A prospective, cross-sectional study on association of serum vitamin D level with musculoskeletal symptoms and blood pressure in adult population

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ABSTRACT

Background: Vitamin D is an important vitamin required to maintain an important physiological function of the body. The body should maintain an optimal level of vitamin D to maintain skeletal and metabolic functions. It was observed that inverse relationship is maintained by vitamin D level in the body with musculoskeletal symptoms and metabolic disorders. Objective: The study is conducted to associate between serum levels of vitamin D with self-reported symptoms (musculoskeletal) and blood pressure. Material and Methods: Venous blood sample was collected from 126 adults with musculoskeletal symptoms. The subjects were stratified based on their vitamin D levels. Groups were tested for the frequency of symptoms and the relationship of different parameters with vitamin D. Results: The frequency of subjects in the study was more in the deficient category (<20 ng/dL). In the study, vitamin D was found to have a significant association with “weakness.” Body mass index (BMI), systolic blood pressure (SBP), and diastolic blood pressure (DBP) were found to have an inverse relation with serum vitamin D level. Conclusion: The study showed the effect of vitamin D level in musculoskeletal symptoms and inverse association of vitamin D with BMI and blood pressure.

Keywords: Blood pressure, body mass index, hypovitaminosis, musculoskeletal symptoms, vitamin D

Introduction

Vitamin D deficiency is prevalent worldwide and it is estimated that about one billion people may have low vitamin D levels across all ethnicities and age groups. Vitamin D is essential for the growth and maintenance of bone and skeletal tissues. Vitamin D3 (cholecalciferol) is produced naturally from skin exposure to sunlight and small amounts of it come from dietary sources. One of the important reasons for this global pandemic is the lack of exposure to the sun and very few foods naturally contain vitamin D (wild-caught salmon and UV-exposed mushrooms). Vitamin D has multiple roles in body functions which include cellular regulation, muscle function, calcium absorption, bone metabolism, and immune function.

Vitamin D deficiency has been found to be associated with other disorders namely secondary hyperparathyroidism, hypertension, diabetes mellitus, inflammatory bowel disease, cardiovascular disease, stroke, osteoporosis and osteoporotic fractures, mental illness, chronic pain, cancers, etc. Vitamin D deficiency causes hypocalcemia, bone loss, and muscle weakness manifested by musculoskeletal pain.
A number of scientific evidence supports the multidimensional consequences of vitamin D deficiency on health. Though, there is a lack of consensus regarding optimum vitamin D serum level, it is defined when the circulating levels of 25-hydroxyvitamin D (25(OH)D) is less than 20 ng/mL. Hence, appropriate evaluation of its serum level and its effect on the organ system will help to select the treatment modalities in terms of dose, dosing interval, and formulation of vitamin D supplementation to maintain the adequate vitamin D level. Recent studies in India have shown increase prevalence of vitamin D deficiency in urban and rural populations. This requires a large number of specialists, primary care physicians, and family physicians to cater to this burden on the society.

Thus, we planned this study to assess the prevalence and its effects on lifestyle and quality of life on the people of northwest India.

**Material and Methods**

An observational and cross-sectional study conducted in the department of general medicine at a tertiary care teaching hospital. The duration of the study was 3 months. Adults (18–65 years of age) attending the out-patients department of general medicine were included in the study based on the following criteria:

**Inclusion criteria:**
1. Patients between 18 and 60 years, of either gender with musculoskeletal symptoms suggestive of vitamin D deficiency.

**Exclusion criteria:**
1. Pregnant and lactating women
2. Patients above 60 years
3. A patient who has taken vitamin D in the last 3 months
4. A patient suffering from thyroid disorders, parathyroid disorders, renal disorders, and metabolic disease
5. Patients on steroids and other factors influencing vitamin D

Sample Size: 126 patients (age between 18 and 60 years) with musculoskeletal features suggestive of vitamin D deficiency were randomly selected for the study duration of 3 months.

**Ethical consideration**

Ethical clearance was taken from the institutional ethical committee with Ethical Clearance Certificate No. AIIMS/IIEC/2017/759 (27/01/2017).

**Sociodemographic clinical profile data**

A structured pro forma was used to record a certain demographic. Body mass index (BMI) was calculated as weight (kilograms) divided by the square of height (meters). On the basis of BMI, the subjects were divided into obese (≥25 BMI), overweight (≥23 BMI but <25 BMI), and normal (<23 BMI) based on the revised consensus guidelines for India.

A clinical profile sheet was designed for the study to record various clinical parameters like age of onset, duration of illness; time spent in episodes/illness exacerbations, clinical features suggesting of musculoskeletal origin, and venous blood samples were collected to measure the level of vitamin D level. As the patients were mostly from a rural area and uneducated, pain analog scale was not used rather all of the responses to the symptoms were categorized into binary scales as yes for symptomatic and no for asymptomatic.

**Procedure of estimation of vitamin D**

25-hydroxy vitamin D estimation was done by chemiluminescence immunoassay (CLIA), a quantitative immunoassay method processed by a fully automated analyzer, (DiaSorin LIASON, Germany), available in the department of biochemistry of the hospital.

The cutoff to define an inefficient/insufficient when circulating concentration of 25(OH) D is above 20 ng/dL but less than equal to 29 ng/dL, while concentrations lower than 20 ng/dL are categorized as deficient. Subjects who were having serum vitamin D level was ≥30 ng/dL are classified as not deficient (ND) or normal.

**Statistical analysis**

Data were compiled using Microsoft Excel and analyzed using SPSS software (IBM-SPSS statistics 21.0; SPSS Inc., Chicago, IL, USA). Quantitative variables were expressed as mean ± standard deviation (Mean ± SD) and numbers (percentages). Normality distribution of data was first determined by the Kolmogorov–Smirnov test. As data were found to be normally distributed, the parametric analysis was used throughout the analysis. Pearson correlation was used to study the correlation between vitamin D and numerical variables. A Chi-square test was used for categorical variables. P values less than 0.05 were considered statistically significant for all tests.

**Results**

In the study, Table 1 presents the demographic data of all patients present with musculoskeletal symptoms. The subjects with self-reported symptoms were stratified according to vitamin D levels into three groups: subjects in the deficient category with vitamin D less than 20 ng/dL, subjects in the insufficient category with vitamin D between 20 and 29 ng/dL, and normal category with vitamin D above and equal to 30 ng/dL. It was found that most of the subjects belong to the category of deficient (76.8%). No significant association was found between age and sex with vitamin D in the study. In the demographic data, it was found that sun exposure had significant effects on the vitamin D level of the subjects (P = 0.040) [Table 1]. Demographic data showed that vitamin D also has a significant effect on the weight and BMI (P < 0.05) in the total population of the sample. It also had a significant effect on diastolic blood pressure (DBP) (P < 0.05) [Table 1]. In the demographic data,
a number of the subject with “weakness” was found more than the other symptoms [Table 1].

In Table 2, the subjects with musculoskeletal symptoms were stratified according to the deficient, insufficient, and normal category of vitamin D level. Descriptive data showed that the number of musculoskeletal symptoms was more in the deficiency category. Weakness (52.8%), bone pain (38.4%), body ache (38.4%), lethargy (13.6%), fatigue (4%), and numbness (4%) were found more in the subjects whose vitamin D level is less than 20 ng/dL. As vitamin D levels improve, the number of symptoms also decreased drastically. No significant associations were also found between symptoms (bone pain, body ache, fatigue, lethargy, and numbness) and vitamin D in the study. Though the impact of vitamin D on musculoskeletal symptoms might not be that significant due to the small sample size but the symptoms due to the vitamin D deficiency are inversely proportional to its level in the body.

The subjects who have less than 20 ng/dL of vitamin D were found to have a statistically significant correlation with exposure to sunlight ($P=0.001$). As the duration of exposure to sunlight increases, the level of vitamin D also improves [Table 3]. On the other hand, subjects with deficient vitamin D levels had consistently higher values of BMI, systolic blood pressure (SBP), and DBP [Table 3]. Although vitamin D does not have statistical significance result in these parameters in the deficient, insufficient, and normal category, the descriptive data indicate that vitamin D has an inverse relation with these parameters.

**Discussion**

Vitamin D is a secosteroid hormone that is essential for skeletal health and the health of non-skeletal tissue such as cardiovascular, endocrine, metabolic, neurological, neoplastic, articular, immunological, etc. Its deficiency is endemic and has been associated with numerous diseases.

Skin is the principal organ for the production of vitamin D in the body. It is produced at an extraordinary speed after a short exposure to sunlight, the quantity produced is more than the dietary sources.$^{[12,13]}$ It was found that fair-skinned people produced more vitamin D (20,000 IU) after 30 min of exposure to sunlight which is comparable to drinking 200 glasses of milk (100 IU/8 oz. glass) or taking 50 standard multivitamins (400 IU/tablet) to obtain the same amount.$^{[14]}$ In fact, many studies were done in India shown the widespread prevalence of hypovitaminosis D and osteomalacia.$^{[15]}$ Many studies have a different opinion regarding the relationship between vitamin D level and its effect on the independent parameters which might vary in our results.$^{[16]}$ Our study showed that there was a positive relationship between the duration of exposure to sunlight and vitamin D level. It was found that almost 76% of subjects are in the deficient vitamin D (0–20 ng/dL) category due to less exposure to sunlight. Maybe because of two reasons: First, study was conducted in the semi-arid region (extreme climate) of the country with increasing urbanization,$^{[17]}$ where-in people are found to be staying indoors, wearing excessive clothing to protect from sunlight, mostly dark-skinned and some were consciously avoiding the sun, thus, landing them into deficiency of vitamin D. Second, more than two-thirds of our study population was vegetarian and was found having less than 30 ng/dL of vitamin D level. As vegetarian population usually has minimal vitamin D in the diet.

The present study finds significant correlations among vitamin D and weakness, one of the most self-reported symptoms which constitute 60% of the symptoms in the overall population. We found that subjects with deficient levels of vitamin D had
The relationship between vitamin D and blood pressure is controversial and unclear. There are several hypotheses to explain the association between vitamin D and obesity. On one hand, it’s proposed that vitamin D deficiency state affects vascular smooth muscle cells and increased vascular stiffness; and last, vitamin D deficiency is also associated with endothelial dysfunction and could promote increased atherosclerosis and systolic hypertension. However, statistically, it was found that the values are significant for DBP than SBP which is contrary to a small trial by Pfeiffer et al.[27]

**Conclusion**

The study showed that the subjects with symptoms of weakness were more in the deficient level (<20 ng/dL). It was also found that sun exposure had a significant effect on the vitamin D level in the total subjects but more for those who are having vitamin D levels less than 20 ng/dL. There was a significant correlation between vitamin D on the BMI of the total subject in the study. The study shows an inverse relationship between SBP, DBP, and vitamin D level. A recently published meta-analysis (14 cross-sectional studies, 4 prospective studies) showed that the pooled odds ratio of hypertension was significant enough and concluded that calcitriol level is having an inverse relationship with hypertension.[21,23] The mechanism proposed for the inverse relationship between vitamin D and hypertension is as follows. First, calcitriol inhibits renin synthesis in the kidney; second, high parathyroid hormone levels to secondary hyperparathyroidism in vitamin D deficiency state affects vascular smooth muscle cells and decreases vascular stiffness; and last, vitamin D deficiency is also associated with endothelial dysfunction and could promote increased atherosclerosis and systolic hypertension. However, statistically, it was found that the values are significant for DBP than SBP which is contrary to a small trial by Pfeiffer et al.[27]

**Table 2: Stratification of patients according to vitamin D level and its relationship with musculoskeletal symptoms**

| Vitamin D (ng/dL) | <20 | 20-29 | ≥30 |
|------------------|-----|-------|-----|
| No. of patients   | 96  | 18    | 11  |
| Weakness†† (%)    |       |       |     |
| Pain†† (%)        |       |       |     |
| Body ache†† (%)   |       |       |     |
| Lethargy†† (%)    |       |       |     |
| Fatigue†† (%)     |       |       |     |
| Numbness†† (%)    |       |       |     |

**Table 3: Stratification of patients according to vitamin D level and its relationship with sun exposure, BMI, SBP, and DBP**

| Vitamin D (ng/dL) | <20 | 20-29 | ≥30 |
|------------------|-----|-------|-----|
| No. of patients   | 96  | 18    | 11  |
| Sun exposure (Hours) / |     |       |     |
| BMI (± SD)         |     |       |     |
| SBP (± SD)         |     |       |     |
| DBP (± SD)         |     |       |     |

Although our findings are similar to other studies,[20] few studies do not support such association[21] which is due to different criteria of inclusion, duration of symptoms, lack of control group, seasonal variation, ethnic homogeneity of populations, and many others.

BMI showed a significant relationship with vitamin D levels in many studies. Low vitamin D level is associated with excess adiposity, due to the sequestration of the fat-soluble vitamin within the adipose tissue or the effect of volume dilution because of the larger body size.[21] The relationship between vitamin D and obesity is controversial and unclear. There are several hypotheses and mechanisms proposed between the associations of vitamin D and obesity. On one hand, it’s proposed that vitamin D deficiency was a consequence of obesity and on the other hand, it was a predisposing factor to obesity. One study found that supplementation of vitamin D3 in healthy overweight and obese women decrease body mass with increasing 25(OH)D concentrations.[22] Another study found that vitamin D deposition in body fat also decreases the serum level of vitamin D.[23]
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Conflicts of interest
There are no conflicts of interest.

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