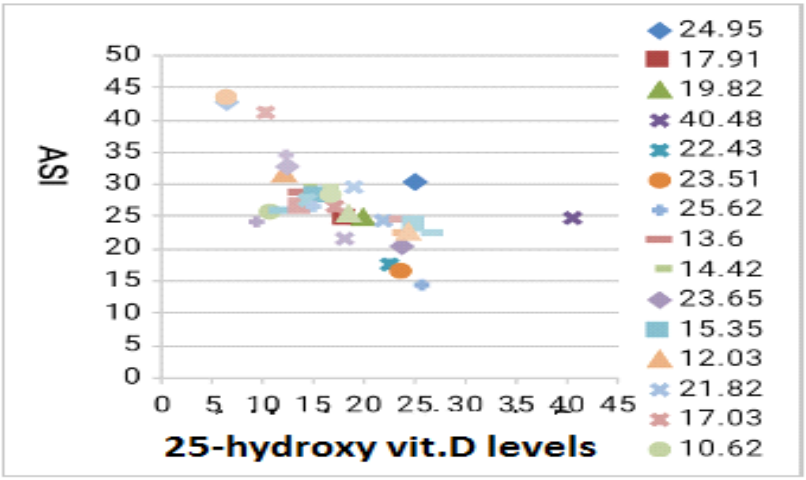

Fig-1: Correlation between ASI and 25-hydroxy vit. D levels

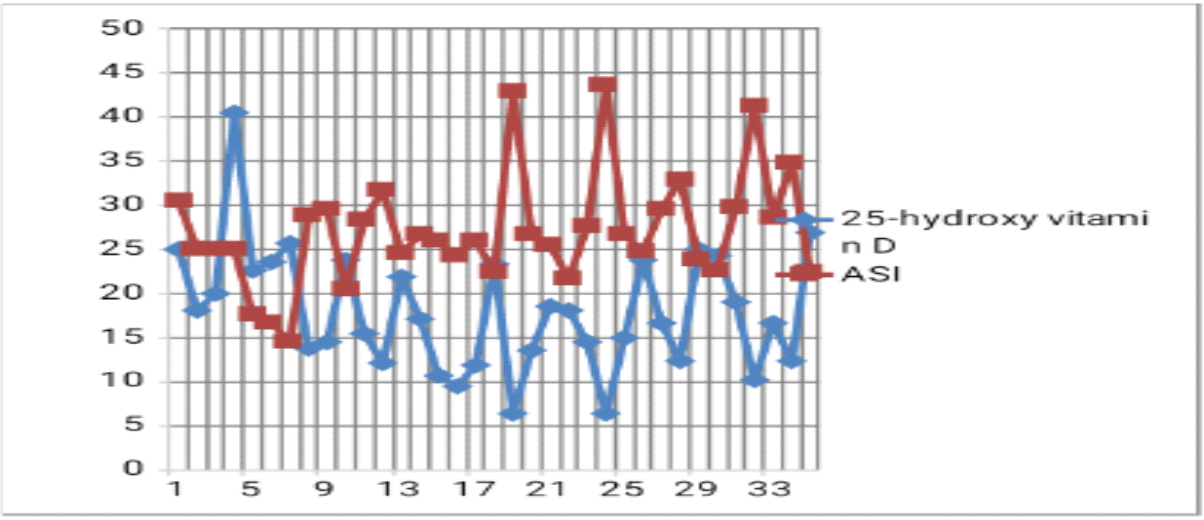

Fig-2: Trend of 25-hydoxy vitamin D and ASI

DISCUSSION

Data of total 35 patients was collected over a period of 2 months. Liver functions test, Renal functions tests, X-ray chest, ECG, Thyroid function tests of these patients were normal.

Mean age of the patients was 50.97 years with standard deviation of 10.722. 25-hydroxy vitamin D levels of maximum patients were below 30 ng/ml. It was seen that arterial stiffness index (ASI) was comparatively higher in patients with lower 25(OH) Vit. D levels. In Pearson's correlation analysis, ASI has a significantly negative correlation with 25(OH) vit. D levels (r= 6.60, p = 0.001). It is also represented on the graphs. Although several previous studies have presented inconsistent findings [12-15], two other cross-sectional studies observed an inverse relationship between serum 25(OH) vit. D level and arterial stiffness [12, 16]. In the Framingham offspring study as well, vitamin D deficiency was found to be associated with an increased incidence of cardiovascular diseases [17]. Our study also suports these previous positive studies.

Several studies have observed a successful decrease in baPWV (brachial-ankle pulse wave velocity) by supplementation with vitamin D [18-22]. However, a cross-sectional analysis of the Korean Longitudinal study on Health and Aging (KLoSHA) (23) showed no association between serum concentration of 25(OH) vit. D and baPWV. A recent cross-sectional study among Korean adults confirmed that the positive association between 25(OH) vit. D and baPWV was reversed when BP was controlled [24]. As mentioned earlier, BP plays a major role in influencing arterial function. Arterial stiffness results from structural and functional changes to the vascular tree [25] and high BP may effect those changes [26].

Our study has several limitations. First, it has less number of participants. Second, this study has a cross-sectional design. The patients were not followed-up and therefore endpoints could not be determined after control of BP and supplementation of vitamin D.

CONCLUSION AND RECOMMENDATIONS

In our study, we have found a negative correlation between arterial stiffness index and 25-hydroxy vitamin D levels among the newly diagnosed untreated hypertensive patients. (p=0.001) Vitamin D insufficiency can increase cardiovascular risk in untreated patients with hypertension.

A prospective especially randomized control trial, comparing vitamin D supplementation with placebo is needed to determine the causative mechanism of association between serum 25 (OH) vitamin D levels and arterial stiffness.

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