Original Research Article

Vitamin D deficiency as a risk factor for Metabolic Syndrome in Hypertensive Subjects

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Abstract

Introduction: Vitamin D deficiency is a highly prevalent condition, present in approximately 30-50% of the general population. Vitamin D deficiency predisposes to insulin resistance, pancreatic beta cell dysfunction, and the metabolic syndrome. The aim of this study was to determine whether vitamin D deficiency is associated with increased risk of metabolic syndrome among adult hypertensive patients.

Materials & Methods: This is a cross sectional study, conducted at Department of General Medicine of a tertiary care centre. All adults (age >18 years) diagnosed as essential hypertension were included in the study. 250 residents of Indore city who gave informed consent and met the inclusion criteria were selected as subjects. All subjects were almost equally divided into three groups; depending on serum 25(OH)D level. Following investigations were also done in all patients: Hb, ESR, serum creatinine, fasting blood sugar, serum TSH, and Lipid profile. The Non-parametric test, Pearson's Chi-Square test has been used for qualitative data.

Results: Hypertensive Subjects were divided into three groups depending on serum 25(OH)D level. Female hypertensive patients were predisposed for vitamin D deficiency. BMI, waist circumference, blood pressure, fasting blood sugar and triglyceride levels were higher in vitamin D deficiency patients. 24% of vitamin D deficiency subjects had metabolic syndrome in comparison to 12% of vitamin D insufficiency subjects and 8% of vitamin D sufficiency subjects had metabolic syndrome.

Conclusion: In summary, vitamin D deficiency also has extra-skeletal effects that impact on the development of various pathologies including those that make up a large majority of morbidity and mortality; metabolic syndromes. Our findings suggested that serum 25(OH)D concentrations were inversely associated with the risk of metabolic syndrome among hypertensive subjects.

Key Words: Vitamin D, hypertension, metabolic syndrome

Introduction

Vitamin D deficiency is a highly prevalent condition, present in approximately 30-50% of the general population. A growing body of data suggests that low 25-hydroxyvitamin D levels may adversely affect cardiovascular health. Vitamin D deficiency activates the renin-angiotensin-aldosterone system and can predispose to hypertension and left ventricular hypertrophy.[1] Additionally, vitamin D deficiency causes an increase in parathyroid hormone, which

increases insulin resistance and is associated with diabetes, hypertension, inflammation, and increased cardiovascular risk. Deficient or insufficient serum 25(OH)D levels have been documented in patients with myocardial infarction[2], stroke[3], heart failure, diabetes, cardiovascular diseases[4], and peripheral arterial disease.[5] Other cross-sectional studies have confirmed the links between vitamin D deficiency and both hypertension and diabetes.[6,7] Additionally, vitamin D deficiency predisposes to insulin resistance, pancreatic beta cell dysfunction[8], and the metabolic syndrome.[9]

The metabolic syndrome is commonly characterized by dyslipidemia, hyperglycemia, abdominal obesity and hypertension. Metabolic syndrome is associated with an increased risk of hypertension and cardiovascular complications. We know that obesity is also one of the risk factors for vitamin D deficiency, because the excess fat absorbs and holds onto the vitamin D so that it cannot be used for bone building or cellular health. Relationships among serum 25(OH)D and dyslipidemia, abdominal obesity, and hypertension have been explored in different regions and various kinds of people[10-12], but data to support those relationships are inconsistent with only a sparse sample from Indian people. Previous studies have indicated that low concentrations of serum 25(OH)D may be associated with an increased risk of metabolic syndrome[13,14] but whether this association exists among hypertensive patients remains unclear.

The aim of this study was to determine whether vitamin D deficiency is associated with increased risk of metabolic syndrome among adult hypertensive patients.

Material & Methods

Study Design: This is a cross sectional study.

Study Setup: This study was conducted at Department of General Medicine of a tertiary care centre.

Study Duration: The duration of study was two years; January-2015 to December-2016.

Sampling: Purposive sampling technique is used for selection of desired samples according to inclusion criterion.

Inclusion criteria: All adults (age >18 years) diagnosed as essential hypertension were included in the study.

Exclusion criteria: Patients with severe hypertension, renal calculi, corticosteroid use, calcitriol or calcium use or any other serious illness were excluded from the study.

Methods: 250 residents of Indore city who gave informed consent and met the inclusion criteria were selected as subjects. All subjects were almost equally divided into three groups; depending on serum 25(OH)D level.

Detailed history was taken and physical examination was done. Peripheral venous blood specimens were collected in gel coagulation tubes from all participants. They were instructed to fast for 12 hours until the early morning before blood collection. Serum 25(OH)D levels were measured with an electrochemical luminescence system. Although a consensus regarding the optimal level of serum 25(OH)D has not yet been established, most experts define vitamin D deficiency as a 25(OH)D level of <20 ng/ml and vitamin D insufficiency as 21 to 29 ng/ml. For all studied end points to date, the optimal concentration of 25(OH)D is at least 30 ng/ml.[15] Following investigations were also done in all patients: Hb, ESR, serum creatinine, fasting blood sugar, serum TSH, Lipid profile. According to

guidelines from the National Heart, Lung, and Blood Institute (NHLBI) and the American Heart Association (AHA), metabolic syndrome is diagnosed when a patient has at least 3 of the following 5 conditions:

- Fasting glucose ≥100 mg/dL (or receiving drug therapy for hyperglycemia)
- Blood pressure ≥130/85 mm Hg (or receiving drug therapy for hypertension)
- Triglycerides ≥150 mg/dL (or receiving drug therapy for hypertriglyceridemia)
- HDL-C <40 mg/dL in men or <50 mg/dL in women (or receiving drug therapy for reduced HDL-C)
- Waist circumference ≥102 cm (40 in) in men or ≥88 cm (35 in) in women

Ethical Consideration: Prior to conduct of the present study, the protocol of the study was submitted to ethical and scientific committee of hospital. After getting due approval from these two committees, the present study was initiated. Also prior to conduct of study related procedure / investigation, a voluntary written informed consent was taken from the patient /legally acceptable representative.

Statistical Technique: The demographic data of 250 subjects was analyzed by statistical software, SPSS version 17.0. Results of continuous measurements are presented on Mean±SD and results of categorical measurements are presented in numbers (%). The Non-parametric test, Pearson's Chi-Square test has been used for qualitative data. The probability value $p<0.05$ was considered as statistically significant.

Observation & Results

The characteristics of all hypertensive subjects are summarized in Table 1. Hypertensive subjects were divided into three groups depending on serum 25(OH)D level. These groups were: Vitamin D deficiency group if serum 25(OH)D level of <20 ng/ml, vitamin D insufficiency group if serum 25(OH)D level 21 to 29 ng/ml and vitamin D sufficiency group if 25(OH)D level > 30 ng/ml. There was no significant difference among three groups for number, age, except for gender. Female hypertensive patients were predisposed for vitamin D deficiency. BMI, waist circumference, blood pressure, fasting blood sugar and triglyceride levels were higher in vitamin D deficiency patients while HDL-C levels were significantly low in vitamin D deficiency group. 24% of vitamin D deficiency subjects had metabolic syndrome in comparison to 12% of vitamin D insufficiency subjects and 8% of vitamin D sufficiency subjects had metabolic syndrome.

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Table.1 Characteristics of All Hypertensive Subjects

Patient's characteristics	Vitamin D Sufficiency	Vitamin D insufficiency	Vitamin D Deficiency	P value
Number	82	84	84	NS
Age (Mean±SD)	42.4±11.8 years	44.3±10.9 years	41.9±12.7 years	NS
Gender (Male %)	68%	52%	38%	0.01
BMI (Mean±SD)	22.4±1.1 kg/M_2	23.4±2.1 kg/M_2	26.4±1.2 kg/M_2	0.01
Waist circumference (Mean±SD)	83.2±4.2 Cm	86.3±5.3 Cm	88.1±5.5 Cm	0.05
Systolic Blood Pressure (Mean±SD)	128.4±10.8 mmHg	134.6±11.9 mmHg`	138.6±16.8 mmHg	0.06
Diastolic Blood Pressure (Mean±SD)	80.8±8.7 mmHg	85.5±7.4 mmHg	90.9±12.5 mmHg	0.05
Fasting blood sugar (Mean±SD)	82.9±4.2 mg/dl	84.7±6.9 mg/dl	96.9±8.6 mg/dl	0.01
Triglyceride Level (Mean±SD)	119.4±22.8 mg/dl	138.9±42.5 mg/dl	149.6±52.4 mg/dl	0.001
HDL-C Level (Mean±SD)	40.6±6.5 mg/dl	39.7±3.8 mg/dl	32.8±7.6 mg/dl	0.04
Metabolic syndrome (%)	8%	12%	24%	<0.0001

NS=nonsignificant

Discussion

Vitamin D is a hormone, which is produced in the skin from 7-dehdrocholesterol (pre-vitamin D_3), derived from cholesterol. Type B ultraviolet rays from sun act on pro-vitamin D_3 and convert it into pre-vitamin D_3, which is then converted to cholecalciferol. Sufficient serum vitamin D concentrations plays a protective role against a range of disease states, including cardiovascular disease, diabetes, multiple sclerosis, cancer and may enhance the immune system.[16]

The classic effect of vitamin D is to facilitate the intestinal absorption of calcium by mediating active calcium transport across the intestinal mucosa. Vitamin D acts in this system by both genomic and non-genomic mechanisms. These mechanisms involve, among other effects, synthesis of calcium from the brush border across to the basolateral side of the mucosal cell.

The principal function of 1,25-dihydroxyvitamin D_3 [1,25(OH)2D_3] in the maintenance of calcium homeostasis is to increase calcium absorption from the intestine. 1,25(OH)2D_3, the harmonically active form of vitamin D, is the major controlling hormone of intestinal calcium absorption.[17]

Vitamin D deficiency has reached pandemic proportions all over the Indian subcontinent accounting to a prevalence of 70-100% in the general population. Vitamin D deficiency affects not only skeletal but also on extra-skeletal diseases. Owing to its multifarious implications on health, the epidemic of vitamin D deficiency in India is likely to significantly contribute to the enormous burden on the healthcare system of India. As per documented

study report, high dose vitamin D_3 (cholecalciferol 60000 IU) is effective in achieving sufficient serum 25(OH)D among population who tend to have lower baseline serum 25(OH)D.[18]

The large population-based Cardiovascular Health Study measured 25(OH)D in 2,314 patients and reported a lower prevalence of hypertension in patients with 25(OH)D ≥20 ng/mL (48%) compared to patients with 25(OH)D <20 ng/mL (61%).[19] Similarly, the German National Health Interview and Examination Survey (GNHIES), which included 1,763 men and 2,2267 women, evaluated the relationship between 25(OH)D and hypertension.[20] The authors reported a prevalence of hypertension of 50% in women with a very low vitamin D (<5 ng/mL) compared to a prevalence of 30% in women with vitamin D levels of at least 20 ng/mL.

A meta-analysis of 28 studies (between 1990 and 2009) including 99745 participants (age range: 40.5-74.5 years) by Parker et al[21] investigated the effects of vitamin D on the risk of CVD, diabetes and the metabolic syndrome.[21] Higher levels of vitamin D were seen to be associated with reduction of all the outcomes studied among middle aged and elderly individuals. The 28 studies reported 33 ORs when considering the association between 25(OH)D and cardiometabolic outcomes; 29 of these ORs suggested an inverse relationship with 3 indicating an opposite effect with 1 analysis remaining non-significant.[21] The pooled OR was 0.57 (95%CI: 0.48-0.57). Prevalence of the metabolic syndrome was the outcome in 8 of the studies; all these showing a significant association between high 25(OH)D levels and reduced metabolic syndrome prevalence (OR = 0.49, 95%CI: 0.38-0.64).

Conclusion

In summary, vitamin D deficiency also has extra-skeletal effects that impact on the development of various pathologies including those that make up a large majority of morbidity and mortality; metabolic syndromes. Our findings suggested that serum 25(OH)D concentrations were inversely associated with the risk of metabolic syndrome among hypertensive subjects.

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